Weill Cornell Medicine
Global Health Education

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Introduction to Global Health
Spring 2021 Syllabus

Faculty Leader
Madelon Finkel, Ph.D.
Professor of Population Health Sciences
Director of the Office of Global Health Education

Administrative Coordinator
Savita Birbal, M.A.
Global Health Teaching Associate
globalhealthTA@med.cornell.edu

Location and Time
February 1, 2021 – March 29, 2021
Mondays, 1:00-2:00pm or 5:00-6:00pm

Course Overview

Introduction to Global Health introduces students to key topics in global health through weekly seminars. Course faculty are drawn from Weill Cornell and other institutions, and have extensive field and research experience in global health. The course is designed as a non-credit elective for first-year medical students.

Expectations of Student

- Attendance is voluntary but we hope that you try to attend all sessions.
- Reading of materials provided for each session.
- Participation in class discussions.
- Completion of mandatory feedback surveys.
- Professionalism during presentations.

*Note: Those who attend ¾ of the sessions will be eligible for a Certificate in Global Health, which is awarded in March of the 4th year.

Course Objectives

By the end of this course participants will be able to

- Understand the principles of screening for cancer in LMICs, especially during a pandemic.
- Recognize issues in women's health in LMICs.
- Recognize the health issues surrounding reproductive health that are common in LMICs
- Identify the leading causes of global blindness, and the potential treatments and interventions to ameliorate the burden of global blindness.
- Become familiar with issues of palliative care in LMICs.
- Compare the similarities and differences between the methods of diagnosis, treatment and prevention of diabetes in developed vs developing nations.
- Become familiar with the difficulty in reducing malaria transmission in places like sub-Saharan Africa.
- Become familiar with issues of "decolonizing" global health.

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DATE	TIME	SPEAKER	TOPIC (and Zoom link)	Zoom ID/ Passcode
February 1, 2021	1:00pm – 2:00pm	Madelon Finkel, Ph.D.	Screening for Cancer in the Age of COVID-19: Focus on LMICs	Meeting ID: 986 2633 1111 Passcode: 886531
February 8, 2021	5:00pm – 6:00pm	Jyoti Mathad, M.D.	Women's Health Issues in LMICs	Meeting ID: 929 3743 6313 Passcode: 214786
February 22, 2021	1:00pm – 2:00pm	Grace Sun, M.D.	Global Blindness	Meeting ID: 950 8203 0968 Passcode: 586713
March 1, 2021	5:00pm – 6:00pm	Lucy Bruell, Randi Diamond, M.D., Howard Eison, M.D., and Jemella Raymore, MD.	Palliative Care MODERATOR: Dr. Madelon Finkel	Meeting ID: 940 3098 9169 Passcode: 546727
March 8, 2021	5:00pm – 6:00pm	Jason Baker, M.D.	Diabetes in the Developing World	Meeting ID: 921 9171 4192 Passcode: 096379
March 15, 2021	1:00pm – 2:00pm	Kirk W. Deitsch, Ph.D.	The Persistent Problem of Malaria in the Developing World	Meeting ID: 938 6466 1904 Passcode: 652267
March 22, 2021	1:00pm – 2:00pm	David Scales, M.D.	Humanitarian Crisis: Global Health	Meeting ID: 985 9146 1353 Passcode: 264130
March 29, 2021	5:00pm – 6:00pm	Leslie Bull, M.A, Luiza Perez, and Nicholas Roberts, M.P.H.	Panel Discussion: Challenges of Global Health Work MODERATOR: Dr. Madelon Finkel	Meeting ID: 916 9178 0417 Passcode: 149562

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Speaker: Madelon Finkel, MD
Date: February 1, 2021
Time: 1:00pm to 2:00pm
Title: Screening for Cancer in the Age of COVID-19: Focus on LMICs

Zoom info: https://weillcornell.zoom.us/j/98626331111 **Meeting ID**: 986 2633 1111 **Passcode**: 886531

Summary: Review of the principles of screening; discussion of how to screen for cancer during a pandemic; focus on challenges of cervical cancer screening in LMICs

Suggested Readings:

Shieh, Y., Eklund, M., Sawaya, G. et al. Population-based screening for cancer: hope and hype. Nat Rev Clin Oncol 13, 550–565 (2016). https://doi.org/10.1038/nrclinonc.2016.50.

del Pilar Estevez-Diz, M., Colombo Bonadio, R., Costa Miranda, V., & Paula Carvalho, J. (2020). Management of cervical cancer patients during the COVID-19 pandemic: a challenge for developing countries. *Ecancermedicalscience*, *14*, 1060. https://doi.org/10.3332/ecancer.2020.1060.

Gorin, S. N. S., Jimbo, M., Heizelman, R., Harmes, K. M., & Harper, D. M. (2020a). The future of cancer screening after COVID-19 may be at home. *Cancer*. https://doi.org/10.1002/cncr.33274.

Case Study:

The coronavirus disease (COVID-19) pandemic has caused huge disruptions in the ability to screen for cancer. Individuals are fearful of going to hospital clinics for screening, and the potential ramifications of such could lead to patients presenting with advanced disease. In low- and middle- income countries (LMICs) the challenges of encouraging individuals to be screened are especially great. Using cervical cancer screening as an example, share your ideas about how to screen for this disease during the COVID-19 pandemic in a LMIC of your choice.

Discussion Questions:

Describe where you will conduct your screening program; define the target population; articulate the proposed screening program; how might your proposals be integrated into clinic screening programs once the pandemic has passed?

Population-based screening for cancer: hope and hype

Yiwey Shieh[1], Martin Eklund[2], George F. Sawaya[3], William C. Black[4], Barnett S. Kramer[5] and Laura J. Esserman[6]

Abstract | Several important lessons have been learnt from our experiences in screening for various cancers. Screening programmes for cervical and colorectal cancers have had the greatest success, probably because these cancers are relatively homogenous, slow-growing, and have identifiable precursors that can be detected and removed; however, identifying the true obligate precursors of invasive disease remains a challenge. With regard to screening for breast cancer and for prostate cancer, which focus on early detection of invasive cancer, preferential detection of slower-growing, localized cancers has occurred, which has led to concerns about overdiagnosis and overtreatment; programmes for early detection of invasive lung cancers are emerging, and have faced similar challenges. A crucial consideration in screening for breast, prostate, and lung cancers is their remarkable phenotypic heterogeneity, ranging from indolent to highly aggressive. Efforts have been made to address the limitations of cancer-screening programmes, providing an opportunity for cross-disciplinary learning and further advancement of the science. Current innovations are aimed at identifying the individuals who are most likely to benefit from screening, increasing the yield of consequential cancers on screening and biopsy, and using molecular tests to improve our understanding of disease biology and to tailor treatment. We discuss each of these concepts and outline a dynamic framework for continuous improvements in the field of cancer screening.

[1]*Division of General Internal Medicine, Department of Medicine, University of California, San Francisco, 1545 Divisadero Street, San Francisco, California 94115, USA*
[2]*Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Nobels väg 12A, 17177 Stockholm, Sweden.*
[3]*Departments of Obstetrics, Gynecology, and Reproductive Sciences, School of Medicine, University of California, San Francisco, 550 16th Street, San Francisco, California 94158, USA.*
[4]*Department of Radiology, Geisel School of Medicine at Dartmouth, Dartmouth-Hitchcock Medical Center, 1 Medical Center Drive, Lebanon, New Hampshire 03756, USA.*
[5]*Division of Cancer Prevention, National Cancer Institute, 9609 Medical Center Drive, Bethesda, Maryland 20892, USA.*
[6]*Departments of Surgery and Radiology, University of California, San Francisco, 1600 Divisadero Street, Box 1710, San Francisco, California 94115, USA.*

Correspondence to L.J.E.
laura.esserman@ucsfmedctr.org

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The proximate goal of cancer screening is the identification of early stage cancer, or precancerous lesions, before a person develops symptoms and at a point in the disease trajectory when treatment is likely to result in cure. This concept is simple, but practicing effective screening on a population level is a complex endeavour. In 1968, Wilson and Jungner[1] of the WHO proposed criteria that should be met before a screening test should be implemented (BOX 1); these principles continue to guide policy in countries where implementation of organized screening programmes is being considered. For a number of common cancers, some of these criteria have been met; however, many continue to present challenges and remain incompletely addressed (BOX 1). Wilson and Jungner's suggestion that "the natural history of the condition, including development from latent to declared disease, should be adequately understood" (REF. 1) seems particularly prophetic. At the time of the WHO report, and for decades after, the prevailing model of carcinogenesis was that of a linear progression from precursor disease to early stage (localized) cancer and, subsequently, to advanced-stage (disseminated) cancer. Indeed, the models of colorectal cancer (CRC) tumorigenesis proposed by Vogelstein *et al.*[2] in the late1980s suggested a relatively slow, stereotyped evolution from colonic polyp to cancer, commensurate with the acquisition of certain mutations over time. A similar paradigm has become established for the natural history of cervical cancer, and health-care organizations in a number of countries, including the USA, introduced screening for breast and prostate cancers, presuming that these diseases also followed this classic developmental framework.

With mass implementation of screening for cancer, our experiences on the population level have deepened our understanding of cancer biology. Screening efforts have revealed a previously unappreciated reservoir of precancerous lesions and indolent cancers that would not have otherwise come to clinical attention. By contrast, other cancers have been recognized to grow so fast that screening assessments performed at predetermined intervals do not enable detection before their spread to local or distant organs. Indeed, we now understand that 'cancer' comprises a heterogeneous collection of diseases, both across and within organ sites. The advent of

Key points

- Tumours within any organ site can have a spectrum of biological phenotypes, ranging from indolent to highly aggressive
- Screening for cancer is most likely to be beneficial when the target tumour type has a relatively uniform biology and a slower rate of progression
- Not all precursor lesions are on an obligate pathway towards invasive-cancer development
- Strategies for early detection of cancer must balance the benefits of mortality reduction (and reduction in invasive-disease incidence with screening for precancers) with the heterogeneity of the target disease and the consequent risk of overdiagnosis
- Screening can be viewed as a 'cascade' involving multiple steps, such as selection of individuals to be screened, administration of the screening test, workup of positive findings, and, ultimately, treatment
- Efforts are underway to individualize decision-making surrounding risk stratification, the modality and frequency of screening, and diagnostic and therapeutic interventions tailored to the biology of the detected tumour

gene-expression profiling and other molecular diagnostic methodologies has advanced our understanding of cancer biology beyond the original model proposed by Vogelstein and colleagues. In fact, treatment decisions are increasingly being guided by gene-expression profiling, rather than by traditional factors, such as disease stage or histopathological features[3].

The challenge in screening for and prevention of disease relates to the concept that it is difficult to make healthy people better off than they already are, but not as difficult to make them worse off. Screening, by virtue of increasing the likelihood of performing a biopsy, will potentially uncover a reservoir of biologically more-indolent cancers, some of which might lack the potential to progress to metastatic disease (the ultimate cause of most cancer-related deaths). Detection of indolent lesions is not intrinsically harmful, but can lead to downstream diagnostic and therapeutic interventions that cause serious adverse effects to patients. Nevertheless, screening can be of benefit when diagnosis and treatment of a precancerous lesion or an early stage tumour will avert progression of disease to metastasis and/or death. This hope continues to form the basis for population screening for cancer, but also fuels the hype that surrounds cancer screening.

Going forward, lessons learned from the careful distillation of several decades of experience in cancer screening can guide practice and drive improvements in cancer screening. Four key lessons and their corollaries form the foundations for this Review of screening for breast, prostate, cervical, colorectal, and lung cancers (BOX 2). These concepts serve to refine — rather than replace — the Wilson and Jungner criteria, by highlighting the corresponding action points that must be considered to continue improving the delivery of screening assessments. We present a framework for improving cancer screening, based on a stepwise examination of the decisions that must be made before, during, and after deployment of a screening test. Owing to the scope of this topic, emerging technological advancements in screening tests are discussed where relevant, but are not otherwise comprehensively covered.

Screening: a population-based view

Cancer screening can contribute to decreasing cancer morbidity and mortality through two mechanisms: the detection of a precursor lesion, or the early detection of invasive cancer. The benefits of screening are greater when the detection of disease at an earlier (or precancerous) stage improves outcomes; therefore, the available treatment should be safe, acceptable, and more effective when implemented earlier in the disease course.

The identification of true precursor lesions through population screening should result in a decrease in the incidence rates of invasive cancer over time. Colonoscopy and colposcopy (following cervical cytology) enable direct visualization of the target organs (rectum and colon, and cervix, respectively), and concurrent or subsequent removal of at-risk tissue. The use of these approaches depletes the reservoir of precancerous lesions, namely colonic polyps and cervical intraepithelial neoplasia (CIN), which has led to a decrease in the overall incidence of the respective invasive cancers[4] (FIG. 1). The success of population-based screening programmes using cervical cytology in reducing the incidence and mortality rates of invasive cervical cancer fuelled enthusiasm surrounding screening for other (pre)cancers. The detection and removal of all suspected precursor lesions, however, does not lead to the same result in all screening programmes. As is discussed herein, widespread use of mammography screening has increased the frequency of intervention to remove *in situ* breast lesions, but has not resulted in a decline in the incidence of invasive breast cancer[5,6]. The underlying biology and heterogeneity of cancers largely determine the tradeoff between the benefits and the harms of screening.

Differences in disease biology between cancers of the same organ site are of particular importance for tests aimed at the early detection of invasive cancer. Such tests rely on either radiographic imaging of a target organ (for example, mammography for breast cancer and low-dose computed tomography (LDCT) for lung cancer), or measurement of a circulating biomarker associated with presence of the disease (for instance, PSA testing for prostate cancer). These tests are beneficial when they detect invasive cancer at an early, localized stage. The desired effect is a 'stage shift', whereby the proportion of patients diagnosed with early stage disease increases over time, accompanied by a decline in incidence of advanced-stage disease — reflecting averted progression of cancers via early detection and treatment. Importantly, the absolute decrease in the incidence rate of advanced-stage disease should be considered, rather than the change in the relative proportions of these cancers versus early-stage disease, as the latter comparison can be falsely reassuring if an excess of early stage cancers that would not otherwise progress to advanced stages is detected through screening[7]. Additionally, one must consider whether the stage shift is associated with an improvement in disease-related mortality, or because this measure is also affected by the efficacy of treatment, the incidence of metastatic cancers[8].

Box 1 | **Cancer screening in 2016: meeting the Wilson and Jungner[1] criteria?**

1. The condition sought should be an important health problem
   - Criterion met
2. There should be an accepted treatment for patients with recognized disease
   - Criterion met
3. Facilities for diagnosis and treatment should be available
   - Criterion met
4. There should be a recognizable latent or early symptomatic stage
   - Criterion not fully met. Owing to the spectrum of disease heterogeneity, more often true for some cancer types (cervical and colorectal), but less often true for other types (breast, prostate, and lung)
5. There should be a suitable test or examination
   - Criterion met
6. The test should be acceptable to the population
   - Criterion met
7. The natural history of the condition, including development from latent to declared disease, should be adequately understood
   - Criterion not fully met. Focus for improvement: cervical intraepithelial neoplasia, ductal carcinoma *in situ*, colonic polyps, lung nodules, and indolent invasive cancers (for example, Gleason 6 prostate cancers)
8. There should be an agreed policy on whom to treat as patients
   - Criterion not fully met. Focus for improvement: management of disease entities listed in above
9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole
   - Criterion not fully met. Focus for improvement: refining targets of screening and biopsy to improve yield and focus on precursor or early stage forms of potentially morbid disease
10. Case-finding should be a continuing process and not a "once and for all" project
    - Criterion not fully met. Focus for improvement: screening registries should be established to facilitate quality improvement

The focusing of screening programmes on the early detection of invasive cancer arose from an incomplete understanding of the heterogeneity in cancer biology. Cancers can have a spectrum of clinical behaviours, ranging from indolent to aggressive. At one end of this spectrum lies a subset of cancers so aggressive that screening will not, ultimately, be of benefit. This subset comprises cancers that are prone to early systemic spread and, therefore, have a poor prognosis[8]. Despite routine screening, patients with these cancers will already have distant metastatic disease at the time of detection. The term 'interval cancer' is commonly applied to symptomatic tumours that arise in between screening intervals. These cancers tend to be more aggressive and are diagnosed at more-advanced stages than screen-detected lesions[9]. Representing more of a limitation of screening, rather than a harm, patients with interval cancers present with clinical symptoms, and at the same disease stages, regardless of screening. Moreover, in clinical studies, these clinically detected cancers are associated with a worse prognosis than those detected as a result of screening[10], thus challenging the paradigm that screening is effective at improving patient outcomes for all tumour phenotypes.

Screening predominantly detects lesions other than interval cancers, which necessarily include tumours with slow and moderate growth velocities. A difficult challenge, therefore, is to avoid preferential detection of indolent (slow-growing) cancers that might not otherwise come to clinical attention; detection of these cancers might increase the incidence of early stage cancers, but is unlikely to substantially reduce the incidence of advanced-stage cancers because they would probably never progress to such a stage during the patient's lifetime. Herein lies a potential harm of screening: in addition to the intrinsic risk of false-negative and false-positive results owing to the imperfect sensitivity and specificity of the screening tests, screening incurs 'overdiagnosis', defined as the detection of cancerous lesions that would not have caused morbidity or mortality. A closely related concept is 'overdetection' — the detection of premalignant lesions that are not destined to progress to malignancy. Patients with premalignant lesions and indolent cancers can be subjected to invasive tests and treatments, or toxic therapies; therefore, the theoretical risks of overdetection can be similar to those of overdiagnosis: 'overtreatment'. Overtreatment refers to therapy that is inappropriately invasive or extensive in relation to the biology of disease and can occur with a variety of diseases.

Overdiagnosis has been observed on the population level since the 1990s, when screening of children for neuroblastoma was associated with this effect[11]; however, a particularly illustrative example is that of thyroid-cancer screening in the Republic of Korea (South Korea). Widespread government-sponsored screening in South Korea led to a fivefold increase in the incidence of papillary thyroid cancers without a concomitant decrease in disease-specific mortality[12]. Organized population-screening for thyroid cancer does not exist in the USA, although the incidence rate of thyroid cancer is increasing most rapidly of all cancers, owing largely to opportunistic ultrasonography screening[13,14].

The uncovering of a large reservoir of indolent thyroid cancers illustrates the potential for overdiagnosis when screening is targeted at cancer types with a large reservoir of nonprogressive disease (BOX 2: Lesson 1). Similarly, not all precancerous lesions are obligate precursors of invasive disease (BOX 2: Lesson 2). As will be explained in the following sections, population-wide trends, such as those seen for thyroid cancer in the Republic of Korea, can provide valuable clues as to whether screening is having unintended consequences (BOX 2: Lesson 3). In these instances, screening exposes a large population of healthy people to unnecessary harms (BOX 2: Lesson 4). Specifically, overdiagnosis leads to subsequent diagnostic and therapeutic interventions that carry risks, but are ultimately of limited or no benefit (overtreatment).

Thus, screening is likely to be of limited benefit at either extreme of cancer aggressiveness. The challenge is to leverage the experience with screening on the population level gained to date, to continue advancing our understanding of cancer biology, in order to avoid overdiagnosis and overtreatment. In the following sections, we review the two major population-based screening strategies, detection of precursor lesions and early detection of invasive cancer, to further illustrate the lessons and corollaries outlined in BOX 2.

Box 2 | **Key lessons surrounding cancer screening and their corollaries**

Lesson 1: The biology of invasive cancers ranges from indolent to aggressive
Corollary: Screening will be of greatest benefit if targeted at detecting progressive, potentially morbid disease while avoiding identification, and/or reflexive treatment, of indolent disease

Lesson 2: Not all precancerous lesions are obligate precursors of invasive cancers; in fact, most are not
Corollary: Treatment of precancerous lesions is of greatest benefit when it prevents potentially morbid disease, or otherwise removes precursors of less-aggressive disease in an effective, nontoxic way

Lesson 3a: Effective screening and removal of early stage cancers should cause a concomitant decline in the incidence of advanced-stage cancers
Lesson 3b: Effective screening and removal of precursor lesions should cause a concomitant decline in the incidence of invasive cancers
Corollary: Population-level trends can be analysed to identify unintended consequences of screening, such as overdiagnosis, and drive efforts aimed at improving outcomes

Lesson 4: Not all individuals will benefit equally from screening
Corollary: Screening should be offered to a carefully defined target population after consideration of risk factors and overall prognosis

Detection of precursor lesions

Cervical-cancer screening was adopted based largely on the results of early observational studies that showed a decrease in incidence of the disease coincident with widespread screening[15,16]. Randomized clinical trials (RCTs) performed in India subsequently revealed a mortality benefit of cervical-cancer-screening programmes[17–19]. Moreover, high usage of cytology-based screening in US women has been accompanied by a decline in cervical-cancer incidence and mortality (FIG. 1). The causal link between screening and reduced cervical-cancer mortality is also supported by the observation that over half of the incident cervical cancer cases reported each year in the USA and other countries occur in the relatively small subpopulation of unscreened women[20,21]. Of note, cervical-cancer risk can be entirely eliminated among women who undergo total hysterectomy; the high prevalence of hysterectomy by the age of 65 years among women in the USA — up to 50% — has contributed heavily to the observed low rates of cervical cancer in this population[22].

The benefits of screening colonoscopy have largely been extrapolated from the results of RCTs of sigmoidoscopy, and from findings of observational studies that demonstrated a reduction in CRC incidence and mortality rates in participants who received colonoscopy[23–25]. The data from RCTs of sigmoidoscopy-based screening, although differing in the number and frequency of assessments, endoscopic equipment used, and trial design, indicate that this approach is associated with reductions in CRC incidence rate by 18–23% and in disease-specific mortality by 22–31%[26]. Of note, the reductions in the incidence rate and mortality were only statistically significant for distal cancers[25], leading to the hypothesis that regular screening with colonoscopy would enable detection of as many distal cancers and more proximal cancers than screening with sigmoidoscopy, given the ability of colonoscopy to enable visualization of the colon proximal to the splenic flexure. Indeed, findings of two early multicentre trials on one-time colonoscopy screening for asymptomatic individuals indicated that sigmoidoscopy alone might result in a substantial burden of high-risk lesions being missed, as approximately 50% of these advanced-stage neoplasms occurred in the proximal colon and were not associated with distal adenomas[27,28]. To date, no completed trial has directly compared the efficacy of sigmoidoscopy and colonoscopy, but pooled analyses of data from cohort studies on colonoscopy have revealed decreases in CRC incidence and mortality related to proximal and distal cancers[25]. These findings mirror the population decline in CRC incidence and mortality since the 1980s (FIG. 1); the sharpest decline in incidence rates occurs after 2000, when data from the above multicentre colonoscopy trials spurred increased uptake of colonoscopy screening. Colonoscopy every 10 years is considered by some experts to be the most-favourable screening strategy, given its sensitivity, ability to detect serrated polyps, and long-lasting protection against future CRC[29]; however, other CRC screening strategies have also been shown to be effective, including sigmoidoscopy every 5 years and/or yearly stool-based testing with faecal immunohistochemical or faecal occult blood tests[30]. Simulation models have estimated that the cumulative effect of the various CRC screening strategies is responsible for 50% of the observed decline in incidence and mortality rates of this disease in the USA[31].

Screening for cervical cancer and CRC capitalizes on the typically slow, stereotyped progression that lesions comprising atypical cervical cells and colonic polyps undergo during their transformation into malignant neoplasms. The discovery of human papillomavirus (HPV) as the aetiological driver of most cervical cancers prompted further change in the approach to screening for this disease to incorporate consideration of HPV-infection status and adjust future interventions accordingly[32]. Cervical cells infected by oncogenic strains of HPV can sometimes develop into CIN, which can progress to cervical cancer if left untreated[33]. Similarly, some colonic polyps progress to malignancy after acquiring genetic mutations, which differ based on the histological type of the polyp; for example, investigators have demonstrated that hyperplastic polyps and tubulovillous polyps have distinct mutagenesis pathways[34]. The lead-time for such transitions spans several years, allowing adequate time for detection and treatment of the polyp before it becomes malignant. The findings regarding the biology of these diseases, and the experience in screening for them demonstrated that screening is most likely to be beneficial when the targeted cancer has a relatively uniform biology and a slower rate of progression (BOX 2: Lesson 1, corollary).

Another important lesson learned is that not all precancerous lesions are obligate precursors to invasive cancers; in fact, most are not (BOX 2: Lesson 2). Even in the absence of screening and removal, many cases of CIN do not progress to cervical cancer — the immune system often clears HPV infections associated with CIN grade 1, and 40% of CIN grade 2 lesions spontaneously regress[32,35]. Similarly, most colonic polyps will not transform into invasive neoplasms, and a substantial

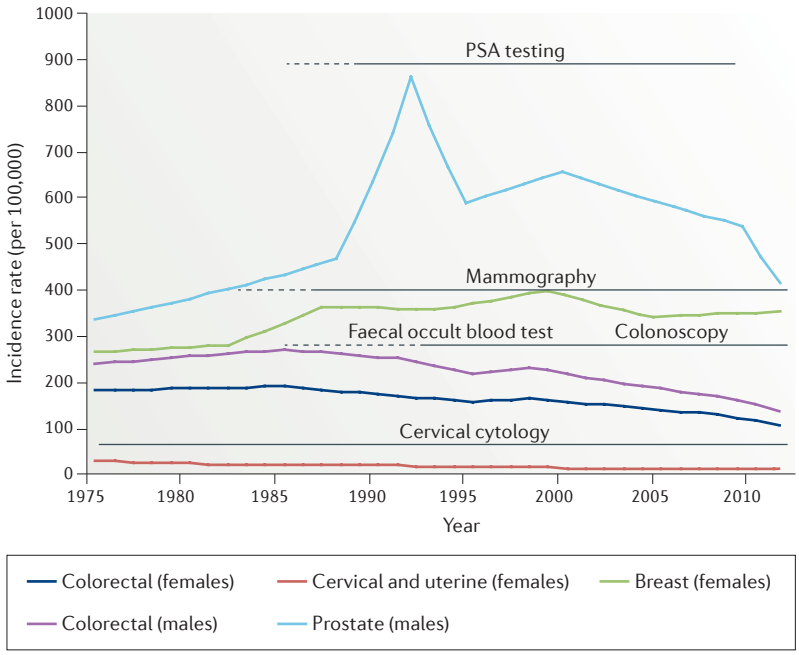

Figure 1 | **Age-adjusted incidence rates of invasive cancers for which population-based screening is practiced in the USA.** Annual incidence rates in men (for prostate and colorectal cancers) and women (for cervical and uterine, breast and colorectal cancers) over the age of 50 years are shown for a 37-year period (1975–2012), based on data from the Surveillance, Epidemiology, and End Results (SEER) registry[4]. Approximate eras of widespread use of the respective screening tests are represented by black lines, with dotted regions representing initial periods of increasing dissemination of the tests following their introduction. The incidence rates of cervical cancer in women and colorectal cancers in both men and women have declined since the early-to-mid 1980s, probably owing to the screening-based detection and subsequent removal of cervical intraepithelial neoplasia and colonic polyps, respectively. On the other hand, the incidence rates of prostate cancer and breast cancer have increased over the same timeframe, probably owing to increased detection of localized cancers as a result of the widespread use of prostate-specific antigen (PSA)-based and mammography screening, respectively.

proportion — perhaps 30% — of small (<6–9 mm) polyps will regress, as suggested by findings of CT-colonography surveillance of unresected polyps[36]. Thus, many resected CIN lesions and colonic polyps would not have otherwise caused morbidity or death. Identification and removal of such lesions represents overdetection and overtreatment, respectively. Treatments for both of these lesion types are generally considered minimally invasive; nevertheless, they have inherent risks. Polypectomy to remove colonic polyps can rarely be complicated by bleeding or colonic perforation[37], and colonoscopy can commonly lead to abdominal pain and bloating[38]. Excisional treatments for cervical lesions, such as loop excision and cone biopsy, carry risks, including bleeding and infection, and have been linked to adverse obstetrical outcomes, such as preterm birth[39]. Treatment harms are difficult to prove with certainty, and the increased risk of preterm birth among women who undergo the most-common cervical excisional technique (loop excision) has been called into question[40]. Nonetheless, current management guidelines recommend restraint in using excisional procedures for the treatment of cervical neoplasia in young women to avoid potential long-term health consequences associated with preterm birth.

Such risks, although not trivial, are generally tolerated because excisional treatments for CIN and colonic polyps are considered effective at preventing the development of invasive cancers, and are less toxic than the treatments that would otherwise be required if the diseases progressed to this stage (BOX 2: Lesson 2, corollary). Additionally, this practice is probably the predominant reason for the observed decline in the incidence of CRC and cervical cancers in the countries where screening is widespread (BOX 2: Lesson 3b). Tailoring the frequency of screening and limiting intervention for lesions that are not believed to be precursors to morbid disease, however, have been key challenges in screening aimed at prevention of these cancers. In guidelines published in 2012, the United States Preventive Services Task Force (USPSTF) recommend increasing the age of initiation of cervical screening cytology from 18 to 21 years, extending screening intervals, and implementing an upper age limit of 65 years for screening of women with prior negative test results[32], reflective of a deeper understanding of the underlying biology of cervical neoplasia (BOX 2: Lesson 4).

On the other hand, the management of ductal carcinoma *in situ* (DCIS) of the breast has been the subject of heavy scrutiny precisely because current treatment strategies are not satisfying the corollary of Lesson 2 (BOX 2): treatment itself is associated with some risks, especially considering that the risk of progression and death for certain types of DCIS and invasive disease is quite low. The incidence of DCIS in the USA increased more than 500% between the early 1980s and late 1990s, largely paralleling the advent of screening mammography, and has stayed relatively constant since then[41,42]. That many cases of DCIS do not progress to invasive breast cancer is widely acknowledged; nevertheless, the standard therapy over the past 25 years or more has been surgical resection (mastectomy, or lumpectomy plus adjuvant radiotherapy) and hormonal therapy[6,43]. Despite treatment of >60,000 DCIS cases per year in the USA, the incidence of invasive breast cancer has not fallen[42]; moreover, breast-cancer mortality has been unaffected by widespread treatment of DCIS (BOX 2: Lesson 3a)[44]. The natural history of DCIS is largely unknown, as most DCIS lesions are surgically resected. According to the available data, the prevalence of invasive cancer in the setting of DCIS might range from 0–50%[45,46]. Notably, the biology of the lesion dictates the risk of associated invasive cancer, with high-grade comedo-type DCIS having a higher likelihood of co-incident invasive cancer[47].

High-grade comedo and low-grade non-comedo DCIS are increasingly recognized to represent distinct disease entities, with the latter probably constituting overdiagnosis. Low-grade DCIS, even if untreated, is unlikely to cause breast-cancer-specific mortality: a recent study reported 10-year survival of 98.8% for women with untreated low-grade DCIS, and 98.6% for those in whom low-grade DCIS was surgically excised[48]. For low-grade DCIS, the risk might be spread over the woman's lifetime, whereas for high-grade DCIS, it might be concentrated within 5 years[46]. Indeed, high-grade DCIS is more-commonly associated

with local recurrence after treatment, distant metastasis, and mortality, and could be considered a true precursor lesion[49,50]. Consideration of DCIS grade alone, however, is unlikely to be sufficient in determining the risk of invasive cancer, and could potentially continue to result in overdiagnosis. In the past 3 years, a gene-expression-profiling test has been introduced as a tool to delineate DCIS biology[45]. In addition, profiling of the tumour immune microenvironment might provide insights into the aetiology of, and inform treatment approaches for, the highest risk DCIS lesions[51].

Early detection/stage shift

Screening approaches aimed at early detection of invasive cancer have been shown to reduce cancer-related mortality rates in some large RCTs with long-term follow up; however, considerable controversy remains over optimal use of the screening tests, and regarding how to balance the benefits and the harms of overdiagnosis and subsequent overtreatment, especially in settings outside of closely monitored clinical trials. For example, mammography-based screening was shown to reduce breast-cancer-related mortality in early RCTs[52–54], although more-recently available long-term follow-up data from completed trials have provided conflicting information on whether mammography decreases breast-cancer mortality[55,56]. Of note, mammography trials have varied in key aspects, such as screening frequency and technique, randomization scheme, and attribution of outcome[57]. In meta-analyses of screening trials, investigators have reported a decrease in disease-specific mortality associated with screening for breast cancer of approximately 20%, although the mortality reduction varies by age[57,58]: the absolute mortality reduction at 10 years is greatest in women aged 60–69 years (21 deaths per 10,000 women), and lowest in those aged 40–49 years (3 deaths per 10,000 women)[59].

At the population level, breast-cancer mortality in the USA has declined since 1990 (REF. 13). Despite some uncertainty, this decline is probably attributable to the combined effects of screening and therapy, and might be dominated by the unquestioned improvements in systemic therapy for locally-advanced and node-positive breast tumours over the past two decades[60]. Microsimulations have yielded a very broad range of estimates for the contribution of screening to the decline in mortality observed in the USA (28–65%)[61]. The magnitudes of these estimates vary dramatically because simulations are influenced by the assumptions and inputs on which each model is based. In fact, even the lower bound estimate might be optimistic. As systemic treatments improve, the mortality reduction attributable to screening diminishes, and accurate modelling of the dissemination of new therapies, or the magnitude of their effects, can be difficult[60]. Likewise, accounting for overdiagnosis and length-time bias in models is challenging, leading to overestimation of the benefits of screening[62]. This consideration is important because 22–31% of breast cancers detected on mammography are estimated to represent overdiagnosis[63].

Thus, two points relevant to screening can be made with the example of breast cancer. First, the mortality reduction attributable to screening diminishes as systemic treatments improve. Notably, most of the screening mammography trials were conducted before the advent of modern adjuvant treatment for breast cancer. Second, a reservoir of indolent disease exists that is detected with screening. After the widespread implementation of mammographic screening in the USA in the mid-to-late 1980s, the overall incidence of invasive breast cancer increased substantially, and remains substantially higher than rates before screening[7] (FIG. 1). This increased incidence largely reflects detection of a greater number of localized (early stage) tumours, accompanied by a disproportionately small decrease in late-stage cancers[7], and whether this trend translates to lowering of disease-related mortality is controversial. Interestingly, an ecological study showed no reduction in breast-cancer-specific mortality in regions of the USA with the highest uptake of mammographic screening[64].

In the face of such complexity, the differing interpretation of the evidence by several guideline-issuing professional bodies around the world is perhaps unsurprising (TABLE 1). In updated guidelines published in February 2016, the USPSTF continued to recommend screening mammography every 2 years for women aged 50–74 years, and that women aged 40–49 years should only be offered screening based on individual circumstances related to patient preferences[65]. These recommendations were based, in part, on a decision analysis[66] and systematic reviews[59,67] commissioned by the USPSTF. In 2015, the American Cancer Society (ACS) modified their guidelines for breast-cancer screening, based on a separate systematic review[58], and their recommendations now more closely resemble the USPSTF guidelines, with the exception of recommended annual screening for women between the ages of 45 and 54 years[68]. American breast-imaging societies and the American College of Obstetrics and Gynecology (ACOG) continue to recommend annual screening beginning at the age of 40 years[69,70], whereas European countries recommend screening every 2–3 years, with starting ages that range between 40 and 50 years[71–73].

A similar picture is seen with screening for prostate cancer. Death from prostate cancer has also declined since the 1990s[13], and this reduction is probably at least partially attributable to screening[74]. In the USA, the incidence of prostate cancer presenting initially as metastatic disease has decreased since the advent of PSA-based screening, indicating that screening and subsequent intervention does avert the progression of some localized tumours[8]. Nevertheless, two major RCTs of PSA-based screening produced discrepant findings related to prostate-cancer-specific mortality: the Prostate, Lung, Colorectal, and Ovarian (PLCO)-study investigators reported no benefit[75], whereas the European Randomized Study of Screening for Prostate Cancer (ERSPC) investigators reported a 21% reduction in the relative risk of prostate-cancer-specific mortality[76]. Differences in the study designs and populations, as well as the relatively high proportions of men in the control

groups who underwent PSA-based screening, might explain these conflicting results[77]. Regardless, the potential for overdiagnosis, with subsequent overtreatment, is widely recognized as a major downside of PSA-based screening. Indeed, a substantial increase in the incidence of prostate cancer has been observed following the dissemination of PSA-based screening (FIG. 1), mostly driven by early stage tumours with a low Gleason score[7]. Many low-grade prostate cancers will not invade beyond the prostatic capsule during the man's lifetime[78], and thus subsequent biopsies, resections, and/or radiation therapy expose the patient to unnecessary harms. Additionally, a normal serum PSA level (typically below 4 ng/ml) does not exclude the possibility of prostate cancer: in the Prostate Cancer Prevention Trial[79], 42.4% of all cancers with Gleason score ≥7 occurred in men with PSA values of ≤3 ng/ml. In the face of an unfavourable risk-to-benefit ratio, the USPSTF has now recommended against the routine use of PSA-based screening, and to date, no country has introduced a national PSA-based screening programme[80,81]. Other major professional societies, however, urge shared decision-making regarding PSA-based screening. For example, the ACS recommends that this discussion should begin at the age of 50 years for men at average risk[82], whereas the American Urological Association (AUA) recommends consideration of screening in men aged 55–69 years[83]. Similarly to the ACS, the European Association of Urology (EAU) recommends that PSA testing should be offered to men over 50 years of age (or earlier in certain risk groups, such as men with a family history of prostate cancer), and can continue until the individual's life expectancy is less than 15 years[84].

Lung cancer screening with LDCT has garnered increased attention based on results of the National Lung Screening Trial (NLST)[85,86]. In this study, 53,454 adults deemed to be at high risk of lung cancer on the basis of age and smoking history were randomly assigned to undergo three annual screenings with either LDCT or chest radiography[85,86]. After a median follow-up duration of 6.5 years, the LDCT arm had three fewer deaths per 1,000 individuals screened than the radiography arm — a 16% reduction in the relative risk of lung-cancer-specific mortality[86,87]. An excess of 120 lung cancers was detected by LDCT versus radiography,

Table 1 | **Summary of mammography guidelines from selected nations**

Country and organisation	Start screening at age (years)	Terminate screening at age (year)	Frequency of assessment	Comments
USA				
United States Preventive Services Task Force (USPSTF)[65]	50	74	Every 2 years (for women at average-risk of breast cancer)	Screening for women aged 40–49 years is a 'grade C' recommendation ('offer or provide this service for selected patients depending on individual circumstances')
American Cancer Society (ACS)[68]	45	As appropriate based on life expectancy	Annually then biennially at 55 years of age and older	Recommend continuing screening as long as the individual is in good health and has a life expectancy exceeding 10 years
American College of Obstetricians and Gynecologists (ACOG)[69]	40	As appropriate based on life expectancy	Annually	Suggest discussing cessation of screening with physician starting at age 75
American College of Radiology (ACR)/Society of Breast Imaging (SBI)[70]	40	As appropriate based on life expectancy	Annually	Suggest continued screening as long as life expectancy exceeds 5–7 years
Canada				
Canadian Task Force on Preventive Health Care[146]	50	74	Every 2–3 years	Not applicable
Sweden				
Socialstyrelsen[73]	40	74	Every 18–24 months	Not applicable
UK				
National Health Service[71]	50	70	Triennially	Expanding the age range of invited women to 47–73 years is being considered
Netherlands				
National Breast Screening Programme[72]	50	75	Biennially	Not applicable
Australia				
Royal Australian College of General Practitioners[147]	50	74	Biennially	Not applicable

however. With the use of modelling to account for lifetime follow up, the overdiagnosis rate for screening with LDCT was estimated to be 11% overall, but was nearly 50% for bronchioloalveolar-cell carcinoma and only 3% for other cell types[88]. The use of LDCT was also associated a cumulative false-positive rate of 37% owing to the detection of benign pulmonary nodules that share imaging characteristics with lung cancer[85]. Results of a retrospective analysis of the NLST data, however, indicate that application of the Lung-RADS reporting system, developed by the American College of Radiology, could potentially reduce the false-positive rate and overdiagnosis[89]. Findings of the Dutch–Belgian NELSON trial[90] of screening for lung cancer with LDCT at 2-year intervals after the initial screen indicated improved specificity compared with annual screening in the NLST[85] (98.6% versus 73.4%), with the tradeoff of lower sensitivity (84.6% versus 93.8%). Nevertheless, a similar percentage of lung cancers were detected at stage 1 in the NELSON trial and the NLST[85,90]. Interval cancers comprised 35 out of 187 diagnosed lung cancers in the NELSON trial, although only 12 of these interval cancers (35%) were not visible on the prior screening scan[90].

A concern is that the efficacy of LDCT seen in the clinical-trial setting will not translate into effectiveness in community practice; some of the success in the NLST might be due to the high level of expertise in LDCT interpretation and patient management at the participating medical centres, 76% of which were National Cancer Institute (NCI)-designated cancer centres[91]. Nevertheless, in the USA, screening for lung cancer is currently recommended for former or current smokers with a 30 pack-year history of tobacco use (and a quit date within 15 years for former smokers) by the USPSTF and other professional societies[92–94]. Beginning screening at the age 55 years is generally advocated, but the recommended age at which to end screening varies between the guidelines[94].

The careful delineation of the candidates for LDCT-based screening illustrates an understanding that not all individuals benefit equally from screening (BOX 2: Lesson 4). The prevailing lesson learned from current experience in screening of lung, breast, and prostate cancers, however, is that these cancers are truly heterogeneous in terms of their biological phenotype (BOX 2: Lesson 1). If the corollary of this lesson is not heeded, screening will disproportionately detect slower growing cancers and has the potential to reveal a reservoir of more-indolent disease. Given the clear excess of early stage cancers detected with population-level screening for breast and prostate cancers, room for improvement of these programmes clearly exists (BOX 2: Lesson 3a). Screening can lead to overdiagnosis and overtreatment if the potential for the detection of indolent cancers is not recognized and treatment decision-making does not account for disease biology. Gene-expression profiling of breast tumours, for example, has revealed a wide array of phenotypic features associated with differences in aggressiveness, and has begun to highlight the important interaction between biological phenotype and approaches to treatment[95–97].

Tempering hype: an eye on improvement

The perception and message surrounding screening for cancer has evolved to acknowledge the complex interplay of risks and benefits inherent to its practice. Hype around screening initially centred around the sound bite that 'early detection saves lives' — an intuitive, powerful message, attractive to practitioners and patients alike. Early campaigns promoting the use of screening tests, such as mammography and colonoscopy, prominently featured (and in some cases, inflated) the purported benefits, while neglecting the potential harms[98]. Wide-reaching population screening was initiated at a time when the linear model of cancer progression prevailed. Reports from cancer registries showed that patients with early stage cancers had good-to-excellent outcomes, and those with advanced-stage disease had much higher mortality rates. This observation led to the belief that detecting cancer at an early stage would uniformly reduce cancer-related mortality; however, this framework did not account for the extensive biological complexity and heterogeneity in cancer, which we are increasingly recognizing, or the associated variability in disease progression. Thus, the nearly uniform enthusiasm for screening contributed to a low-value, or 'more is better', approach to screening[99]. Admittedly, conceptualizing the rewards from less screening is difficult, and the lay public, based on decades of public-health messaging, tend to overestimate the benefits and underestimate the harms of screening[100]. Findings suggest that the concept of overdiagnosis, a clear harm that can be incurred in healthy, asymptomatic people, is discussed relatively infrequently between patients and health-care providers[101].

A guiding principle of cancer prevention and screening is that making healthy people better off than they already are is difficult. Prasad *et al.*[102] have argued that no clear evidence indicates that any of the current cancer screening protocols convincingly reduce all-cause mortality, except LDCT-based screening for lung cancer — and even then, raise the possibility that the reduction in all-cause mortality in the NLST might be smaller than reported. The downstream harms of overdiagnosis and overtreatment probably dilute or even nullify disease-related benefits of cancer screening in general, and exposure to such harms is more difficult to justify in the healthy population than in the management of patients with symptomatic disease. The frequency of screening should, therefore, be optimized based on detection of the tumour types for which beneficial outcomes of intervention are most likely. Those patients with tumours that progress too fast will not benefit from more-intensive screening, which would, however, increase the rates of false-positive findings and overdiagnosis on the population level.

In Europe, such harms are ameliorated, to some extent, by the centralized approach to screening; programmes are organized with fixed budgets, and with formal consideration of the tradeoffs, as opposed to the opportunistic approach used in the USA. In each setting, the same data are viewed and interpreted through different metaphorical lenses — relating to,

for example, the financing and organization of health care, malpractice litigation and cultural attitudes toward risk, interventions, and the politics behind the 'war on cancer'. In Europe, such considerations have led to the generally more-conservative approach to the dissemination of screening. Consider breast-cancer screening, for example: each European nation follows one guideline, and screening of women is usually recommended to begin at 50 years of age, occur every other year, and end at the age of 65–70 years (TABLE 1). Currently, no organized population-screening programmes for lung or prostate cancer are active in Europe. Moreover, government-based screening in European nations affords several additional benefits. Firstly, comprehensive registries of screening outcomes are assembled. Secondly, quality measures can be better implemented, which probably explains the lower recall rates and higher cancer-to-biopsy ratios reported in Europe compared with the USA. Factors relevant to the latter advantage include the minimum requirement for mammogram reads (960 every 2 years in the USA compared with 5,000 per year in Denmark and the UK); double reading (having two radiologists review each image); and the centralization of reading, possibly making mammograms easier to compare, with an emphasis on high specificity[103–105].

Nevertheless, important efforts are emerging in the USA to acknowledge the limitations and tackle the knowledge gaps with regard to cancer screening. These efforts have brought about renewed hope that screening programmes will meet the hype that initially accompanied them. First of all, increased awareness of overdiagnosis has prompted major professional groups to revise their guidelines[68,106]. Furthermore, the NCI convened a working group on overdiagnosis, which made several key recommendations to guide practice and research[107]. The American College of Physicians has also focused attention on high-value care in cancer screening[99,108]. Moreover, increased coverage in the press and other lay-publications in response to these actions has helped disseminate the screening debate among the general public.

Taking the key lessons learned from past experience and their corollaries (BOX 2), we can formulate corresponding action points to improve cancer-screening efforts. In the face of a heterogeneous disease biology (BOX 2: Lesson 1), efforts should be made to identify the true 'targets' of screening — namely, better defining a positive test result based on molecular phenotyping of lesions. Given the uncertainty regarding whether all precursor lesions are predecessors to clinically consequential disease (BOX 2: Lesson 2), a prevention or risk-reduction strategy, rather than treatment intervention, should be considered as the initial approach for some of these lesions. Considering the heterogeneity of risk in the population (BOX 2: Lesson 3), risk stratification might better identify the individuals who are most likely to benefit from screening. Population-based data on screening outcomes should be compiled into registries to provide continued feedback and thus enable quality improvement (BOX 2: Lesson 4). Lastly, similarly to treatment, screening should be based on both prognostic and predictive diagnostics, informed by a better understanding of disease phenotype, with a goal of characterizing and correlating screening abnormalities with the specific type of cancer biology using emerging prognostic and predictive tools. We posit that progress is being made across all five of these goals, with evidence of application and progress across all of the five cancers that are key targets for screening (that is, those of the breast, prostate, lung, cervix, and colon/rectum).

We have integrated the lessons learned with the screening 'cascade' proposed by Harris *et al.*[109] to illustrate how tailored innovations are being incorporated at each step of the screening process (FIG. 2). We believe that such innovations set the stage for 'precision screening', which incorporates individualized risk-prediction, based on clinical factors and biomarkers integrated with molecular characterization of the cancers detected. This approach should improve elucidation of the targets for cancer screening and prevention. Individualized data and patient values should be taken into account when making key decisions on whom to screen, when to initiate and cease screening, how often to screen, and what action to take for patients with abnormal findings. Efforts are already well underway to generate the information that will enable us to harness this knowledge to improve screening. The 'output' generated at each step of the screening cascade is linked with valuable opportunities for continued improvement. We have summarized the tools that will facilitate improvements in screening practices (BOX 3).

Precision along the screening cascade

Persons who are screened

Initiation of screening has to be undertaken acknowledging that "overdiagnosis exists and is common," which is one of five recommendations made by an NCI-sponsored think-tank working group on overdiagnosis[107]. The decision to screen should factor in an individual's pretest probability of cancer, a threshold risk level at which testing is most likely to have a net benefit, and patient values and attitudes towards risk tolerance. Risk stratification has been practiced in a rudimentary form since the advent of screening, as the cumulative risk of nearly all cancers increases with age; therefore, minimum ages at which to begin screening in individuals at low-to-average risk have been recommended — be it faecal occult blood testing, sigmoidoscopy, or colonoscopy at the age of 50 years, or cervical cytology at 21 years of age. Differences in interpretation of the available evidence, however, continue to spur disagreement over these age thresholds[110]. Additionally, the presence of familial risk syndromes or a concurrent disease state associated with an elevated cancer risk places an individual in a high-risk group, warranting consideration of earlier and more-frequent screening. Examples include hereditary nonpolyposis colorectal syndromes[111] or inflammatory bowel disease[112,113] and CRC risk.

Beyond age and conditions associated with an increased risk of malignancy, exposure history is increasingly considered in risk-stratification. For example,

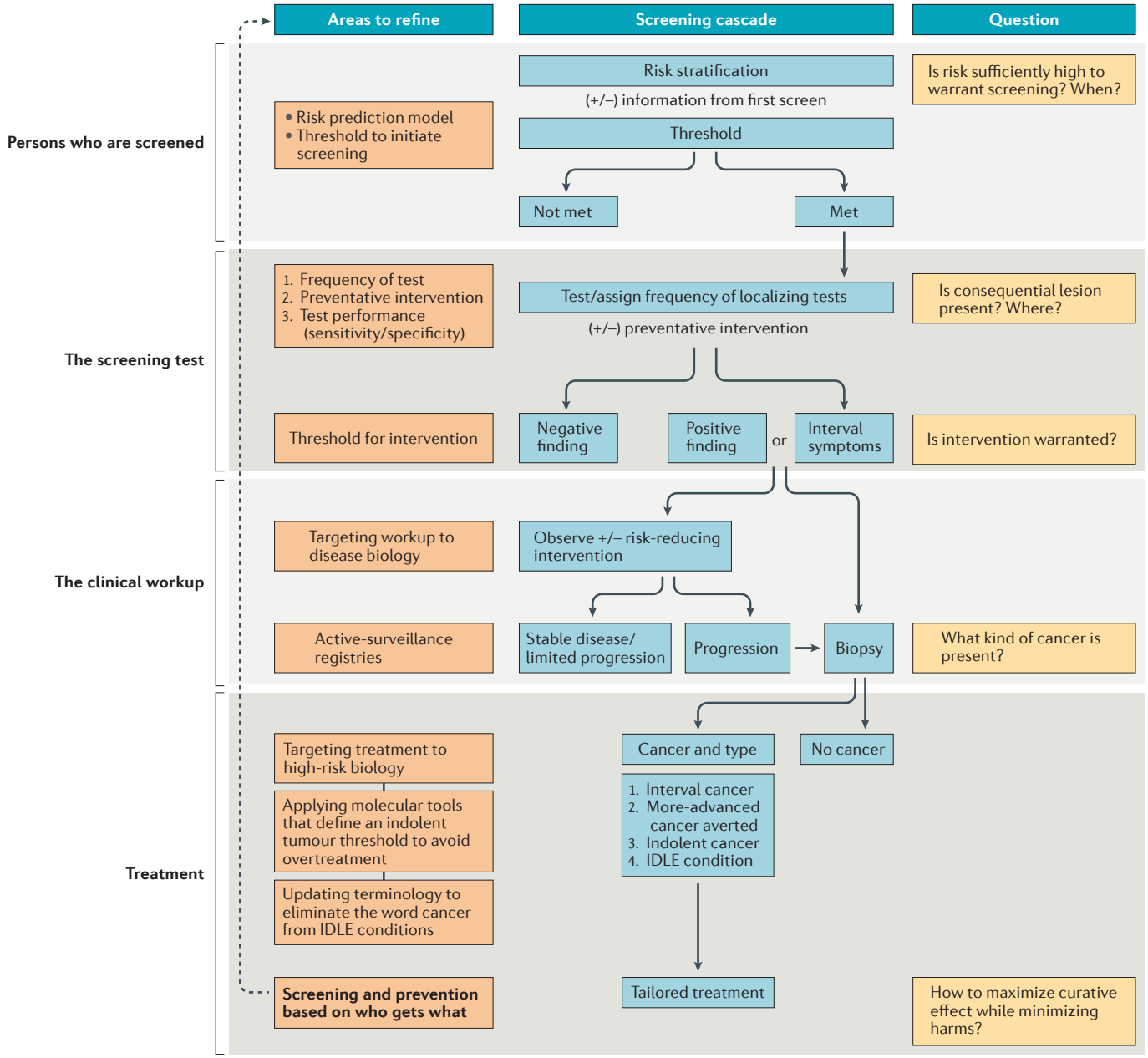

Figure 2 | **A framework for ongoing improvement of cancer-screening programmes.** We present a modified version of the screening cascade proposed by the High-Value Care Task Force of American College of Physicians[109]. Our recommendations for cancer-screening programmes focus on incorporation of key clinical questions at each step of the cascade, as well as components of the 'feedback loop' (areas to refine) — aspects of screening decision-making that can be actively improved using outcomes from the corresponding step on the cascade. IDLE, indolent lesions of epithelial origin.

given the robust, dose-dependent association between cigarette smoking and lung cancer, the NLST investigators selectively enrolled participants who met a minimum of 30 pack-years of smoking history and, if former smokers, had quit less than 15 years before study entry[85]. Most screening guidelines and reimbursement criteria for lung-cancer screening reflect the participant demographics of the NLST, namely limiting use of LDCT to people with a minimum smoking history of 30 pack-years[92,114]. Similar risk-stratification tools have been developed for CRC screening[115] and lung-cancer screening[116], and their clinical utility is currently being studied. Newer proposed algorithms for cervical-cancer screening suggest that HPV testing alone can identify a low-risk population (those with a negative test result), or that type-specific testing of HPV types 16 and/or 18 might help to further refine risk-stratification, such that women with evidence of oncogenic HPV types should have more-diligent evaluation[117,118].

Risk-prediction models are increasingly being used for risk-stratification. The Breast Cancer Risk Assessment Tool, one of the earliest risk prediction tools,

Box 3 | **Toolkit for improving screening**

Site-specific tools

- Risk-prediction models
- Molecular-based tests to inform risk-stratification and treatment decisions
- Feedback-based modification of screening interval and modality, and thresholds for initiating and stopping screening
- Registry of outcomes as a resource for continued quality improvement
- Standardization of test delivery and interpretation
- Shared decision-making tools
- Continued study of the biology, natural history, and treatment response of precancerous and cancerous lesions

Generalized strategies (applicable across all organ sites)

- Integration of comorbidity assessment into decisions about screening, workup, and treatment
- Common molecular classification of indolent tumours, for example, 'IDLE' (indolent lesions of epithelial origin) conditions — that is, redefinition of the term 'cancer'
- Screening systems that includes invitation to screen, recall, and outcomes tracking: 'registry 2.0'

was developed to identify women for inclusion in trials of preventive interventions for breast cancer, and considers exposure to endogenous hormones, in addition to other clinical risk factors[119]. Other risk-prediction models are targeted at individuals suspected of having familial breast cancer[120,121]. The Breast Cancer Surveillance Consortium (BCSC) risk-prediction tool incorporates age, race, family history, mammographic breast density, history of prior breast biopsy (and type of benign breast disease, if present) to calculate a woman's 5-year and 10-year risks of developing breast cancer[122,123]. Beyond risk factors commonly incorporated in prediction models, some specific exposures clearly identify women at risk (for example, history of mantle radiation), and these women are recommended to undergo annual screening with MRI and mammography[124]. In addition, biomarkers have been combined with risk-prediction tools in the hope of improving their performance. A polygenic risk score based on 76 single nucleotide polymorphisms (SNPs) has been shown to independently predict breast-cancer risk, and improved risk-prediction when incorporated into the existing BCSC model[125]. To date, more than 90 SNPs have been associated with breast-cancer risk[126], and incorporation of additional SNPs might further enhance the predictive value of the polygenic risk score. In the upcoming WISDOM trial[127], investigators will use the BCSC model, genetic mutation analysis, and a SNP panel to estimate the 5-year breast-cancer risk score of the women enrolled and, ultimately, assign them a tailored plan, personalizing the starting age, stopping age, and frequency of screening — all within the bounds of the USPSTF guidelines at study initiation. Over time, the risk model will be refined, as will screening-test assignment[127].

The screening test

Screening should follow another of the goals raised at the NCI-sponsored think-tank: to "mitigate overdiagnosis by testing strategies that lower the chance of detecting unimportant lesions" (REF. 107). One can pursue this within three domains, as discussed in the following sections.

Choice of screening test. Imaging tests serve to localize lesions and provide visual clues about the likelihood of malignancy and aggressiveness. With regard to prostate-cancer screening, following up detection of an elevated PSA level with prostate MRI can help to rule out a false-positive result, and if a lesion is present, to improve the yield of tumour tissue upon biopsy[128]. Women at very high risk of breast cancer, such as *BRCA*-mutation carriers, first-degree relatives of *BRCA*-mutation carriers, or those with a 20–25% lifetime risk according to prediction models, should be screened annually with MRI, as an adjunct to mammography, given the superior sensitivity of MRI in this population[124,129–131]. Conversely, use of less invasive or costly strategies is a possibility for individuals on the other end of the risk spectrum. For example, less-frequent screening might be appropriate for individuals considered to be at 'very low' to 'low' risk of CRC according to the prediction model discussed in the previous section[115]. Of note, all current cervical screening guidelines by the ACS, USPSTF, and ACOG incorporate HPV testing as an alternative to cytology-only strategies[108].

Frequency of screening. The frequency of testing is a question that has long been central to quality-improvement efforts in cervical-cancer and CRC screening. In both scenarios, results of the first test or previous tests are used to inform decisions about how and when to repeat screening. In cervical-cancer screening, a combination of a normal cytology-test result and a test result showing no evidence of infection with high-risk (oncogenic) HPV types among women aged ≥30 years predicts a particularly low risk of CIN and invasive cancer[33]; a 5-year screening interval is currently recommended for these women[32]. Women with evidence of infection with oncogenic HPV types can have more-diligent evaluation, whereas those with non-oncogenic HPV infections can be followed less intensively[117,118].

Likewise, the absence of colonic polyps on colonoscopy (and even the presence of small polyps that lack concerning histological features) is associated with a low risk of CRC development over the next decade, and the next screen can, therefore, occur in 10 years[132]. Breast-density measurements obtained from initial mammograms (breast imaging-reporting and data system (BI-RADS) density) has been strongly linked to breast-cancer risk; for example, extremely dense breasts in the setting of elevated risk, such as a family history of breast cancer, or in a woman aged 40–49 years support annual (rather than biennial) screening with mammography[133]. In the Stockholm-3 (STHLM3 trial)[134], a baseline PSA threshold of 1 ng/ml informed the frequency

of prostate cancer screening: if a participant had a PSA level <1 ng/ml, he was not recommended to undergo screening during the following 6 years.

Definition of a positive test result. Experience with precursor lesions has shown that not every 'positive' result warrants further immediate investigation or a biopsy. Historically, the standard of care for young women with abnormal cytology was follow-up colposcopy; however, newer screening approaches integrate watchful waiting (active surveillance). The 2012 management guidelines of the American Society for Colposcopy and Cervical Pathology[135], for example, recommend that women aged 21–24 years with minimally abnormal cytological findings be followed with annual cytology testing, as many such lesions regress spontaneously. Incorporating strict criteria for embarking on a clinical workup into the screening cascade is important. Active surveillance, which will be covered in detail in the next section, can be used for individuals with indeterminate lesions, or those that probably represent indolent disease or its precursors. Additionally, according to the Lung-RADS reporting criteria, pulmonary nodules <6 mm in diameter detected on an initial LDCT screen do not constitute a 'positive' result given they do not require intervention, or necessitate changes to the screening frequency or modality[136]. This example illustrates an important concept, and one that is applicable to any screening study: a 'finding' does not necessarily constitute a 'positive' result. Lastly, results from the STHLM3 trial[134] indicate that combining information on PSA levels, SNP genotype, circulating protein markers, and clinical variables can improve the accuracy of detection for prostate cancers with a Gleason score of ≥7. This demonstration that the STHLM3 model outperformed PSA testing alone for detection of these high-risk prostate cancers might usher in an era in which screening tests have more-narrowly-defined targets related to clinically consequential cancers[134].

The clinical workup

The aim of a clinical workup in an individual with a positive screening-test result is to establish a pathological diagnosis of cancer or high-risk neoplasia, and gather the data necessary for precision treatment. In many cases, a positive result will trigger an invasive diagnostic test, for example, an image-guided biopsy for a suspicious breast mass detected on mammography. In addition to standard pathological review for histology, extent of disease, and tumour markers, increasing options are available for molecular characterization of tumours. Gene-expression-profiling tests have been developed to enable prediction of recurrence risk after treatment for invasive cancers and to support treatment decisions. Notable examples are the Oncotype DX® and MammaPrint® assays for gene-expression profiling of breast cancers[95,96]. Further refinements to these tests, such as establishment of an 'indolent threshold' for the MammaPrint® 70-gene signature[137], have enabled identification of a particularly indolent form of the disease. These advances have enabled gene-expression profiling to be performed on biopsy samples of screen-detected tumours to facilitate risk-stratification and thus prevent overtreatment.

Molecular profiling has changed the view that a standard treatment is uniformly beneficial for all invasive cancers. Approximately one-third of breast cancers detected using modern screening modalities are defined as 'ultra-low risk' based on gene-expression profiling[138]. These cancers are associated with no risk of breast-cancer-related death in the first 15 years after surgical treatment and a <5% risk of late breast-cancer-related death (17–20 years after surgical treatment) with a short course of tamoxifen[137]. Certainly, identification of a precursor of this kind of indolent cancer has no rationale. Low-histological-grade DCIS, as defined by pathologists, is probably a risk factor for the development of such indolent cancers, and this disease entity closely matches the definition of indolent lesions of epithelial origin, or 'IDLE' conditions, that was proposed by the working group convened by the NCI[107]. Other candidate IDLE conditions include the subset of indolent lung cancers identified within the NLST and Gleason 3 + 3 prostate cancers[107]. Setting up observational registries for IDLE conditions will enrich our understanding of the natural history of these tumours and provide guidance on how to incorporate information on disease dynamics (that is, whether the tumours progress, remain stable, or regress) into individualized management approaches. These efforts would parallel the NCI working group's recommendation of creating observational registries for IDLE conditions[107].

This approach has already been shown to hold promise with regard to lung-cancer screening. The rollout of LDCT occurred in an era when the risks associated with screening and subsequent diagnostic testing were recognized, and as such, quality measures were formulated to standardize the clinical workup. For example, the Lung-RADS tool can be used to guide the management of nodules detected on LDCT[136]: on the basis of size, appearance, and growth rate, nodules are assigned a probability of malignancy using this tool, as well as a recommended timeframe and modality for surveillance. This strategy limits unnecessary imaging (only nodules larger than 6 mm, or 4 mm if new, require follow-up assessment) and tissue sampling, which is reserved for 'Category 4B and 4X' lesions, such as >1.5 cm solid nodules[136]. Likewise, the investigators of the NELSON study used strictly defined criteria for a 'positive' test result based on nodule volume or volume-doubling time, which probably improved the positive predictive value of LDCT (40.4%, 95% CI 35.9–44.7%), compared with the performance of this modality reported in other studies, such as the NLST (3.8%, 95% CI 3.4–4.3%)[85,90].

The observation that CIN grade 2 lesions have a high spontaneous regression rate has led to recommendations that these lesions be followed, rather than treated, especially in young women in whom treatments might lead to adverse reproductive outcomes[135]. Repeating colposcopy with cytology at 6-month intervals is specifically recommended for women aged 21–24 years, but

can be offered to women of any age with CIN grade 2 in whom the harms of treatment are believed to outweigh the benefits[135].

Treatment

A comprehensive discussion of cancer therapy is outside the scope of this Review, but tailored therapy is discussed briefly, in the context of limiting overtreatment of indolent tumours. Gene-expression profiling has deepened our understanding of the range of disease entities that are currently classified as 'cancer' based on the classic criteria of histological appearance. In the cases with diagnostic test results that suggest indolent disease, less-aggressive therapies should be pursued. For instance, low-grade DCIS is more likely to be an indicator for an increased risk of future invasive cancer, similarly to its closely related pathological entity atypical ductal hyperplasia[46], rather than an indication for immediate surgery and radiation therapy; a potentially better alternative is to consider these lesions as an opportunity for prevention, using selective oestrogen-receptor modulators or aromatase inhibitors. Thus, for certain women with breast lesions, endocrine therapy alone might be sufficient[96,137].

Moreover, if the workup reveals an IDLE tumour, consideration should be given to active surveillance. When appropriate, changing the nomenclature of IDLE lesions, to reflect their typically benign clinical course, will help frame the decision between patients and providers. The NCI-sponsored think-tank members recommended removing terms related to 'cancer' — as has been instituted for some CIN grade 3 lesions, formerly known as carcinoma *in situ* [107]. A consortium of seven centres (funded by grants from the NCI) are working together to identify common biological criteria for indolent cancers and IDLE conditions, to help redefine 'cancer' in the era of modern molecular medicine[139].

Systems-level improvements

Across the entire screening cascade, several advancements have the potential to improve screening programmes. For example, outcomes registries can support continued improvement by providing real-time feedback. National cancer registries have long been a mainstay in Europe, and have provided an opportunity for detailed cohort studies on screening outcomes[140,141]. In the USA, more-limited registries, such as the Breast Cancer Screening Consortium[142], have linked data from regional mammography registries to form a representative sample of the country. The American College of Radiology's lung-cancer-screening registry represents a burgeoning attempt to form a national screening registry with an aim towards quality improvement[143]. The ultimate goals of this and similar ventures are to promote evidence-based practices (such as management of incidental findings) and improve reporting in order to enable continued assessment of screening practices. Participation in this registry enables screening centres to meet the quality-reporting requirements mandated by the Centers for Medicare and Medicaid Services[143].

One key knowledge gap is centred on screening in the elderly and particularly those with considerable comorbidities — demographics in which few clinical trials of screening interventions have been conducted. Screening should proceed cautiously in the elderly, frail population; for example, many smokers aged within the 55–74 year range who represent the target for LDCT screening for lung cancer, based on the NLST results[85,87], have concurrent cardiac or pulmonary disease that will limit their lifespan. Across the screening cascade, ideally, the individual's underlying comorbidities and frailty should be incorporated into decision-making on the risk–benefit tradeoff. One such example of this approach is provided by e-Prognosis, a prediction tool that is available online (http://eprognosis.ucsf.edu/) and as a smartphone application, and can be used to guide cancer screening in the elderly. The tool juxtaposes the predicted mortality benefit from screening with competing risks, based on a synthesis of published geriatric risk indices[144]. Integration of such tools into screening decisions is a promising area of future research, and the development of a tool that could be applied widely across all screening indications should be a research priority.

Finally, engaging individuals through shared decision-making and the routine offer of participation in studies should be major goals. Many decision tools have been created to facilitate discussions around screening, and tackle the complex interplay between risks, benefits, and each individual's preferences[145]. Patient-oriented studies, such as the WISDOM trial[127], are probing the feasibility and acceptability of precision screening, and should provide critically needed data and key insights. Moreover, the Centers for Medicare and Medicaid Services has mandated that a "lung cancer screening counselling and shared decision making visit" must occur before a LDCT scan being ordered, and is a requirement for reimbursement, emphasizing the need to consider patient preferences[143].

Patient preference could have an important role at the points in the screening cascade at which a biopsy or treatment is recommended. If potentially morbid disease is unlikely to be present, or the suspected lesion is thought to be associated with low mortality, then such uncertainties should be communicated to the patient. Patients' values and levels of risk tolerance can help direct decision-making: those intolerant of the risks of a potential malignancy might favour an aggressive approach and, therefore, intervention, whereas others might favour a watchful-waiting approach. Those in the latter group should be cautioned of the potential need for more-frequent diagnostic testing, and the associated risks and benefits.

Conclusions

We now recognize that cancer encompasses a heterogeneous collection of conditions, and approaches to screening are changing accordingly. Opportunities for improvement are demonstrated by advancements in each of the screening programmes for lung, breast, prostate, colorectal, and cervical cancers, and can inform efforts to further advance the state of the art of screening. Learning who is at risk of which cancers, in terms of both site and

biology, will be a critical underpinning for improvements in screening. The tools required to conduct studies to elucidate these data are coming online, owing to our increasing understanding of the genetic and biological basis of cancer risk, as well as the immunotypes, genotypes, and phenotypes of the tumours that arise. Herein, we have assembled the lessons learned from screening for five major cancers (breast, lung, prostate, cervical, and colorectal cancers; BOX 2) into a quality framework to accelerate our ability to introduce precision screening (FIG. 2), tailored to biology, patient preference, and clinical performance status.

1. Wilson, J. M. & Jungner, Y. G. Principles and practice of screening for disease. *Public Health Pap.* **34**, 1–163 (1968).
2. Vogelstein, B. *et al.* Genetic alterations during colorectal-tumor development. *N. Engl. J. Med.* **319**, 525–532 (1988).
3. Gyorffy, B. *et al.* Multigene prognostic tests in breast cancer: past, present, future. *Breast Cancer Res.* **17**, 11 (2015).
4. National Cancer Institute. U.S. population data — 1969–2013. [online], http://www.seer.cancer.gov/popdata (2015).
5. Bleyer, A. & Welch, H. G. Effect of three decades of screening mammography on breast-cancer incidence. *N. Engl. J. Med.* **367**, 1998–2005 (2012).
6. Worni, M. *et al.* Trends in treatment patterns and outcomes for ductal carcinoma *in situ*. *J. Natl Cancer Inst.* **107**, djv263 (2015).
7. Esserman, L., Shieh, Y. & Thompson, I. Rethinking screening for breast cancer and prostate cancer. *JAMA* **302**, 1685–1692 (2009).
8. Welch, H. G., Gorski, D. H. & Albertsen, P. C. Trends in metastatic breast and prostate cancer — lessons in cancer dynamics. *N. Engl. J. Med.* **373**, 1685–1687 (2015).
9. Kirsh, V. A. *et al.* Tumor characteristics associated with mammographic detection of breast cancer in the Ontario breast screening program. *J. Natl Cancer Inst.* **103**, 942–950 (2011).
10. Shen, Y. *et al.* Role of detection method in predicting breast cancer survival: analysis of randomized screening trials. *J. Natl Cancer Inst.* **97**, 1195–1203 (2005).
11. Woods, W. G. *et al.* Screening of infants and mortality due to neuroblastoma. *N. Engl. J. Med.* **346**, 1041–1046 (2002).
12. Ahn, H. S., Kim, H. J. & Welch, H. G. Korea's thyroid-cancer 'epidemic' — screening and overdiagnosis. *N. Engl. J. Med.* **371**, 1765–1767 (2014).
13. Siegel, R. L., Miller, K. D. & Jemal, A. Cancer statistics, 2016. *CA Cancer J. Clin.* **66**, 7–30 (2016).
14. O'Grady, T. J., Gates, M. A. & Boscoe, F. P. Thyroid cancer incidence attributable to overdiagnosis in the United States 1981–2011. *Int. J. Cancer* **137**, 2664–2673 (2015).
15. Peirson, L., Fitzpatrick-Lewis, D., Ciliska, D. & Warren, R. Screening for cervical cancer: a systematic review and meta-analysis. *Syst. Rev.* **2**, 35 (2013).
16. Whitlock, E. P. *et al.* Liquid-based cytology and human papillomavirus testing to screen for cervical cancer: a systematic review for the U.S. Preventive Services Task Force. *Ann. Intern. Med.* **155**, 687–697 (2011).
17. Sankaranarayanan, R. *et al.* Effect of visual screening on cervical cancer incidence and mortality in Tamil Nadu, India: a cluster-randomised trial. *Lancet* **370**, 398–406 (2007).
18. Sankaranarayanan, R. *et al.* HPV screening for cervical cancer in rural India. *N. Engl. J. Med.* **360**, 1385–1394 (2009).
19. Shastri, S. S. *et al.* Effect of VIA screening by primary health workers: randomized controlled study in Mumbai, India. *J. Natl Cancer Inst.* **106**, dju009 (2014).
20. Andrae, B. *et al.* Screening-preventable cervical cancer risks: evidence from a nationwide audit in Sweden. *J. Natl Cancer Inst.* **100**, 622–629 (2008).
21. National Institute of Health. Cervical cancer. NIH Consensus Statement. *NIH Consensus Development Program* [online], https://consensus.nih.gov/1996/1996cervicalcancer102html.htm (1996).
22. Rositch, A. F., Nowak, R. G. & Gravitt, P. E. Increased age and race-specific incidence of cervical cancer after correction for hysterectomy prevalence in the United States from 2000 to 2009. *Cancer* **120**, 2032–2038 (2014).
23. Nishihara, R. *et al.* Long-term colorectal-cancer incidence and mortality after lower endoscopy. *N. Engl. J. Med.* **369**, 1095–1105 (2013).
24. Brenner, H., Chang-Claude, J., Seiler, C. M., Rickert, A. & Hoffmeister, M. Protection from colorectal cancer after colonoscopy: a population-based, case–control study. *Ann. Intern. Med.* **154**, 22–30 (2011).
25. Brenner, H., Stock, C. & Hoffmeister, M. Effect of screening sigmoidoscopy and screening colonoscopy on colorectal cancer incidence and mortality: systematic review and meta-analysis of randomised controlled trials and observational studies. *BMJ* **348**, g2467 (2014).
26. Weinberg, D. S. & Schoen, R. E. Screening for colorectal cancer. *Ann. Intern. Med.* **160**, ITC5-1 (2014).
27. Lieberman, D. A. *et al.* Use of colonoscopy to screen asymptomatic adults for colorectal cancer. Veterans Affairs Cooperative Study Group 380. *N. Engl. J. Med.* **343**, 162–168 (2000).
28. Imperiale, T. F. *et al.* Risk of advanced proximal neoplasms in asymptomatic adults according to the distal colorectal findings. *N. Engl. J. Med.* **343**, 169–174 (2000).
29. Rex, D. K. Colonoscopy: the current king of the hill in the USA. *Dig. Dis. Sci.* **60**, 639–646 (2015).
30. United States Preventive Services Task Force. Screening for colorectal cancer: U.S. Preventive Services Task Force recommendation statement. *Ann. Intern. Med.* **149**, 627–637 (2008).
31. Zauber, A. G. The impact of screening on colorectal cancer mortality and incidence: has it really made a difference? *Dig. Dis. Sci.* **60**, 681–691 (2015).
32. Moyer, V. A. Screening for cervical cancer: U.S. Preventive Services Task Force recommendation statement. *Ann. Intern. Med.* **156**, 880–891 (2012).
33. Vesco, K. K. *et al. Screening for Cervical Cancer: A Systematic Evidence Review for the U.S. Preventive Services Task Force* (Agency for Healthcare Research and Quality, 2011).
34. Grady, W. M. & Markowitz, S. D. The molecular pathogenesis of colorectal cancer and its potential application to colorectal cancer screening. *Dig. Dis. Sci.* **60**, 762–772 (2015).
35. ASCUS-LSIL Triage Study (ALTS) Group. Results of a randomized trial on the management of cytology interpretations of atypical squamous cells of undetermined significance. *Am. J. Obstet. Gynecol.* **188**, 1383–1392 (2003).
36. Pickhardt, P. J. *et al.* Assessment of volumetric growth rates of small colorectal polyps with CT colonography: a longitudinal study of natural history. *Lancet Oncol.* **14**, 711–720 (2013).
37. Levin, T. R. *et al.* Complications of colonoscopy in an integrated health care delivery system. *Ann. Intern. Med.* **145**, 880–886 (2006).
38. Ko, C. W. *et al.* Incidence of minor complications and time lost from normal activities after screening or surveillance colonoscopy. *Gastrointest. Endosc.* **65**, 648–656 (2007).
39. Kyrgiou, M. *et al.* Fertility and early pregnancy outcomes after conservative treatment for cervical intraepithelial neoplasia. *Cochrane Database Syst. Rev.* **9**, CD008478 (2015).
40. Conner, S. N. *et al.* Loop electrosurgical excision procedure and risk of preterm birth: a systematic review and meta-analysis. *Obstet. Gynecol.* **123**, 752–761 (2014).
41. Ernster, V. L., Barclay, J., Kerlikowske, K., Grady, D. & Henderson, C. Incidence of and treatment for ductal carcinoma *in situ* of the breast. *JAMA* **275**, 913–918 (1996).
42. Ozanne, E. *et al.* Characterizing the impact of 25 years of DCIS treatment. *Breast Cancer Res. Treat.* **129**, 165–173 (2011).
43. Baxter, N. N., Virnig, B. A., Durham, S. B. & Tuttle, T. M. Trends in the treatment of ductal carcinoma *in situ* of the breast. *J. Natl Cancer Inst.* **96**, 443–448 (2004).
44. Narod, S. A., Iqbal, J., Giannakeas, V., Sopik, V. & Sun, P. Breast cancer mortality after a diagnosis of ductal carcinoma *in situ*. *JAMA Oncol.* **1**, 888–896 (2015).
45. Solin, L. J. *et al.* A multigene expression assay to predict local recurrence risk for ductal carcinoma *in situ* of the breast. *J. Natl Cancer Inst.* **105**, 701–710 (2013).
46. Sanders, M. E. *et al.* Continued observation of the natural history of low-grade ductal carcinoma *in situ* reaffirms proclivity for local recurrence even after more than 30 years of follow-up. *Modern Pathol.* **28**, 662–669 (2014).
47. Leonard, G. D. & Swain, S. M. Ductal carcinoma *in situ*, complexities and challenges. *J. Natl Cancer Inst.* **96**, 901–920 (2004).
48. Sagara, Y. *et al.* Survival benefit of breast surgery for low-grade ductal carcinoma *in situ*: a population-based cohort study. *JAMA Surg.* **150**, 739–745 (2015).
49. Bijker, N. *et al.* Risk factors for recurrence and metastasis after breast-conserving therapy for ductal carcinoma-*in-situ*: analysis of European Organization for Research and Treatment of Cancer Trial 10853. *J. Clin. Oncol.* **19**, 2263–2271 (2001).
50. Fisher, E. R. *et al.* Pathologic findings from the National Surgical Adjuvant Breast Project (NSABP) eight-year update of Protocol B-17: intraductal carcinoma. *Cancer* **86**, 429–438 (1999).
51. Campbell, M. J., *et al.* Characterizing the tumor immune microenvironment (TIME) in high-risk ductal carcinoma *in situ* [abstract]. *Cancer Res.* **75**, PD1-5 (2015).
52. Habbema, J. D., van Oortmarssen, G. J., van Putten, D. J., Lubbe, J. T. & van der Maas, P. J. Age-specific reduction in breast cancer mortality by screening: an analysis of the results of the Health Insurance Plan of Greater New York study. *J. Natl Cancer Inst.* **77**, 317–320 (1986).
53. Nystrom, L. *et al.* Long-term effects of mammography screening: updated overview of the Swedish randomised trials. *Lancet* **359**, 909–919 (2002).
54. Tabar, L. *et al.* Efficacy of breast cancer screening by age. New results from the Swedish Two-County Trial. *Cancer* **75**, 2507–2517 (1995).
55. Miller, A. B. *et al.* Twenty five year follow-up for breast cancer incidence and mortality of the Canadian National Breast Screening Study: randomised screening trial. *BMJ* **348**, g366 (2014).
56. Moss, S. M. *et al.* Effect of mammographic screening from age 40 years on breast cancer mortality in the UK Age trial at 17 years' follow-up: a randomised controlled trial. *Lancet Oncol.* **16**, 1123–1132 (2015).
57. Gotzsche, P. C. & Jorgensen, K. J. Screening for breast cancer with mammography. *Cochrane Database Syst. Rev.* **6**, CD001877 (2013).
58. Myers, E. R., Moorman, P., Gierisch, J. M., Havrilesky, L. J. & Grimm, L. J. Benefits and harms of breast cancer screening: a systematic review. *JAMA* **314**, 1615–1634 (2015).
59. Nelson, H. D. *et al.* Effectiveness of breast cancer screening: systematic review and meta-analysis to update the 2009 U.S. Preventive Services Task Force Recommend. *Ann. Intern. Med.* **164**, 244–255 (2016).
60. Birnbaum, J., Gadi, V. K. & Markowitz, E. The effect of treatment advances on the mortality results of breast cancer screening trials: a microsimulation model. *Ann. Intern. Med.* **164**, 236–243 (2016).
61. Berry, D. A. *et al.* Effect of screening and adjuvant therapy on mortality from breast cancer. *N. Engl. J. Med.* **353**, 1784–1792 (2005).
62. Autier, P. Efficient treatments reduce the cost-efficiency of breast cancer screening. *Ann. Intern. Med.* **164**, 297–308 (2016).
63. Welch, H. G. & Passow, H. J. Quantifying the benefits and harms of screening mammography. *JAMA Intern. Med.* **174**, 448–454 (2014).

64. Harding, C. *et al.* Breast cancer screening, incidence, and mortality across US counties. *JAMA Intern. Med.* **175**, 1483–1489 (2015).
65. Siu, A. L. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern. Med.* **164**, 279–296 (2016).
66. Mandelblatt, J. S., Stout, N. K. & Schechter, C. B. Collaborative modeling of the benefits and harms associated with different U.S. breast cancer screening strategies. *Ann. Intern. Med.* **164**, 215–225 (2016).
67. Nelson, H. D., Pappas, M. & Cantor, A. Harms of breast cancer screening: systematic review to update the 2009 U.S. Preventive Services Task Force recommendation. *Ann. Intern. Med.* **164**, 256–267 (2016).
68. Oeffinger, K. C. *et al.* Breast cancer screening for women at average risk: 2015 guideline update from the American Cancer Society. *JAMA* **314**, 1599–1614 (2015).
69. American College of Obstetricians–Gynecologists. Practice bulletin no. 122: breast cancer screening. *Obstet.Gynecol.* **118**, 372–382 (2011).
70. Mainiero, M. B. *et al.* ACR appropriateness criteria breast cancer screening. *J. Am. Coll. Radiol.* **10**, 11–14 (2013).
71. Liston, J. & Wilson, R. (eds) Clinical guidelines for breast cancer screening assessment. *GOV.UK* [online], https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/465528/nhsbsp49_June2010.pdf (2010).
72. de Jong, N., Lock, A., Carpay, M. & Hoebee, B. Dutch Breast Cancer Screening Program: organization and effectiveness. [online], *National Institute for Public Health and the Environment* http://rivm.nl/dsresource?objectid=rivmp:239950&type=org (2014).
73. Socialstyrelsen. Screening för bröstcancer — rekommendation och bedömningsunderlag. [online], http://www.socialstyrelsen.se/publikationer2014/2014-2-32 (2014).
74. Etzioni, R. *et al.* The prostate cancer conundrum revisited: treatment changes and prostate cancer mortality declines. *Cancer* **118**, 5955–5963 (2012).
75. Andriole, G. L. *et al.* Mortality results from a randomized prostate-cancer screening trial. *N. Engl. J. Med.* **360**, 1310–1319 (2009).
76. Schroder, F. H. *et al.* Screening and prostate-cancer mortality in a randomized European study. *N. Engl. J. Med.* **360**, 1320–1328 (2009).
77. Schroder, F. H. & Roobol, M. J. ERSPC and PLCO prostate cancer screening studies: what are the differences? *Eur. Urol.* **58**, 46–52 (2010).
78. Yin, M., Bastacky, S., Chandran, U., Becich, M. J. & Dhir, R. Prevalence of incidental prostate cancer in the general population: a study of healthy organ donors. *J. Urol.* **179**, 892–895; discussion 895 (2008).
79. Thompson, I. M. *et al.* Prevalence of prostate cancer among men with a prostate-specific antigen level ≤4.0 ng per milliliter. *N. Engl. J. Med.* **350**, 2239–2246 (2004).
80. Moyer, V. A. Screening for prostate cancer: U. S. Preventive Services Task Force recommendation statement. *Ann. Intern. Med.* **157**, 120–134 (2012).
81. Arnsrud Godtman, R., Holmberg, E., Lilja, H., Stranne, J. & Hugosson, J. Opportunistic testing versus organized prostate-specific antigen screening: outcome after 18 years in the Goteborg randomized population-based prostate cancer screening trial. *Eur. Urol.* **68**, 354–360 (2015).
82. Wolf, A. & Wender, R. C. American Cancer Society guideline for the early detection of prostate cancer: update 2010. *CA Cancer J. Clin.* **60**, 70–98 (2015).
83. Carter, H. B. *et al.* Early detection of prostate cancer: AUA guideline. *J. Urol.* **190**, 419–426 (2013).
84. Heidenreich, A. *et al.* EAU guidelines on prostate cancer. Part 1: screening, diagnosis, and local treatment with curative intent — update 2013. *Eur. Urol.* **65**, 124–137 (2014).
85. National Lung Screening Trial Research Team. Results of initial low-dose computed tomographic screening for lung cancer. *N. Engl. J. Med.* **368**, 1980–1991 (2013).
86. Pinsky, P. F., Church, T. R., Izmirlian, G. & Kramer, B. S. The National Lung Screening Trial: results stratified by demographics, smoking history, and lung cancer histology. *Cancer* **119**, 3976–3983 (2013).
87. Aberle, D. R. *et al.* Reduced lung-cancer mortality with low-dose computed tomographic screening. *N. Engl. J. Med.* **365**, 395–409 (2011).
88. Patz, E. F. Jr *et al.* Overdiagnosis in low-dose computed tomography screening for lung cancer. *JAMA Intern. Med.* **174**, 269–274 (2014).
89. Pinsky, P. F. *et al.* Performance of Lung-RADS in the National Lung Screening Trial: a retrospective assessment. *Ann. Intern. Med.* **162**, 485–491 (2015).
90. Horeweg, N. *et al.* Detection of lung cancer through low-dose CT screening (NELSON): a prespecified analysis of screening test performance and interval cancers. *Lancet Oncol.* **15**, 1342–1350 (2014).
91. Bach, P. B. *et al.* Benefits and harms of CT screening for lung cancer: a systematic review. *JAMA* **307**, 2418–2429 (2012).
92. Moyer, V. A. Screening for lung cancer: U.S. Preventive Services Task Force recommendation statement. *Ann. Intern. Med.* **160**, 330–338 (2014).
93. Wender, R. *et al.* American Cancer Society lung cancer screening guidelines. *CA Cancer J. Clin.* **63**, 106–117 (2015).
94. Tanoue, L. T., Tanner, N. T., Gould, M. K. & Silvestri, G. A. Lung cancer screening. *Am. J. Respir. Crit. Care Med.* **191**, 19–33 (2015).
95. van 't Veer, L. J. *et al.* Gene expression profiling predicts clinical outcome of breast cancer. *Nature* **415**, 530–536 (2002).
96. Paik, S. *et al.* A multigene assay to predict recurrence of tamoxifen-treated, node-negative breast cancer. *N. Engl. J. Med.* **351**, 2817–2826 (2004).
97. Sorlie, T. *et al.* Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications. *Proc. Natl Acad. Sci. USA* **98**, 10869–10874 (2001).
98. Woloshin, S., Schwartz, L. M., Black, W. C. & Kramer, B. S. Cancer screening campaigns — getting past uninformative persuasion. *N. Engl. J. Med.* **367**, 1677–1679 (2012).
99. Wilt, T. J., Harris, R. P. & Qaseem, A. Screening for cancer: advice for high-value care from the American College of Physicians. *Ann. Intern. Med.* **162**, 718–725 (2015).
100. Hoffman, T. C. & Del Mar, C. Patients' expectations of the benefits and harms of treatments, screening, and tests: a systematic review. *JAMA Intern. Med.* **175**, 274–286 (2015).
101. Moynihan, R. *et al.* Public opinions about overdiagnosis: a national community survey. *PLoS ONE* **10**, e0125165 (2015).
102. Prasad, V., Lenzer, J. & Newman, D. H. Why cancer screening has never been shown to 'save lives' — and what we can do about it. *BMJ* **352**, h6080 (2016).
103. Smith-Bindman, R. *et al.* Comparison of screening mammography in the United States and the United Kingdom. *JAMA* **290**, 2129–2137 (2003).
104. Kemp Jacobsen, K. *et al.* Comparing sensitivity and specificity of screening mammography in the United States and Denmark. *Int. J. Cancer* **137**, 2198–2207 (2015).
105. Esserman, L. *et al.* Improving the accuracy of mammography: volume and outcome relationships. *J. Natl Cancer Inst.* **94**, 369–375 (2002).
106. US Preventive Services Task Force. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. *Ann. Intern. Med.* **151**, 716–726 (2009).
107. Esserman, L. J. *et al.* Addressing overdiagnosis and overtreatment in cancer: a prescription for change. *Lancet Oncol.* **15**, e234–e242 (2014).
108. Sawaya, G. F. *et al.* Cervical cancer screening in average-risk women: best practice advice from the Clinical Guidelines Committee of the American College of Physicians. *Ann. Intern. Med.* **162**, 851–859 (2015).
109. Harris, R. P., Wilt, T. J. & Qaseem, A. A value framework for cancer screening: advice for high-value care from the American College of Physicians. *Ann. Intern. Med.* **162**, 712–717 (2015).
110. Jorgensen, K. J. & Gotzsche, P. C. Breast cancer: updated screening guidelines — much ado about small improvements. *Nat. Rev. Clin. Oncol.* **13**, 139–140 (2016).
111. Stoffel, E. M. *et al.* Hereditary colorectal cancer syndromes: American Society of Clinical Oncology Clinical Practice Guideline endorsement of the familial risk-colorectal cancer: European Society for Medical Oncology Clinical Practice Guidelines. *J. Clin. Oncol.* **33**, 209–217 (2015).
112. Cairns, S. R. *et al.* Guidelines for colorectal cancer screening and surveillance in moderate and high risk groups (update from 2002). *Gut* **59**, 666–689 (2010).
113. Kornbluth, A. & Sachar, D. B. Ulcerative colitis practice guidelines in adults: American College of Gastroenterology, Practice Parameters Committee. *Am. J. Gastroenterol.* **105**, 501–523; quiz 524 (2010).
114. Ruparel, M. & Navani, N. Fulfilling the dream. Toward reducing inequalities in lung cancer screening. *Am. J. Respir. Crit. Care Med.* **192**, 125–127 (2015).
115. Imperiale, T. F., Monahan, P. O., Stump, T. E., Glowinski, E. A. & Ransohoff, D. F. Derivation and validation of a scoring system to stratify risk for advanced colorectal neoplasia in asymptomatic adults: a cross-sectional study. *Ann. Intern. Med.* **163**, 339–346 (2015).
116. Tammemagi, M. C. *et al.* Selection criteria for lung-cancer screening. *N. Engl. J. Med.* **368**, 728–736 (2013).
117. Wright, T. C. *et al.* Primary cervical cancer screening with human papillomavirus: end of study results from the ATHENA study using HPV as the first-line screening test. *Gynecol. Oncol.* **136**, 189–197 (2015).
118. Huh, W. K. *et al.* Use of primary high-risk human papillomavirus testing for cervical cancer screening: interim clinical guidance. *Gynecol. Oncol.* **136**, 178–182 (2015).
119. Gail, M. H. *et al.* Projecting individualized probabilities of developing breast cancer for white females who are being examined annually. *J. Natl Cancer Inst.* **81**, 1879–1886 (1989).
120. Tyrer, J., Duffy, S. W. & Cuzick, J. A breast cancer prediction model incorporating familial and personal risk factors. *Stat. Med.* **23**, 1111–1130 (2004).
121. Mavaddat, N., Rebbeck, T. R., Lakhani, S. R., Easton, D. F. & Antoniou, A. C. Incorporating tumour pathology information into breast cancer risk prediction algorithms. *Breast Cancer Res.* **12**, R28 (2010).
122. Tice, J. A. *et al.* Using clinical factors and mammographic breast density to estimate breast cancer risk: development and validation of a new predictive model. *Ann. Intern. Med.* **148**, 337–347 (2008).
123. Tice, J. A. *et al.* Breast density and benign breast disease: risk assessment to identify women at high risk of breast cancer. *J. Clin. Oncol.* **33**, 3137–3143 (2015).
124. Saslow, D. *et al.* American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *CA Cancer J. Clin.* **57**, 75–89 (2007).
125. Vachon, C. M. *et al.* The contributions of breast density and common genetic variation to breast cancer risk. *J. Natl Cancer Inst.* **107**, dju397 (2015).
126. Michailidou, K. *et al.* Genome-wide association analysis of more than 120,000 individuals identifies 15 new susceptibility loci for breast cancer. *Nat. Genet.* **47**, 373–380 (2015).
127. Wisdom. About the study. [online], https://wisdom.secure.force.com/portal/WsdSiteStudy (2015).
128. Schoots, I. G. *et al.* Magnetic resonance imaging-targeted biopsy may enhance the diagnostic accuracy of significant prostate cancer detection compared to standard transrectal ultrasound-guided biopsy: a systematic review and meta-analysis. *Eur. Urol.* **68**, 438–450 (2015).
129. Warner, E. *et al.* Surveillance of *BRCA1* and *BRCA2* mutation carriers with magnetic resonance imaging, ultrasound, mammography, and clinical breast examination. *JAMA* **292**, 1317–1325 (2004).
130. Kriege, M. *et al.* Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. *N. Engl. J. Med.* **351**, 427–437 (2004).
131. Lee, C. H. *et al.* Breast cancer screening with imaging: recommendations from the Society of Breast Imaging and the ACR on the use of mammography, breast MRI, breast ultrasound, and other technologies for the detection of clinically occult breast cancer. *J. Am. Coll. Radiol.* **7**, 18–27 (2010).
132. Lieberman, D. A. *et al.* Guidelines for colonoscopy surveillance after screening and polypectomy: a consensus update by the US Multi-Society Task Force on Colorectal Cancer. *Gastroenterology* **143**, 844–857 (2012).

133. Kerlikowske, K. *et al.* Outcomes of screening mammography by frequency, breast density, and postmenopausal hormone therapy. *JAMA Intern. Med.* **173**, 807–816 (2013).
134. Grönberg, H. *et al.* Prostate cancer screening in men aged 50–69 years (STHLM3): a prospective population-based diagnostic study. *Lancet Oncol.* **16**, 1667–1676 (2015).
135. Massad, L. S. *et al.* 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. *Obstet. Gynecol.* **121**, 829–846 (2013).
136. American College of Radiology. Lung CT Screening Reporting and Data System (Lung-RADS™). [online], http://www.acr.org/~/media/ACR/Documents/PDF/QualitySafety/Resources/LungRADS/AssessmentCategories.pdf (2015).
137. Lindstrom, L. S. *et al.* MammaPrint accurately predicts long-term survival (25 years) and adjuvant tamoxifen therapy benefit in lymph node and negative patients (abstract). *Cancer Res.* **75** (Suppl. 9), P4-11-12 (2015).
138. Esserman, L. J. *et al.* Impact of mammographic screening on the detection of good and poor prognosis breast cancers. *Breast Cancer Res. Treat.* **130**, 725–734 (2011).
139. National Cancer Institute Division of Cancer Prevention. Consortium for Molecular Characterization of Screen-Detected Lesions Created: eight grants awarded. [online], http://prevention.cancer.gov/news-and-events/news/consortium-molecular (2015).
140. Bennett, R. L., Blanks, R. G., Patnick, J. & Moss, S. M. Results from the UK NHS Breast Screening Programme 2000–2005. *J. Med. Screen.* **14**, 200–204 (2007).
141. Fracheboud, J. *et al.* Interval cancers in the Dutch breast cancer screening programme. *Br. J. Cancer* **81**, 912–917 (1999).
142. Breast Cancer Surveillance Consortium. Evaluating screening performance in practice. *NIH National Cancer Institute* [online], http://breastscreening.cancer.gov/espp.pdf (2004).
143. Centers for Medicare & Medicaid Services. Decision memo for screening for lung cancer with low dose computed tomography (LDCT) (CAG-00439N). [online], https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=274 (2015).
144. Yourman, L. C., Lee, S. J., Schonberg, M. A., Widera, E. W. & Smith, A. K. Prognostic indices for older adults: a systematic review. *JAMA* **307**, 182–192 (2012).
145. Stacey, D. *et al.* Decision aids for people facing health treatment or screening decisions. *Cochrane Database Syst. Rev.* **1**, CD001431 (2014).
146. The Canadian Task Force on Preventive Health Care. Recommendations on screening for breast cancer in average-risk women aged 40–74 years. *CMAJ* **183**, 1991–2001 (2011).
147. The Royal Australian College of General Practitioners. Guidelines for preventive activities in general practice, 8th edition. [online], http://www.racgp.org.au/your-practice/guidelines/redbook/

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M.E. is named on four patents applications for prostate-cancer diagnostics. G.F.S. is Principal Investigator of an NCI-funded grant that aims to identify the range of reasonable options for cervical-cancer screening from a patient-centred and economic perspective (R011CA169093). Y.S., W.C.B., B.S.K., and L.J.E. declare no competing interests.

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Management of cervical cancer patients during the COVID-19 pandemic: a challenge for developing countries

Maria del Pilar Estevez-Diz[1,2], Renata Colombo Bonadio[1,2], Vanessa Costa Miranda[1,2] and Jesus Paula Carvalho[1]

[1]Instituto do Cancer do Estado de Sao Paulo—Faculdade de Medicina da Universidade de Sao Paulo, Sao Paulo 01246-000 2, Brazil
[2]Oncologia D'Or, Sao Paulo 04501-000, Brazil

Abstract

During the COVID-19 pandemic, health services worldwide are going through important adaptations to assist patients infected with COVID-19, at the same time as continuing to provide assistance to other potentially life-threatening diseases. Although patients with cancer may be at increased risk for severe events related to COVID-19 infection, their oncologic treatments frequently cannot be delayed for long periods without jeopardising oncologic outcomes. Considering this, a careful consideration for treatment management of different malignancies is required.

Cervical cancer is concentrated mainly in low-middle income countries (LMICs), which face particular challenges during the COVID-19 pandemic due to the scarcity of health resources in many places. Although cervical cancer is the fourth cause of cancer death among women, it receives little attention from international Oncology societies and scientific research studies. In this review paper, we discuss the cervical cancer landscape and provide specialists recommendations for its management during the COVID-19 pandemic, particularly focused on LMICs' reality.

Keywords: *COVID-19, coronavirus, pandemic, cervical cancer, developing countries*

Policy

Introduction

Since December 2019, the outbreak of a new coronavirus, the SARS-COV-2 (COVID-19) has been observed with a fast spread worldwide. Currently, countries from all over the world are dealing with the consequences of the COVID-19 pandemic. By the end of May 2020, more than 340,000 fatal COVID-19 cases have been registered and numbers continue to rise exponentially [1]. Facing this, governments have been adopting incisive strategies to minimise the number of individuals with COVID-19 infection and prepare health facilities to assist these cases.

An increased risk of complications from COVID-19 infection has been observed in certain groups such as older patients and those with chronic diseases. Regarding patients with cancer, the data available suggest higher rates of severe events. In a prospective Chinese cohort, among 1506 patients with acute respiratory symptoms with confirmed

Correspondence to: Maria del Pilar Estevez-Diz
Email: maria.pilardiz@gmail.com

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COVID-19 infection who were hospitalised, 18 patients had a history of cancer. Despite the small sample size and its heterogeneity in terms of primary tumour and phase of treatment, the study suggested that patients with cancer history had 3.56 times (95% CI 1.8–16.1) higher rates of severe events in comparison with those without cancer [2]. In another study with 28 COVID-19 infected cancer patients, receiving oncologic treatment in the last 14 days previous to infection was identified as a risk factor for severe events (HR 4.07, 95% CI 1.08–15.3) [3].

The presence of an active malignancy and the oncologic treatment can lead to the impairment of physical capacity (performance-status) and immunosuppressive states and can increase the requirement for health service visits and hospitalisation [4]. All these factors may contribute to the increased risk of COVID-19 infection and the occurrence of severe events. Considering this, as well as the global efforts to minimise the overwhelming of health services in general, many cancer centres and oncology societies have been discussing the need for clinic visits and oncologic treatment procedures in different scenarios; however, many malignancies represent a considerable threat to patients' lives and treatment delays may impact oncologic outcomes. Thus, management recommendations should be adapted considering many factors, including the type of cancer, type of oncologic treatment, COVID-19 incidence on the location, and availability of health care facilities.

A concern in low-middle income countries (LMICs) is the treatment of cervical cancer. Cervical cancer is the fourth most incident cancer and the fourth cause of cancer death among women, with 85% of the cases occurring in LMICs [5]. In these countries, the availability of radiotherapy equipment, which is essential for cervical cancer treatment, is frequently insufficient, leading to the need to rationalise its use [6, 7]. When facing the COVID-19 pandemic, this need for rationalisation increases. In LMICs, access to COVID-19 tests is also lower than in high-income countries and represents an additional challenge [8].

Another important particularity is that most cervical cancer cases are diagnosed in young women (median age of 50 years) and as localised potentially curable disease [9]. Despite the relevant impact of cervical cancer, scientific research and discussions by international societies are scarce due to the low frequency of this neoplasia in places as Europe and the United States of America.

In this paper, we aim to discuss the cervical cancer scenario during the COVID-19 pandemic and provide specialists recommendations for its management in LMICs.

General recommendations

In addition to all the measures recommended to the overall population in terms of social distancing, hand hygiene and education on COVID-19 infection symptoms, some recommendations can be made for cancer patients in general. First of all, it is important to highlight that any treatment decision should be based on a case-by-case analysis, which should balance the risks associated with treatment delay or discontinuation versus the risks of COVID-19 exposure and infection.

Building lasting recommendations for all the cases is almost impossible. The complexity of patients and disease varies in different scenarios. In the decision-making process, it is also important to consider the working conditions of health professionals' teams and the availability of resources. The isolation measures of medical staff, restrictions on face-to-face meetings and losses of professionals affected by Covid19 are additional difficulties. Given this situation, the maintenance of a virtual tumour board is a measure that can be very useful. Different existing communication platforms can be used, providing possibilities for discussing cases with the participation of a multidisciplinary team.

Whenever possible, the treatment should be done in the outpatient setting, avoiding unnecessary hospitalisations. This strategy helps to minimise the risk of patient exposure to the COVID-19 virus and decreases the demand for health care services.

Patients who attend to cancer care facilities should be screened for COVID-19 symptoms. In the case of COVID-19 suspicion, they should be ideally transferred to units focused on COVID-19 care. Additionally, the number of patients' companions for clinic visits should be limited to one person at most. Visits to hospitalised patients should be restricted as well and visitors should also be screened for COVID-19 symptoms.

In terms of oncologic treatment during the COVID-19 pandemic, anti-cancer treatments have been associated with increased risk of severe events as already mentioned [3]. Considering this, treatment interruptions should be considered for the patients with active COVID-19 infection until patient recovery with resolution of symptoms, especially in cases of immunosuppressive treatments such as cytotoxic chemotherapy [10]. Despite the low availability of COVID-19 tests in LMIC, we highly recommend testing patients who are currently receiving oncologic treatments since test results will guide treatment decisions.

Active COVID-19 infection should be determined by the presence of symptoms associated with a positive reverse transcription-polymerase chain reaction (RT-PCR) assay for SARS-CoV-2 from an upper respiratory sample [11]. Since false-negative results occur frequently with RT-PCR assay, especially in the first days of the disease, this test should be repeated if initially negative and the presumptive diagnosis of COVID-19 infection based on characteristic findings of chest computed tomography is also acceptable [12, 13].

For cancer patients without COVID-19 infection, the start or continuation of treatment should be evaluated individually. In cases of advanced incurable cancer that has been treated with systemic therapy with satisfactory disease control, treatment pauses can be considered during the pandemic period. On the other hand, if a procedure delay may impact negatively patient's health, an effort should be made to avoid this delay, as recommended by the Society of Gynecologic Oncology [14, 15].

Priorities in cervical cancer management

Treatment for localised potentially curable cervical cancer (stages I-IVA) should be considered a cancer treatment priority. Thus, as long as local conditions allow it, definitive treatments should be started and continued. Most patients with this diagnosis have less than 60 years, representing a group with great life expectancy after successful curative treatment [16].

For patients with early-stage cervical cancer, both surgery and radiation therapy are acceptable treatment strategies. To decide between the two treatment options during the COVID-19 pandemic, local conditions of the health systems should be considered. Although surgery has the disadvantage of requiring patient hospitalisation, it allows the conclusion of treatment in a single moment. If required by local conditions, a surgical procedure delay of 4–8 weeks would be acceptable in this situation [17, 18].

Radiation therapy, otherwise, requires multiple daily visits to the health care facility. During this period in which individuals' dislocations are restricted, this may represent a major challenge. Especially in LMIC, radiation therapy facilities are not largely available and are localised in a few reference centres, which difficult importantly patient access during the COVID-19 pandemic. In the face of this, the surgery for early-stage cervical cancer may be a more suitable option in many locations.

For locally advanced cervical cancer, the standard treatment is definitive chemoradiation. Once again, since this treatment is potentially curative, it should remain a priority. Previous studies have shown that delays to initiate chemoradiation after diagnosis of locally advanced cervical cancer and duration greater than 8 weeks to conclude the therapy are both associated with poorer overall survival [19–21]. Thus, an early chemoradiation therapy, ideally without interruptions, should continue to be pursued. To decrease the number of visits to the health care facility, hypofractionated radiation therapy could be discussed in selected cases [17].

Of note, in many situations, the oncologic treatment may represent an urgency rather than an elective procedure. This is the case of patients who presents with complications related to cancer, such as bleeding, which requires immediate measures.

Finally, for patients with metastatic cervical cancer, first-line chemotherapy (with or without bevacizumab, according to availability) should also be considered as a priority treatment. This therapy is associated with a clear survival benefit, justifying its continuation as long as local conditions allow it [22, 23].

Non-priorities in cervical cancer management

Oncotic colpocytology (Pap smear) is a valuable screening tool, allowing the identification and treatment of premalignant lesions and early cervical cancer. Nevertheless, postponing Pap smear during the COVID-19 pandemic is an acceptable strategy to minimise contact of individuals with health care units. Additionally, the treatment of intraepithelial neoplasia may be postponed [24].

Decreasing health services burden and preserving its resources is essential. The postponement of elective screening procedures is also a recommendation of the American Society of Clinical Oncology [10].

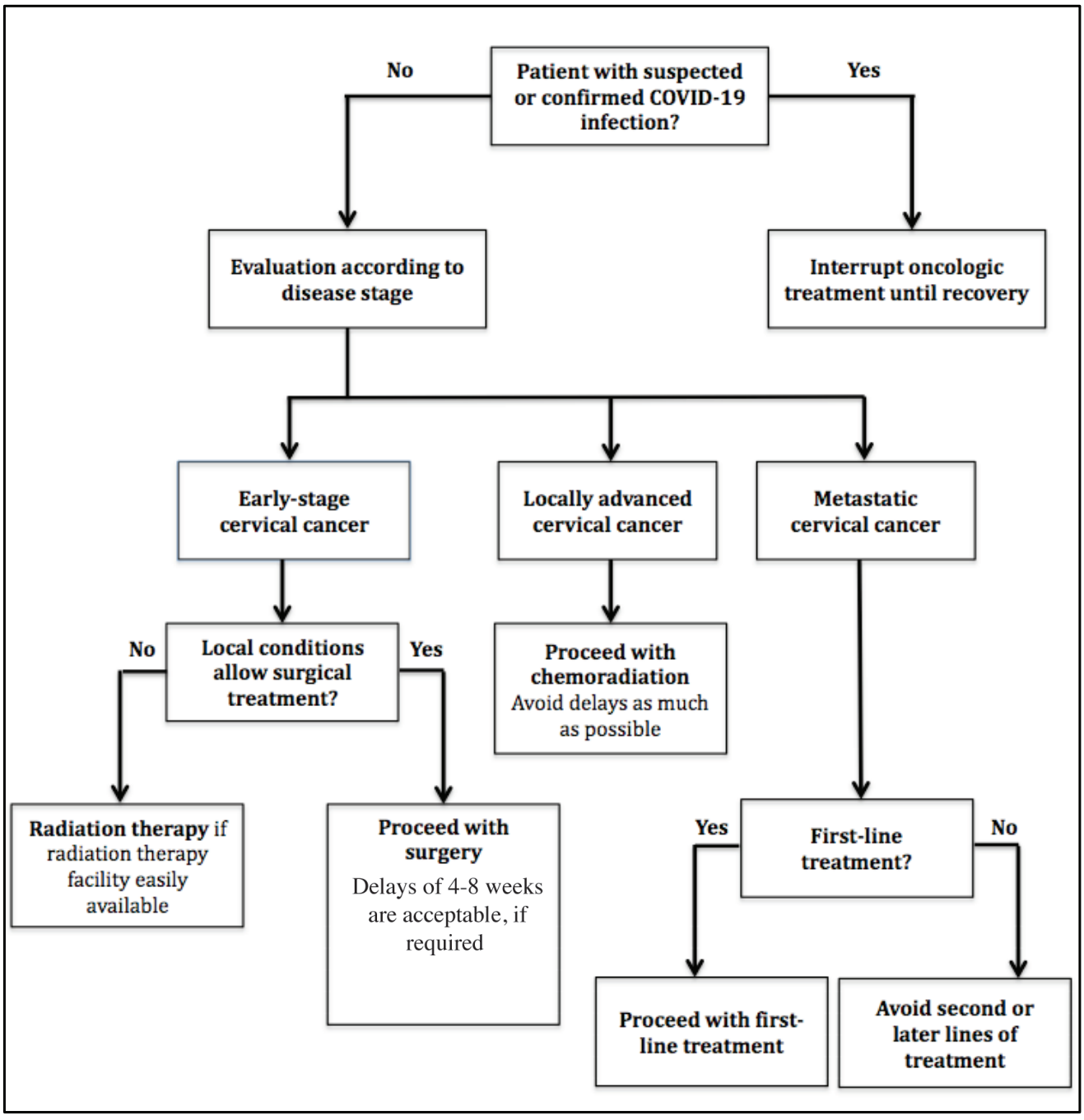

Figure 1. Flowchart of recommendations for the management of cervical cancer patients in active treatment during the COVID-19 pandemic.

Table 1. Recommendations on priority and non-priority procedures for cervical cancer management during COVID-19 pandemic.

Priority	Non-priority
Surgery for early-stage cervical cancer—consider deferring until 4–8 weeks in regions with high COVID-19 risk. Radiation therapy is an acceptable altern-ative in case of easy access to a radiation therapy facility.	Oncotic colpocytology for cervical cancer screening—can be postponed to preserve health care resources and minimise contact of an individual with health care units
Chemoradiation for locally advanced cervical cancer—delays for treatment initiation and conclusion have a negative impact on overall survival.	Systemic therapy after progression on first-line for metastatic cervical cancer—no overall survival benefit
First-line chemotherapy (with or without bevacizumab, according to availability) for patients with metastatic cervical cancer.	Neoadjuvant chemotherapy before chemoradiation for localised cervical cancer—should be avoided due to the lack of a clear benefit and the possibility of a detrimental effect.
Surgical or non-surgical procedures to treat urgent complications (e.g., bleeding) in patients with a potentially curative disease.	Follow-up visits after curative treatment—in case of asymptomatic patients, clinic visits can be postponed or replaced for telemedicine

Moreover, as another strategy to decrease health services burden, surgical staging for locally advanced cervical cancer should be avoided. In a randomised trial with 255 patients, no statistically significant difference in overall survival was observed with surgical staging in comparison with standard clinical/radiological staging [25].

Systemic treatment for metastatic cervical cancer after progression on first-line chemotherapy is not a priority in the time being. Currently, no treatment in subsequent lines has been shown to improve overall survival in comparison with best supportive care [26]. Due to this lack of survival benefit and the risks of an immunosuppressive agent during the COVID-19 pandemic, the use of second or later lines of therapy is discouraged.

In other types of cancer, such as breast cancer, the use of neoadjuvant chemotherapy has been suggested during the COVID-19 pandemic as a strategy to delay surgical treatment [27]. In cervical cancer, however, no clear benefit of neoadjuvant chemotherapy before chemoradiation has been shown. Additionally, a randomised phase II study suggested a potentially detrimental effect on the use of neoadjuvant chemotherapy [28]. Considering this, we do not recommend the use of neoadjuvant chemotherapy to postpone the definitive chemoradiation for locally advanced cervical cancer, unless it is used in a clinical trial context.

For patients who have been successfully treated with curative therapy and are currently in follow-up, clinic visits should be postponed for the maximum interval acceptable if the patient is asymptomatic [10]. As an alternative, telemedicine should be considered where available for the follow-up visits [10, 29].

A summary of the recommendations for cervical cancer management during the COVID-19 pandemic is shown in Figure 1 and Table 1.

Conclusions

The world faces a uniquely challenging moment with the COVID-19 pandemic. Significant adaptation of health care services has been required to assist the COVID-19 patients, at the same time as continuing to assist other patients who cannot have their treatments postponed. During this crisis, careful attention is required for some high-risk groups such as cancer patients.

Cervical cancer patients are a particularly delicate group due to patients' young ages and the potentially curative disease for the majority of cases, occurring mainly in LMICs. We provided a series of recommendations for the management of these patients during the COVID-19 pandemic, especially focused on LMICs. Although oncology societies have provided helpful general recommendations for cervical cancer management, recommendations based on the health services particularities in these countries were lacking.

Finally, we highlight that the management for each patient should be decided on a case-by-case basis, balancing the risks and benefits of each strategy during this period.

Authors' contributions

All authors participated in the study conception and design, literature search and data collection and interpretation.

Maria del Pilar Estevez-Diz and Renata Colombo Bonadio participated in the manuscript writing and construction of tables and figures.

All authors reviewed the manuscript and approved the final version.

All authors are accountable for all aspects of the work.

Disclosures/conflicts of interest

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References

1. **Worldometer. COVID-19 Coronovirus Pandemic** [https://www.worldometers.info/coronavirus/countries-where-coronavirus-has-spread/] Date accessed: 23/05/20
2. Liang W, Guan W, and Chen R, *et al* (2020) **Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China** *Lancet Oncol* **21**(3) 335–337 https://doi.org/10.1016/S1470-2045(20)30096-6 PMID: 32066541 PMCID: 7159000
3. Zhang L, Zhu F, and Xie L, *et al* (2020) **Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China** *Ann Oncol* https://doi.org/10.1016/j.annonc.2020.03.296 PMCID: 7270947
4. Al-Shamsi HO, Alhazzani W, and Alhuraiji A, *et al* (2020) **A practical approach to the management of cancer patients during the novel coronavirus disease 2019 (COVID-19) pandemic: An International Collaborative Group** *Oncologist* https://doi.org/10.1634/theoncologist.2020-0213
5. Bray F, Ferlay J, and Soerjomataram I, *et al* (2018) **Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries** *CA Cancer J Clin* **68**(6) 394–424 https://doi.org/10.3322/caac.21492 PMID: 30207593
6. Barton MB, Zubizarreta E, and Gospodarowicz M (2017) **Radiotherapy in low- and middle-income countries. what can we do differently?** *Clin Oncol (R Coll Radiol)* **29**(2) 69–71 https://doi.org/10.1016/j.clon.2016.11.009
7. Yap ML, Zubizarreta E, and Bray F, *et al* (2016) **Global access to radiotherapy services: have we made progress during the past decade?** *J Glob Oncol* **2**(4) 207–215 https://doi.org/10.1200/JGO.2015.001545 PMID: 28717703 PMCID: 5497622
8. **Coronavirus (COVID-19) Testing** [https://ourworldindata.org/coronavirus-testing] Date accessed: 23/05/20

9. Rodrigues A, de Melo A, and Calabrich A, *et al* (2018) **Association of age, race, and public health insurance with stage of cervical cancer at diagnosis in Brazil: results of the EVITA cohort study (LACOG0215)** *J Clin Oncol* **36**(15_suppl) e17509. https://doi.org/10.1200/JCO.2018.36.15_suppl.e17509
10. American Society of Clinical Oncology **ASCO coronavirus resources** [https://www.asco.org/asco-coronavirus-information] Date accessed: 23/05/20
11. World Health Organization **Laboratory testing for 2019 novel coronavirus (2019-nCoV) in suspected human cases** [https://www.who.int/publications-detail/laboratory-testing-for-2019-novel-coronavirus-in-suspected-human-cases-20200117] Date accessed: 23/05/20
12. Simpson S, Kay FU, and Abbara S, *et al* (2020) **Radiological Society of North America expert consensus statement on reporting chest CT findings related to COVID-19. Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA** *J Thorac Imaging* https://doi.org/10.1097/RTI.0000000000000524 PMID: 32324653 PMCID: 7255403
13. Ai T, Yang Z, and Hou H, *et al* (2020) **Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases** *Radiology* 200642 https://doi.org/10.1148/radiol.2020200642 PMID: 32101510 PMCID: 7233399
14. Society of Gynecologic Oncology **Anti-cancer therapy and clinical trial considerations for gyn-onc patients** [https://www.sgo.org/clinical-practice/management/covid-19-resources-for-health-care-practitioners/anti-cancer-therapy-and-clinical-trial-considerations-for-gyn-onc-patients/] Date accessed: 23/05/20
15. Society of Gynecologic Oncology **Surgical considerations for gynecologic oncologists during the COVID-19 pandemic** [https://www.sgo.org/clinical-practice/management/covid-19-resources-for-health-care-practitioners/surgical-considerations-for-gynecologic-oncologists-during-the-covid-19-pandemic/] Date accessed: 23/05/20
16. **SEER Cancer Stat Facts: Cervix Uteri Cancer** [https://seer.cancer.gov/statfacts/html/cervix.html] Date accessed: 23/05/20
17. Ramirez PT, Chiva L, and Eriksson AGZ, *et al* **COVID-19 global pandemic: options for management of gynecologic cancers** *Int J Gynecol Cancer*
18. Dowdy S and Fader A **Surgical considerations for gynecologic oncologists during the COVID-19 pandemic** [https://www.sgo.org/wp-content/uploads/2020/03/Surgical_Considerations_Communique.v14.pdf] Date accessed: 23/05/20
19. Chen CP, Kung PT, and Wang YH, *et al* (2019) **Effect of time interval from diagnosis to treatment for cervical cancer on survival: a nationwide cohort study** *PLoS One* **14**(9) e0221946 https://doi.org/10.1371/journal.pone.0221946 PMID: 31483834 PMCID: 6726236
20. Song S, Rudra S, and Hasselle MD, *et al* (2013) **The effect of treatment time in locally advanced cervical cancer in the era of concurrent chemoradiotherapy** *Cancer* **119**(2) 325–331 https://doi.org/10.1002/cncr.27652
21. Hong JC, Foote J, and Broadwater G, *et al* (2017) **Data-derived treatment duration goal for cervical cancer: should 8 weeks remain the target in the era of concurrent chemoradiation?** *JCO Clin Cancer Inform* **1** 1–15 https://doi.org/10.1200/CCI.16.00072
22. Moore DH, Blessing JA, and McQuellon RP, *et al* (2004) **Phase III study of cisplatin with or without paclitaxel in stage IVB, recurrent, or persistent squamous cell carcinoma of the cervix: a gynecologic oncology group study** *J Clin Oncol* **22**(15) 3113–3119 https://doi.org/10.1200/JCO.2004.04.170 PMID: 15284262
23. Tewari KS, Sill MW, and Long HJ, *et al* (2014) **Improved survival with bevacizumab in advanced cervical cancer** *N Engl J Med* **370**(8) 734–743 https://doi.org/10.1056/NEJMoa1309748 PMID: 24552320 PMCID: 4010094
24. **ASCCP Interim Guidance for Timing and Treatment Procedures for Patients with Abnormal Cervical Screening Tests** [https://www.asccp.org/covid-19-resources] Date accessed: 23/05/20

25. Marnitz-Schulze S, Tsunoda A, and Martus P, *et al* (2019) **UTERUS-11 STUDY: A randomized clinical trial on surgical staging versus ct-staging prior to primary chemoradiation in patients with FIGO2009 stages IIB-IVA cervical cancer** *Int J Gynecol Cancer* **29**(Suppl 3) A15

26. McLachlan J, Boussios S, and Okines A, *et al* **The impact of systemic therapy beyond first-line treatment for advanced cervical cancer** *Clin Oncol (R Coll Radiol)* **29**(3) 153–160

27. Society of Surgical Oncology **Resource for Management Options of Breast Cancer During COVID-19** [https://www.surgonc.org/wp-content/uploads/2020/03/Breast-Resource-during-COVID-19-3.30.20.pdf] Date accessed: 23/05/20

28. da Costa SCS, Bonadio RC, and Gabrielli FCG, *et al* (2019) **Neoadjuvant chemotherapy with cisplatin and gemcitabine followed by chemoradiation versus chemoradiation for locally advanced cervical cancer: a randomized phase ii trial** *J Clin Oncol* **37**(33) 3124–3131 https://doi.org/10.1200/JCO.19.00674 PMID: 31449470

29. Lambertini M, Toss A, and Passaro A, *et al* (2020) **Cancer care during the spread of coronavirus disease 2019 (COVID-19) in Italy: young oncologists' perspective** *ESMO Open* **5**(2) https://doi.org/10.1136/esmoopen-2020-000759

The Future of Cancer Screening After COVID-19 May Be at Home

Sherri N. Sheinfeld Gorin, PhD, FSBM [1]; Masahito Jimbo, MD, PhD, MPH[1]; Robert Heizelman, MD[1]; Kathryn M. Harmes, MD, MHSA[1]; and Diane M. Harper, MD, MPH, MS[1,2,3,4]

LAY SUMMARY:

- During the coronavirus disease 2019 (COVID-19) pandemic, cancer screening decreased precipitously; home screening for colorectal cancer diminished less than that for colonoscopy and breast and cervical cancer screening.
- The authors have highlighted approaches for home cancer screening in addition to telemedicine.

KEYWORDS: breast, COVID-19, cancer, cervical, colorectal, home, screening.

INTRODUCTION

The coronavirus disease 2019 (COVID-19; severe acute respiratory syndrome coronavirus 2; SARS-CoV-2) pandemic has triggered dramatic and rapid actions. With shelter-in-place policies implemented throughout the United States, and patients fearful of exposure to COVID-19 in health care facilities and physicians' offices, in-office visits were no longer possible, and instead were replaced by video and telephone visits, as institutional support would allow. Professional societies such as the American Cancer Society issued recommendations that no one should go to a health care facility for routine (nondiagnostic) cancer screening until further notification.[1] Other national professional societies issued similar recommendations (the American Society of Clinical Oncology, American Society of Breast Surgeons, American College of Radiology, and American Society for Colposcopy and Cervical Pathology) to postpone regular cancer screening until health care facilities resumed preventive visits.[2-4] Prior to the pandemic, population screening rates for breast, cervical, and colorectal cancers among age-eligible adults at average risk were rising, reaching parity among diverse population subgroups, although still not meeting the Healthy People 2020 goals.[5-7] During the pandemic, analyses of national cancer screening patterns[8] as of April 25, 2020, revealed a precipitous drop in cervical cytology and breast cancer screening of 94% each and of 86% for colorectal cancer screening.

Other analyses of national claims data have suggested that, at current positivity rates, there could be 36,000 missed or delayed diagnoses of breast cancer during the 3-month period from early March through early June. Missed diagnoses of cervical cancer are estimated at 2500 cases and at 18,800 cases for colorectal cancer.[9] The dramatic reductions in cancer screening have created considerable challenges for cancer detection, with later stages of disease at the time of diagnosis, increased cancer incidence (particularly for cervical and colorectal cancer), and greater morbidity and mortality.[10-14]

The US Preventive Services Task Force (USPSTF) recommends regular screening for breast, cervical, and colorectal cancers. In the United States, cancer screening has become predominantly an office-based and physician-directed activity, with colonoscopy performed under sedation, even though effective colorectal cancer screening can be done at home.[10] In 2016, the USPSTF added the multitarget stool DNA (mt-sDNA) Cologuard test to the other recommended home screening options, including the guaiac fecal occult blood test (gFOBT) and fecal immunochemical test (FIT). In-office speculum examinations for specimen retrieval currently are the standard of care for cervical cancer screening; however, home sampling kits for cervical cancer screening currently are under evaluation for approval by the US Food and Drug Administration. Specialist-led bilateral mammography is normative for breast cancer screening. The USPSTF recommends low-dose computed tomography for lung cancer screening, but

Corresponding Author: Sherri N. Sheinfeld Gorin, PhD, FSBM, Department of Family Medicine, University of Michigan School of Medicine, 1018 Fuller St, Ann Arbor, MI 48105 (ssgorin@med.umich.edu).

[1]Department of Family Medicine, University of Michigan School of Medicine, Ann Arbor, Michigan; [2]Department of Obstetrics and Gynecology, University of Michigan School of Medicine, Ann Arbor, Michigan; [3]Department of Women's Studies, College of Literature, Science, and the Arts, University of Michigan, Ann Arbor, Michigan; [4]Hub Research Capacity Core, Michigan Institute for Clinical and Health Research, University of Michigan, Ann Arbor, Michigan

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only for those individuals aged 55 to 80 years with a smoking history of at least 30 pack-years who currently smoke or have quit within the past 15 years. Their new draft deadlines propose to drop the pack-year exposure to 20 years, and the age at which to initiate screening to 50 years, but these recommendations likely will not be finalized until next year. Because the current commentary discussed USPSTF-recommended cancer screening tests among those at average risk, lung cancer will not be discussed further.

Although commercial analytic and electronic medical records (EMR) firms have shared national data, to our knowledge to date there have been no systematic studies of the variations in the use of the individual in-office or home screening tests, nor the implications of these changes in cancer screening within a local health care system. The objective of the current study was to describe the patterns of cancer screening in response to a statewide shelter-in-place executive order within a large, midwestern private medical center.

MATERIALS AND METHODS

Under a state executive order, Michigan Medicine (an affiliate of the University of Michigan) closed all of its clinics to nonessential care from March 19, 2020, to May 9, 2020, and initiated vigorous programs in telemedicine. We evaluated the EMR of 42,974 unique adult outpatients receiving routine cancer screening across 3 cancer types over the past 3 years between the periods March 19 to May 9 and May 10 to June 7 in 2017, 2018, 2019, and 2020. We selected the most common cancer screenings conducted for average-risk individuals at the health care center. We chose these time periods to compare patient visits during the shelter-in-place orders with similar time periods in the previous years to account for secular variations. We added an additional time period to show recovery rates as restrictions were being lifted. In accordance with USPSTF age-specific screening guidelines,[11,13,14] we evaluated men and women aged 50 to 75 years for colorectal cancer screening via colonoscopy, the mt-sDNA test (Cologuard), and FIT; we assessed women aged 50 to 74 years for breast cancer screening via bilateral mammography; and reviewed women aged 21 to 65 years for cervical cancer screening via ThinPrep and/or the human papillomavirus DNA high-risk profile. We used both laboratory reports for cervical cancer screening and procedure codes for colorectal and breast cancer screening within the time periods under study. We excluded any patients who had been diagnosed with cervical, colorectal, or breast neoplasms between 2017 and 2020 to eliminate patients who were undergoing surveillance. We used Slicer Dicer, a self-service analytics engine, to collect and select the EMR data regarding cancer screening in EPIC software. For the outpatient visits, we used regular reports from the EMR and billing claims.

RESULTS

We compared cancer screening for breast, cervical, and colorectal cancers year to year for the periods between March 19 and May 9 in 2017, 2018, 2019, and 2020 and during the clinic reopening between May 10 and June 7, 2020, by comparison with a similar period in 2017, 2018, and 2019 (Fig. 1). Patterns within these time periods were relatively similar prior to March 19 through May 9, 2020. By comparison with the same time period of March 19 through May 9, 2019, prior to the shelter-in-place orders, unique patient visits for cancer screening decreased markedly with mammograms for breast cancer (3339 to 6) and colonoscopy for colorectal cancer (1291 to 8) (Fig. 1). Cervical cancer screening also decreased considerably during the shelter-in-place orders (4990 to 444 overall). By comparison with comparable monthly time periods in 2019 prior to the shelter-in-place orders, all family medicine outpatient in-person visits decreased by approximately 91% (Table 1).

By contrast, although home mt-sDNA testing was less common than colonoscopy prior to the shelter-in-place orders, testing only decreased by approximately 65% during the pandemic (109 to 38 unique patients) (Fig. 1), while the home-based FIT decreased from 101 to 13 unique patients (87%). Similar to other recommended stool-based tests for colorectal cancer (eg, gFOBT), however, both the FIT and the mt-sDNA tests were performed at home by the patient, and therefore were feasible whereas in-office visits were limited.

After the clinic reopenings took place between May 10 to June 7, 2020, cervical cancer screenings increased slightly. Colonoscopy screenings only increased slightly after the clinics reopened, despite their high economic value to medical centers.[15] Neither mt-sDNA screening using Cologuard nor FIT increased. Screening mammograms were not resumed until June 29, 2020, which was a later stage in the reopening of the medical center, and therefore these data reflected as-needed diagnostic mammograms. After reopening of the clinics in 2020, family medicine outpatient visits increased to approximately 80% of the total between May 10 and June 7, 2019, but in-person visits dropped by approximately 88%. Concurrently, video, telephone, and portal visits have continued to follow a steep upward trajectory, far above the use of these approaches in a comparable period in 2019.

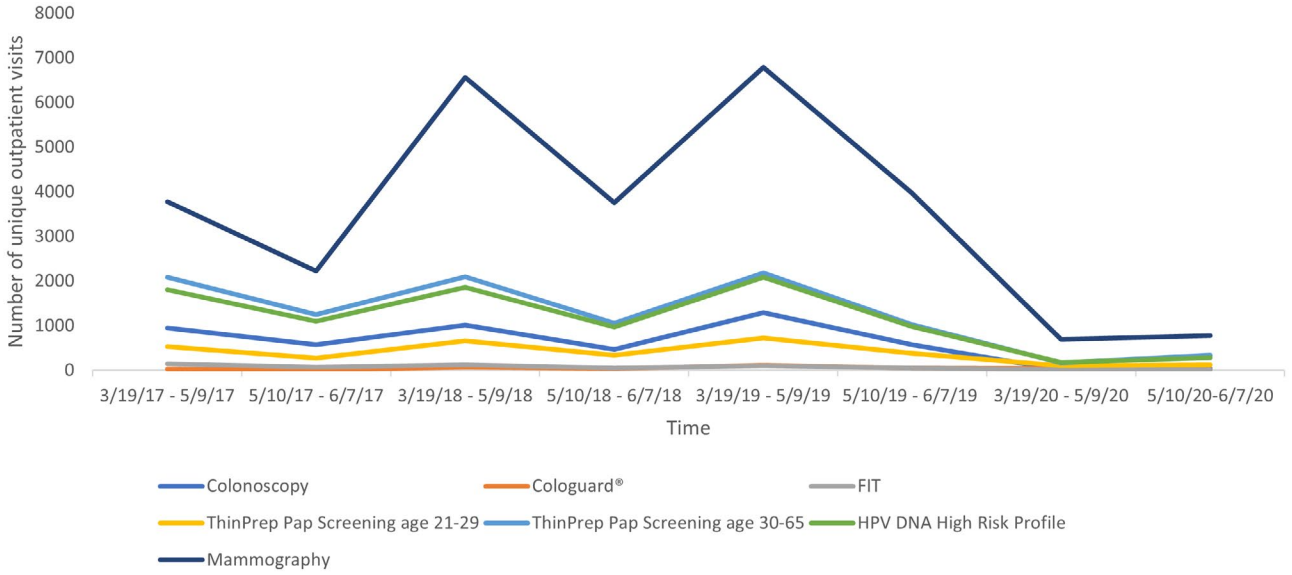

Figure 1. Colorectal, cervical, and breast cancer screening before, during, and after coronavirus disease 2019 (COVID-19) shelter-in-place orders in Michigan.

TABLE 1. Number of Family Medicine Outpatient Visits in Comparable Months Before, During, and After the COVID-19 Pandemic-related clinic closures[a,b]

Type of Visit	3/19/17 to 5/9/17 No. (%)	5/10/17 to 6/7/17 No. %	3/19/18 to 5/9/18 No. %	5/10/18 to 6/7/18 No. %	3/19/19 to 5/9/19 No. %	5/10/19 to 6/7/19 No. %	3/19/20 to 5/9/20 No. %	5/10/20 to 6/7/20 No. %
In person	21,123 (99.7)	11,723 (99.9)	21,891 (99.9)	11,844 (99.9)	22,667 (99.9)	12,514 (99.9)	2120 (15)	1492 (15)
Video	2 (<0.1)	1 (<0.1)	6 (<0.1)	8 (<0.1)	11 (<0.1)	5 (<0.1)	4462 (31)	3519 (35)
Telephone	46 (0.2)	6 (<0.1)	5 (<0.1)	0 (0)	1 (<0.1)	3 (<0.1)	6997 (48)	4551 (45)
Patient portal[c]	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	833 (6)	459 (5)
Total no. of visits	21,171 (100)	11,730 (100)	21,902 (100)	11,852 (100)	22,679 (100)	12,522 (100)	14,412 (100)	10,021 (100)

[a]Only completed visits that could be assigned to a specific provider were reported. Over time, visit types changed (eg, with the addition of a nurse practitioner care navigator).
[b]Source: The electronic medical record using EPIC software.
[c]Source: Michigan Medicine billing reports.

DISCUSSION

We observed an abrupt decrease with in-office breast, cervical, and colorectal cancer screening via colonoscopy between March 19 and June 9, 2020, in accordance with national claims data.[16] However, we observed a more modest decrease in home screening for colorectal cancer via the mt-sDNA test and FIT. Because we captured both the ordering and the performance of these tests within the time periods under study, the at-home tests likely occurred during the suspension of nonessential services. Data from Kaiser Permanente Washington have found that the median time from ordering to the return of FIT among those who adhere is 2 weeks.[17] This suggests the generalizability of the current study findings regarding at-home testing during the pandemic.

With the reopenings taking place after the COVID-19 restrictions, all cancer screenings, both those performed in the office and at home, are beginning to trend upward. However, the number of cancer screening visits remains vastly below those occurring in previous years during the same period of time.

Nonetheless, these data have indicated a potential path forward for home-based cancer screening after the pandemic in addition to telemedicine. Perhaps at-home testing is more immune to the impacts of a pandemic, and its after effects, on the use of and access to primary health care.

Based on the evidence for mt-sDNA testing and FIT, and the emerging findings regarding cervical self-screening, home-based patient screening is both accessible and acceptable to patients[18-22] across diverse

populations, reducing the embarrassment that often accompanies these tests in a medical office.[23-27] There are cost differences, however. Cologuard has a lower cost per screening than colonoscopy, but the screening intervals are more frequent, and therefore the overall cost per patient is higher.[28,29] However, Cologuard is reported to be approximately 99% effective for the general asymptomatic population, and compares favorably with other, similar tests.[30,31] Furthermore, although not yet approved by the US Food and Drug Administration, several studies have found primary human papillomavirus testing using self-sampling to be nearly as effective as speculum-based specimen retrieval.[32,33]

Home self-screening can be taught to and performed by patients.[34,35] Home screening can be integrated into the primary care provider workflow[36,37] for effective screening follow-up that is critical to the earlier detection of cancer, hence to reducing morbidity and mortality. Over time, as clinically relevant biomarkers emerge for the early detection of breast cancer,[38] these tests too may be conducted at home. Home screening for more than one cancer (eg, colorectal and cervical) may significantly boost detection, particularly among populations that have limited access to medical care such as rural-dwelling Native Americans and individuals residing in frontier areas, as well as many minority communities who experienced increased morbidity and mortality after the COVID-19 pandemic. We currently are conducting studies to test this hypothesis.

Michigan Medicine at the University of Michigan treated only approximately 500 patients who were diagnosed with COVID-19. Nonetheless, the health care system quickly increased the use of remote visits and developed centralized management structures and specialized clinical sites. Some of this structural flexibility remains in the organization after COVID-19. However, similar to many other medical centers nationwide, the institution continues to struggle to regain the patient visits that are key to health care settings.[39] In addition, in rural areas, fewer primary care offices are reopening after COVID-19 restrictions.[40,41] The rapid transformation that the health care institution underwent during the pandemic demonstrates that changes can be made in workflow, provider training, and patient engagement to facilitate growth in self-screening for cervical and colorectal cancers, however.

There are several limitations to the current descriptive study. Most important, the cancer screening tests are age-specific counts, but are not necessarily up-to-date screening. To reduce this limitation, we excluded patients from the analyses who were diagnosed with neoplasms. Although year-to-year screening was relatively stable, we limited our analyses to within-screening test comparisons. We evaluated a limited set of tests for colorectal cancer screening within 1 institution, although colonoscopy is the most common test for colorectal cancer nationwide, and the study institution is a major medical center with a diverse and large patient population.[5] Cologuard, which demonstrated the lowest decrease in adherence during the clinic closings, has demonstrated an adherence rate of 71% in a Medicare population.[42] Nonetheless, the baseline testing rates for both mt-sDNA testing and FIT were low compared with colonoscopy, and continued to decline after the clinics reopened. This likely reflects both the high value of colonoscopy to the medical center[15] and physician preference for colonoscopy when all choices are available.[43-45] Although no formal statistical tests were conducted, the changes in screening that were depicted were clinically relevant.

Cancer screening in the United States is opportunistic and therefore, to enhance its effectiveness across populations, it is optimally supported by multilevel intervention approaches, from policy communities, health care organization, physicians, provider teams, and patients.[46] At a time when resources (staff, equipment, and supplies) are devoted to fighting the COVID-19 pandemic and preparing for potential further rebounds, coordinated public health policy and multilevel approaches to implementation are warranted to support continued cancer screening in health care settings. As examples, organized national screening programs for breast, colorectal, and cervical cancers across Europe and the United Kingdom have generally yielded reductions in cancer-related mortality as in the US; nevertheless, implementation still is incomplete, and participation rates vary.[47-49] Nonetheless, during a pandemic, these organized, nationally supported programs still can systematically offer cancer screening.

A positive outcome from the devastation of COVID-19 could be a growth in home screening for 2 cancers: colorectal and cervical. Longer-term study of these changes in cancer screening on patient health after COVID-19 is our future.

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CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

AUTHOR CONTRIBUTIONS

Conceptualization: **Sherri N. Sheinfeld Gorin**. Data curation: **Sherri N. Sheinfeld Gorin**, **Masahito Jimbo**, **Robert Heizelman**, **Kathryn M. Harmes**, and **Diane M. Harper**. Formal analysis: **Sherri N. Sheinfeld Gorin** and **Robert Heizelman**. Writing–original draft: **Sherri N. Sheinfeld Gorin**. Writing–review and editing: **Sherri N. Sheinfeld Gorin**, **Masahito Jimbo**, **Robert Heizelman**, **Kathryn M. Harmes**, and **Diane M. Harper**.

REFERENCES

1. American Cancer Society. Common questions about the new coronavirus outbreak. Accessed April 26, 2020. https://www.cancer.org/latest-news/common-questions-about-the-new-coronavirus-outbreak.html
2. American Society of Clinical Oncology. Cancer screening, diagnosis, staging and surveillance. Accessed April 26, 2020. https://www.asco.org/asco-coronavirus-resources/care-individuals-cancer-during-covid-19/cancer-screening-diagnosis-staging
3. American Society for Colposcopy and Cervical Pathology. Interim guidance for timing of diagnostic and treatment procedures for patients with abnormal cervical screening tests. Site updated March 19, 2020. Accessed April 28, 2020. https://www.asccp.org/covid-198
4. The American Society of Breast Surgeons. ASBrS and ACR Joint Statement on Breast Screening Exams During the COVID-19 Pandemic. Site updated March 26, 2020. Accessed April 28, 2020. https://www.breastsurgeons.org/news/?id=45
5. National Cancer Institute. Cancer Trends Progress Report. Online Summary of Trends in US Cancer Control Measures Centers for Disease Control and Prevention: colorectal cancer screening. Accessed June 2, 2020. https://progressreport.cancer.gov/detection/colorectal_cancer
6. National Cancer Institute. Cancer Trends Progress Report. Online Summary of Trends in US Cancer Control Measures Centers for Disease Control and Prevention: cervical cancer screening. Accessed June 2, 2020. https://progressreport.cancer.gov/detection/cervical_cancer
7. National Cancer Institute. Cancer Trends Progress Report. Online Summary of Trends in US Cancer Control Measures Centers for Disease Control and Prevention: breast cancer screening. Accessed June 2, 2020. https://progressreport.cancer.gov/detection/breast_cancer
8. EPIC Health Research Network (EHRN). Preventive cancer screenings during COVID-19 pandemic. Published May 2020. Accessed June 12, 2020. https://ehrn.org/wp-content/uploads/Preventive-Cancer-Screenings-during-COVID-19-Pandemic.pdf
9. IQVIA Institute for Human Data Science. Three months of COVID-19 may mean 80,000 missed cancer diagnoses. Accessed June 12, 2020. https://www.medscape.com/viewarticle/929986
10. Wernli KJ, Hubbard RA, Johnson E, et al. Patterns of colorectal cancer screening uptake in newly eligible men and women. *Cancer Epidemiol Biomarkers Prev*. 2014;23:1230-1237.
11. US Preventive Services Task Force. Colorectal cancer: screening. Accessed April 25, 2020. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/colorectal-cancer-screening
12. Kim JJ, Burger EA, Regan C, Sy S. Screening for cervical cancer in primary care: a decision analysis for the US Preventive Services Task Force. *JAMA*. 2018;320:706-714.
13. US Preventive Services Task Force. Final recommendation statement. Cervical cancer: screening. Accessed April 25, 2020. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/cervical-cancer-screening
14. US Preventive Services Task Force. Final recommendation statement. Breast cancer: screening. Accessed April 25, 2020. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/breast-cancer-screening
15. Knudsen AB, Zauber AG, Rutter CM, et al. Estimation of benefits, burden, and harms of colorectal cancer screening strategies: modeling study for the US Preventive Services Task Force. *JAMA*. 2016;315:2595-2609. doi:10.1001/jama.2016.682816
16. Martin K, Kurowski D, Given P, Kennedy K, Clayton E. Health Care Cost Institute. The Impact of COVID-19 on the Use of Preventive Health Care. Accessed October 15, 2020. https://healthcostinstitute.org/hcci-research/the-impact-of-covid-19-on-the-use-of-preventive-health-care
17. Haas CB, Phipps AI, Hajat A, Chubak J, Wernli KJ. Time to fecal immunochemical test completion for colorectal cancer screening. *Am J Manag Care*. 2019;25:174-180.
18. Caleia AI, Pires C, Pereira JF, Pinto-Ribeiro F, Longatto-Filho A. Self-sampling as a plausible alternative to screen cervical cancer precursor lesions in a population with low adherence to screening: a systematic review. *Acta Cytol*. 2020;64:332-343.
19. Imperiale TF, Ransohoff DF, Itzkowitz SH, et al. Multitarget stool DNA testing for colorectal-cancer screening. *N Engl J Med*. 2014;370:1287-1297.
20. Kisiel JB, Yab TC, Nazer Hussain FT, et al. Stool DNA testing for the detection of colorectal neoplasia in patients with inflammatory bowel disease. *Aliment Pharmacol Ther*. 2013;37:546-554.
21. Prince M, Lester L, Chiniwala R, Berger B. Multitarget stool DNA tests increases colorectal cancer screening among previously noncompliant Medicare patients. *World J Gastroenterol*. 2017;23:464-471.
22. Chubak J, Bogart A, Fuller S, Laing SS, Green BB. Uptake and positive predictive value of fecal occult blood tests: a randomized controlled trial. *Prev Med*. 2013;57:671-678. doi:10.1016/j.ypmed.2013.08.032
23. Ritvo P, Myers RE, Paszat L, Serenity M, Perez DF, Rabeneck L. Gender differences in attitudes impeding colorectal cancer screening. *BMC Public Health*. 2013;13:500.
24. Datta GD, Mayrand MH, Qureshi S, Ferre N, Gauvin L. HPV sampling options for cervical cancer screening: preferences of urban-dwelling Canadians in a changing paradigm. *Curr Oncol*. 2020;27:e171-e181.
25. Hermansson RS, Olovsson M, Gustavsson C, Lindstrom AK. Elderly women's experiences of self-sampling for HPV testing. *BMC Cancer*. 2020;20:473.
26. Jede F, Brandt T, Gedefaw M, et al. Home-based HPV self-sampling assisted by a cloud-based electronic data system: lessons learnt from a pilot community cervical cancer screening campaign in rural Ethiopia. *Papillomavirus Res*. 2020;9:100198.
27. Pimple SA, Mishra GA, Deodhar KK. Evidence based appropriate triage strategies for implementing high risk HPV as primary technology in cervical cancer screening. *Minerva Ginecol*. 2020;72:96-105.
28. Davies R, Miller R, Coleman N. Colorectal cancer screening: prospects for molecular stool analysis. *Nat Rev Cancer*. 2005;5:199-209.
29. Simon K. Colorectal cancer development and advances in screening. *Clin Interv Aging*. 2016;11:967-976.
30. US Preventive Services Task Force, Bibbins-Domingo K, Grossman DC, et al. Screening for colorectal cancer: US Preventive Services Task Force recommendation statement. *JAMA*. 2016;315:2564-2575.
31. Ouyang DL, Chen JJ, Getzenberg RH, Schoen RE. Noninvasive testing for colorectal cancer: a review. *Am J Gastroenterol*. 2005;100:1393-1403.
32. US Food and Drug Administration. Self-collection devices for Pap test: FDA public workshop. Published January 11, 2018. Accessed June 2, 2020. https://www.fda.gov/media/110292/download
33. Buist DSM, Tiro JA, Thayer C, et al. Improving the promise of embedded pragmatic trials: surmountable barriers encountered in an evaluation of home-based HPV self-sampling to increase cervical cancer screening in overdue women. *Contemp Clin Trials Commun*. 2019;15:100413.
34. Tiro JA, Betts AC, Kimbel K, et al. Understanding patients' perspectives and information needs following a positive home human papillomavirus self-sampling kit result. *J Womens Health (Larchmt)*. 2019;28:384-392.
35. Winer RL, Lin J, Tiro JA, et al. Effect of mailed human papillomavirus test kits vs usual care reminders on cervical cancer screening uptake, precancer detection, and treatment: a randomized clinical trial. *JAMA Netw Open*. 2019;2:e1914729.
36. Health Center Network New York. EHR best practice workflow and documentation guide to support colorectal cancer screening improvement in eClinicalWorks. Accessed June 2, 2020. http://nccrt.org/wp-content/uploads/CRC-Screening-eCW-Best-Practices-Guide-HCNNY-112015.pdf

37. Paxton A.For one laboratory, a workflow transformation. Published June 2018. Accessed June 2, 2020. https://www.captodayonline.com/one-laboratory-workflow-transformation/
38. Bacolod MD, Huang J, Giardina SF, et al. Prediction of blood-based biomarkers and subsequent design of bisulfite PCR-LDR-qPCR assay for breast cancer detection. *BMC Cancer*. 2020;20:85.
39. Mehrotra A, Chernew M, Linetsky D, Hatch H, Cutler D, Schneider EC.The impact of the COVID-19 pandemic on outpatient visits: changing patterns of care in the newest COVID-19 hot spots. Published August 13, 2020. Accessed September 24, 2020. https://www.commonwealthfund.org/publications/2020/aug/impact-covid-19-pandemic-outpatient-visits-changing-patterns-care-newest
40. NPR, Robert Wood Johnson Foundation. Harvard T.H. Chan School of Public Health survey. The Impact of Coronavirus on Households in Rural America. Accessed October 18, 2020. https://cdn1.sph.harvard.edu/wp-content/uploads/sites/94/2020/10/Rural-Report_100520-FINAL.pdf
41. 174 Rural Hospital Closures: January 2005 – Present (132 since 2010). Accessed October 18, 2020. https://www.shepscenter.unc.edu/programs-projects/rural-health/rural-hospital-closures/
42. Weiser E, Parks PD, Swartz RK, et al. Cross-sectional adherence with the multi-target stool DNA test for colorectal cancer screening: real-world data from a large cohort of older adults. *J Med Screen*. 2020 Feb 13:969141320903756. doi:10.1177/0969141320903756
43. Klabunde CN, Lanier D, Nadel MR, McLeod C, Yuan G, Vernon SW. Colorectal cancer screening by primary care physicians: recommendations and practices, 2006-2007. *Am J Prev Med*. 2009;37:8-16.
44. McQueen A, Bartholomew LK, Greisinger AJ, et al. Behind closed doors: physician-patient discussions about colorectal cancer screening. *J Gen Intern Med*. 2009;24:1228-1235.
45. Hawley S, Lillie S, Cooper G, Elston Lafata J. Managed care patients' preferences, physician recommendations, and colon cancer screening. *Am J Manag Care*. 2014;20:555-561.
46. Community Preventive Services Task Force. All Active Recommendations September 2020. Accessed September 11, 2020. https://www.thecommunityguide.org/sites/default/files/assets/CPSTF-Recommendations-508.pdf
47. Peintinger F. National breast screening programs across Europe. *Breast Care (Basel)*. 2019;14:354-358. doi:10.1159/000503715
48. Koo S, Neilson LJ, Von Wagner C, Rees CJ. The NHS Bowel Cancer Screening Program: current perspectives on strategies for improvement. *Risk Manag Healthc Policy*. 2017;10:177-187.
49. Eriksson EM, Lau M, Jonsson C, et al. Participation in a Swedish cervical cancer screening program among women with psychiatric diagnoses: a population-based cohort study. *BMC Public Health*. 2019;19:313. doi:10.1186/s12889-019-6626-3

Speaker: Jyoti Mathad, M.D.
Date: February 8, 2021
Time: 5:00pm - 6:00pm
Title: Women's health issues in LMICs

Zoom info: https://weillcornell.zoom.us/j/92937436313 **Meeting ID**: 929 3743 6313 **Passcode**: 214786

Summary: Focus on health issues that are more common in LMICs or diseases that may be managed differently in LMICs. The talk will also include issues surrounding reproductive health with discussion focused on how social and environmental factors intersect with the provision of appropriate health care in resource-limited settings.

Suggested Readings:

List of Recommendations from the Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC)

The Sustainable Development Goals and the Global Strategy for Women's, Children's and Adolescents' Health

Mendenhall, E., & Weaver, L. J. (2014). Reorienting women's health in low- and middle-income countries: the case of depression and Type 2 diabetes. *Global Health Action*, *7*(1), 22803. https://doi.org/10.3402/gha.v7.22803

Case Study:

Women's Health in LMIC's Case Study: A sick postpartum women in India

Cc: dizzy and weak

HPI: 24 yo female in India presents with dizziness and weight loss for two weeks. The patient recently delivered a baby boy 8 weeks ago. Her pregnancy was uneventful except that she has a history of HIV and was only intermittently adherent to her antiretroviral therapy. At the time of delivery her HIV viral load was in the low thousands.

Two weeks ago, she was seen for her 6-wk postpartum visit and was noted to have cough, fevers, and weight loss. At that time she submitted a sputum sample that was acid fast bacilli (AFB) stain negative. However her chest Xray was notable for a left upper lobe lesion and her sputum was Gene Xpert positive. She was started on anti tuberculosis therapy that day and was encouraged to stay adherent to her antiretroviral therapy as well.

Today she presents with continued weight loss and cough and was found to be hypotensive (78/42) in the clinic. Of note, she has not been adherent with her HIV medications or her TB medications.

Discussion Questions:

· What is your differential diagnosis?

· How would you manage this patient?

List of Recommendations from the Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC)

This information comes from the PRGLAC Report to the HHS Secretary and Congress, September 2018 (/sites/default/files/2018-09/PRGLAC_Report.pdf) (PDF 7 MB).

The Task Force submits the following recommendations to the Secretary of HHS regarding research and the development of safe and effective therapies specific to pregnant women and lactating women based on information gleaned during four meetings and a public comment period. The Task Force developed these recommendations in open, public sessions and voted on each recommendation at the May 2018 meeting (/about/meetings/2018/051418).

The central theme of all recommendations is the need to alter cultural assumptions that have significantly limited scientific knowledge of therapeutic safety, effectiveness, and dosing for pregnant and lactating women. It is critical to facilitate and augment research on therapies for these populations.

1. Include and integrate pregnant women and lactating women in the clinical research agenda
   - Remove pregnant women as an example of a vulnerable population in the Common Rule
   - The Food and Drug Administration (FDA) should harmonize with the Common Rule and remove pregnant women as a vulnerable population
   - The Department of Health and Human Services (HHS) should develop guidance to facilitate the conduct of research in pregnant women and lactating women
2. Increase the quantity, quality, and timeliness of research on safety and efficacy of therapeutic products used by pregnant women and lactating women
   - Provide additional resources and funding for research to obtain clinically meaningful and relevant data for specific and co-existing conditions in pregnant women and lactating women, including but not limited to:
     - Develop preclinical models
     - Expand basic science research to inform drug development
     - Develop new tools and methods to assay therapeutic products, such as those that utilize small volumes and are sensitive to detect minute quantities in human milk
     - Develop new tools to assess pharmacodynamic response in pregnant women, lactating women, and children
     - Fund clinically relevant research and studies to inform therapeutic product use in pregnant women and lactating women
     - Design trials to capture long-term maternal, obstetric, and child outcomes
   - Utilize longer award periods by government funders (beyond the typical 5-year award), when needed, for study design and data collection

3. Expand the workforce of clinicians and research investigators with expertise in obstetric and lactation pharmacology and therapeutics
   - Develop and support training and career development opportunities in obstetric and lactation pharmacology and therapeutics for both clinical and basic science
   - Develop mentors in obstetric and lactation pharmacology and therapeutics for both clinical and basic science
   - Increase the knowledge and engagement of health care providers regarding obstetric and lactation pharmacology and therapeutics
4. Remove regulatory barriers to research in pregnant women
   - Modify subpart B of the Common Rule
     - Change 46.204(e) in subpart B to maternal consent alone
       - Given the recognized autonomy of a pregnant woman, the evolution of family structure, that for a child only one parental signature is required for research to benefit the child and to align with parental consent for pediatrics
     - Add in the option of "Minor increase over minimal risk" from subpart D to 36.046
5. Create a public awareness campaign to engage the public and health care providers in research on pregnant women and lactating women
   - Highlight the importance of research on therapeutic products in pregnant women and lactating women, including the impact of not taking the medication during pregnancy and lactation as well as the impact of not breastfeeding on mother and child
   - Engage stakeholders such as Department of Health and Human Services (HHS), professional societies, industry, advocacy groups, and public and global partners
6. Develop and implement evidence-based communication strategies with health care providers on information relevant to research on pregnant women and lactating women
   - Increase the knowledge of health care providers regarding obstetric and lactation therapeutics and research needs
   - Increase the engagement of health care providers to disseminate information from research findings to their patients
   - Increase the engagement of health care providers to discuss participation in clinical trials, research, and registries
   - Develop appropriate strategies for sharing and interpreting research findings and risk
7. Reduce liability to facilitate an evidence base for new therapeutic products that may be used by women who are, or may become, pregnant and by lactating women
   - Implement a liability-mitigation strategy for conducting research and evaluating new therapeutic products in pregnant women and lactating women
     - Using the Vaccine Injury Compensation Program (VICP) as a model, however include mitigation whether or not the therapeutic product achieves marketing approval
   - If liability mitigation is insufficient, consider implementing a targeted incentive program and/or strengthening FDA authority to require clinically relevant data (such as pharmacologic and clinical data) on pregnant women and lactating women to inform dosing and safety

8. Develop separate programs to study therapeutic products used off-patent in pregnant women and lactating women using the NIH BPCA as a model
   - Provide specific funding
   - Develop separate prioritization processes for therapies and/or conditions in pregnant women and lactating women
9. Develop programs to drive discovery and development of therapeutics and new therapeutic products for conditions specific to pregnant women and lactating women
   - Create separate prioritization processes for pregnant women and lactating women
     - Unmet need examples in lactation: low milk supply, mastitis
     - Unmet need examples in pregnancy: preterm labor, hyperemesis
   - Consider a Biomedical Advanced Research and Development Authority (BARDA)-like model and the NIH vaccine model that takes clinical development up to phase II
10. Implement a proactive approach to protocol development and study design to include pregnant women and lactating women in clinical research
    - Investigators/sponsors must specifically justify exclusion in study design
    - Ensure studies are designed to capture the time dependency of physiologic changes in pregnancy and lactation
    - Develop a systematic plan on how data for pregnant women and lactating women will be obtained in a timely fashion to include pharmacokinetics/pharmacodynamics and safety
    - Develop guidance for institutional review boards and investigators about the inclusion of pregnant women and lactating women in research
    - Develop a systematic plan for if a woman becomes pregnant in a study to include whether product should continue, if un-blinding is necessary, how to capture opportunistic information on pharmacology, clinical data, and pregnancy outcome information
11. Leverage established and support new infrastructures/collaborations to perform research in pregnant women and lactating women
    - Provide financial support and incentives to established and develop new multicenter infrastructures that capitalize on standard of care procedures (opportunistic studies), innovative designs, and methodologies.
    - Broaden focus of ongoing research networks to include research on therapeutic products in pregnant women and lactating women
    - Encourage networks/collaborations to engage in public-private partnerships to facilitate research
12. Utilize and improve existing resources for data to inform the evidence and provide a foundation for research on pregnant women and lactating women
    - Design health record systems to link mother and infant records
    - Leverage large studies and databases including health systems, health plans, surveillance systems, electronic medical records, registries
    - Use novel data resources
    - Use innovative methods of data analytics
    - Require common data elements to facilitate collaboration and use

13. Optimize registries for pregnancy and lactation
    - Create a user-friendly website for registry listing
    - Develop registry standards and common data elements that facilitate input of pertinent data with easy, transparent access to obtain information in real time
        - Include maternal, obstetric, and child outcomes, along with birth defects
    - Facilitate access to data and transparency of information in registries
        - Use the ART registry as a model
    - Develop disease/condition-focused registries
        - Move toward a single registry for all therapeutic products with input from stakeholders
14. The Department of Health and Human Services Secretary should consider exercising the authority provided in law to extend the PRGLAC Task Force when its charter expires in March 2019 (Extended March 13, 2019 – March 13, 2021)
15. Establish an Advisory Committee to monitor and report on implementation of recommendations, updating regulations, and guidance, as applicable, regarding the inclusion of pregnant women and lactating women in clinical research (*Deferred*)

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World Health Organization

Maternal mortality

16 February 2018

Key facts

- **Every day, approximately 830 women die from preventable causes related to pregnancy and childbirth.**
- **99% of all maternal deaths occur in developing countries.**
- **Maternal mortality is higher in women living in rural areas and among poorer communities.**
- **Young adolescents face a higher risk of complications and death as a result of pregnancy than other women.**
- **Skilled care before, during and after childbirth can save the lives of women and newborn babies.**
- **Between 1990 and 2015, maternal mortality worldwide dropped by about 44%.**
- **Between 2016 and 2030, as part of the Sustainable Development Goals, the target is to reduce the global maternal mortality ratio to less than 70 per 100 000 live births.**

Maternal mortality is unacceptably high. About 830 women die from pregnancy- or childbirth-related complications around the world every day. It was estimated that in 2015, roughly 303 000 women died during and following pregnancy and childbirth. Almost all of these deaths occurred in low-resource settings, and most could have been prevented *(1)*.

In sub-Saharan Africa, a number of countries halved their levels of maternal mortality since 1990. In other regions, including Asia and North Africa, even greater headway was made. Between 1990 and 2015, the global maternal mortality ratio (the number of maternal deaths per 100 000 live births) declined by only 2.3% per year between 1990 and 2015. However, increased rates of accelerated decline in maternal mortality were observed from 2000 onwards. In some countries, annual declines in maternal mortality between 2000–2010 were above 5.5%.

The Sustainable Development Goals and the Global Strategy for Women's, Children's and Adolescents' Health

Seeing that it is possible to accelerate the decline, countries have now united behind a new target to reduce maternal mortality even further. One target under Sustainable Development Goal 3 is to reduce the global maternal mortality ratio to less than 70 per 100 000 births, with no country having a maternal mortality rate of more than twice the global average.

Where do maternal deaths occur?

The high number of maternal deaths in some areas of the world reflects inequities in access to health services, and highlights the gap between rich and poor. Almost all maternal deaths (99%) occur in developing countries. More than half of these deaths occur in sub-Saharan Africa and almost one third occur in South Asia. More than half of maternal deaths occur in fragile and humanitarian settings.

The maternal mortality ratio in developing countries in 2015 is 239 per 100 000 live births versus 12 per 100 000 live births in developed countries. There are large disparities between countries, but also within countries, and between women with high and low income and those women living in rural versus urban areas.

The risk of maternal mortality is highest for adolescent girls under 15 years old and complications in pregnancy and childbirth is a leading cause of death among adolescent girls in developing countries *(2)*, *(3)*.

Women in developing countries have, on average, many more pregnancies than women in developed countries, and their lifetime risk of death due to pregnancy is higher. A woman's lifetime risk of maternal death – the probability that a 15 year old woman will eventually die from a maternal cause – is 1 in 4900 in developed countries, versus 1 in 180 in developing countries. In countries designated as fragile states, the risk is 1 in 54; showing the consequences from breakdowns in health systems.

Why do women die?

Women die as a result of complications during and following pregnancy and childbirth. Most of these complications develop during pregnancy and most are preventable or treatable. Other complications may exist before pregnancy but are worsened during pregnancy, especially if not managed as part of the woman's care. The major complications that account for nearly 75% of all maternal deaths are *(4)*:

- severe bleeding (mostly bleeding after childbirth)
- infections (usually after childbirth)
- high blood pressure during pregnancy (pre-eclampsia and eclampsia)
- complications from delivery
- unsafe abortion.

The remainder are caused by or associated with diseases such as malaria, and AIDS during pregnancy.

How can women's lives be saved?

Most maternal deaths are preventable, as the health-care solutions to prevent or manage complications are well known. All women need access to antenatal care in pregnancy, skilled care during childbirth, and care and support in the weeks after childbirth. Maternal health and newborn health are closely linked. It was estimated that approximately 2.7 million newborn babies died in 2015 *(5)*, and an additional 2.6 million are stillborn *(6)*. It is particularly important that all births are attended by skilled health professionals, as timely management and treatment can make the difference between life and death for both the mother and the baby.

Severe bleeding after birth can kill a healthy woman within hours if she is unattended. Injecting oxytocin immediately after childbirth effectively reduces the risk of bleeding.

Infection after childbirth can be eliminated if good hygiene is practiced and if early signs of infection are recognized and treated in a timely manner.

Pre-eclampsia should be detected and appropriately managed before the onset of convulsions (eclampsia) and other life-threatening complications. Administering drugs such as magnesium sulfate for pre-eclampsia can lower a woman's risk of developing eclampsia.

To avoid maternal deaths, it is also vital to prevent unwanted and too-early pregnancies. All women, including adolescents, need access to contraception, safe abortion services to the full extent of the law, and quality post-abortion care.

Why do women not get the care they need?

Poor women in remote areas are the least likely to receive adequate health care. This is especially true for regions with low numbers of skilled health workers, such as sub-Saharan Africa and South Asia. Globally in 2015, births in the richest 20 per cent of households were more than twice as likely to be attended by skilled health personnel as those in the poorest 20 per cent of households (89 per cent versus 43 per cent). This means that millions of births are not assisted by a midwife, a doctor or a trained nurse.

In high-income countries, virtually all women have at least four antenatal care visits, are attended by a skilled health worker during childbirth and receive postpartum care. In 2015, only 40% of all pregnant women in low-income countries had the recommended antenatal care visits.

Other factors that prevent women from receiving or seeking care during pregnancy and childbirth are:

- **poverty**
- **distance**
- **lack of information**
- **inadequate services**
- **cultural practices.**

To improve maternal health, barriers that limit access to quality maternal health services must be identified and addressed at all levels of the health system.

WHO response

Improving maternal health is one of WHO's key priorities. WHO works to contribute to the reduction of maternal mortality by increasing research evidence, providing evidence-based clinical and programmatic guidance, setting global standards, and providing technical support to Member States.

In addition, WHO advocates for more affordable and effective treatments, designs training materials and guidelines for health workers, and supports countries to implement policies and programmes and monitor progress.

During the United Nations General Assembly 2015, in New York, UN Secretary-General Ban Ki-moon launched the Global Strategy for Women's, Children's and Adolescents' Health, 2016-2030 *(7)*. The Strategy is a road map for the post-2015 agenda as described by the Sustainable Development Goals and seeks to end all preventable deaths of women, children and adolescents and create an environment in which these groups not only survive, but thrive, and see their environments, health and wellbeing transformed.

As part of the Global Strategy and goal of Ending Preventable Maternal Mortality, WHO is working with partners towards:

- **addressing inequalities in access to and quality of reproductive, maternal, and newborn health care services;**
- **ensuring universal health coverage for comprehensive reproductive, maternal, and newborn health care;**
- **addressing all causes of maternal mortality, reproductive and maternal morbidities, and related disabilities; and**
- **strengthening health systems to collect high quality data in order to respond to the needs and priorities of women and girls; and**
- **ensuring accountability in order to improve quality of care and equity.**

(1) Global, regional, and national levels and trends in maternal mortality between 1990 and 2015, with scenario-based projections to 2030: a systematic analysis by the UN Maternal Mortality Estimation Inter-Agency Group.
Alkema L, Chou D, Hogan D, Zhang S, Moller AB, Gemmill A, et al. Lancet. 2016; 387 (10017): 462-74.

(2) Maternal-perinatal morbidity and mortality associated with adolescent pregnancy in Latin America: Cross-sectional study.
Conde-Agudelo A, Belizan JM, Lammers C. American Journal of Obstetrics and Gynecology, 2004, 192:342–349.

(3) Global patterns of mortality in young people: a systematic analysis of population health data.
Patton GC, Coffey C, Sawyer SM, Viner RM, Haller DM, Bose K, Vos T, Ferguson J, Mathers CD. Lancet, 2009, 374:881–892.

(4) Global Causes of Maternal Death: A WHO Systematic Analysis.
Say L, Chou D, Gemmill A, Tunçalp Ö, Moller AB, Daniels JD, et al. Lancet Global Health. 2014;2(6): e323-e333.

(5) Levels and Trends in Child Mortality. Report 2015.
The Inter-agency Group for Child Mortality Estimation (UN IGME). UNICEF, WHO, The World Bank, United Nations Population Division. New York, USA, UNICEF, 2015.

(6) National, regional, and worldwide estimates of stillbirth rates in 2015, with trends from 2000: a systematic analysis.
Blencowe H, Cousens S, Jassir FB, Say L, Chou D, Mathers C et al. Lancet Glob Health. 2016 Feb;4(2):e98-e108. doi: 10.1016/S2214-109X(15)00275-2.

(7) Global Strategy for Women's, Children's and Adolescents' Health, 2016-2030.
New York: United Nations; 2015.

Global Health Action

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SPECIAL ISSUE: EPIDEMIOLOGICAL TRANSITIONS – BEYOND OMRAN'S THEORY

Reorienting women's health in low- and middle-income countries: the case of depression and Type 2 diabetes

Emily Mendenhall[1]* and Lesley Jo Weaver[2]

[1]Science, Technology, and International Affairs Program, School of Foreign Service, Georgetown University, Washington, DC, USA; [2]Department of Anthropology, Emory University, Atlanta, Georgia, USA

Women's health in low- and middle-income countries (LMICs) has historically focused on sexual and reproductive health. However, understanding how women acquire, experience, and treat non-reproductive health conditions, such as non-communicable diseases, has become a fundamental public health concern. Special attention to the social determinants of LMIC women's health can provide socially and culturally relevant knowledge for implementation of policies and programs for women increasingly confronting these 'New Challenge Diseases'. This article uses the example of depression and Type 2 diabetes comorbidity to illustrate how attending to the social determinants of mental and physical health beyond the reproductive years contributes to a more holistic agenda for women's health. For instance, we must address the plurality of experiences that shape women's health from social determinants of depression, such as gendered subjugation within the home and public sphere, to the structural determinants of obesity and diabetes, such as poor access to healthy foods and health care. Attending to the complexities of health and social well-being beyond the reproductive years helps the women's global health agenda capture the full spectrum of health concerns, particularly the chronic and non-communicable conditions that emerge as life expectancy increases.

Keywords: *women's health*; *depression*; *Type 2 diabetes*; *life course*; *social determinants*; *epidemiological transition*

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*Correspondence to: Emily Mendenhall, Science, Technology, and International Affairs Program, School of Foreign Service, Georgetown University, Washington, DC, USA, Email: em1061@georgetown.edu

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The contemporary landscape of women's health in low- and middle-income countries (LMICs) is more complex than public health approaches in previous decades reflected, when the focus was primarily on sexual and reproductive health. As populations age, no longer are sexual and reproductive health the dominant themes that shape how women can live longer, healthier lives. Instead, a combined perspective of the social determinants of mental and physical health across the life course comes to the forefront. Understanding how women acquire, experience, and treat non-reproductive health conditions, such as non-communicable diseases, over the course of their lives is particularly important for women living in resource-constrained settings, who are socially and economically marginalized and often experience limited access to healthcare. This article uses the example of depression and Type 2 diabetes comorbidity to illustrate how attending to the social determinants of mental and physical health beyond the reproductive years contributes to a more holistic agenda for women's health.

This shift in priorities requires that we break down the traditional distinctions between 'chronic' and 'acute', 'communicable' and 'non-communicable' diseases because in fact they often occur together. For instance, diabetes and tuberculosis not only coexist within a given population but also can coexist within a single individual. Likewise, over- and under-nutrition can exist simultaneously in communities, households, or even individuals during different phases of their lives. In light of these complex scenarios, Knaul and Frenk have suggested that we rethink public health paradigms for the challenges of aging populations as 'New Challenge Diseases' rather than 'non-communicable diseases' (1). This approach requires that we move beyond diseased-focused silos in public health. Instead, we must address the plurality of experiences that shape women's health from social determinants of depression, such as gendered subjugation within the home and public sphere, to the structural determinants of obesity and diabetes, such as poor access to healthy foods and health care. Women living in LMICs require special attention not only because their

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experiences are unique to women living in affluent nations but also because such limited research is available on their social and health problems. Bias of research from high-income nations may construe LMIC women's experiences and contribute not only to knowledge displaced from women's social experiences but also policies and programs that do not reflect the social, economic, and cultural factors surrounding women's mental and physical health problems in LMICs.

As opposed to traditional disease-based approaches in medicine and public health, a life course approach encompasses the powerful role of social and economic determinants of health in women's lives from infancy to old age (2, 3). This approach is particularly important for women who may experience disproportionate social disadvantage, gendered discrimination, and chronic, untreated depression when compared to men (4). Indeed, new global data demonstrates that women's health is overall poorer than their male counterparts around the world (5), and this is largely due to socially driven inequalities. Recognizing this is crucial for understanding and managing chronic diseases, which typically have complex etiologies rooted in long-term lifestyle choices as well as intergenerationally heritable characteristics, both genetic and behavioral. A life course perspective acknowledges, for instance, that social and economic problems related to poverty both fuel poor health and result from it, creating cycles that are difficult to break.

We present complexities of the comorbidity between Type 2 diabetes and depression to illustrate the need for a life course perspective in women's health. Type 2 diabetes, an adult-onset chronic disease, is widely known as a disease of 'modernization' that is emerging in LMICs and shifting from affluent to lower income groups all over the world (6, 7). Biologists and epidemiologists identify depression as both a cause and consequence of diabetes (8, 9), while medical social scientists have elucidated some of the complex socioeconomic and psychophysiological pathways linking the two chronic conditions (10). Despite increasing diabetes prevalence in LMICs, the research on social experiences of those living with diabetes, depression, and their comorbidity is limited. The few existing qualitative studies suggest that experiences differ between men and women (11) as well as between income groups (12).

Social and economic determinants of women's health are fundamental in the relationship of depression and diabetes, particularly among people of lower socioeconomic status (6, 13). As underscored in the 2010 Global Burden of Disease studies, experiences of social problems such as various forms of interpersonal abuse, and psychological problems such as depression and anxiety, have escalated either by detection or actual incidence among women on a global scale (5). Stress throughout the life course rooted in childhood trauma, abuse, or the chronicity of poverty may be key risk factors for depression and/or poor eating and activity patterns that lead to obesity and its complications, such as Type 2 diabetes (10). Complicating matters is the dual burden associated with living in poverty in rapidly modernizing cities that make unhealthy foods accessible and affordable, fueling obesity epidemics in LMIC settings (7). These inequalities create a negative feedback loop, whereby social and economic problems increase the likelihood of developing depression, diabetes, and their overlap, and these illnesses together promote the development of diabetes-related complications such as loss of limbs or eyesight and subsequent physical disability, further compounding socioeconomic inequalities (10). Finally, because of stigma and limited mental healthcare services in LMICs (14), women experiencing this comorbidity are more likely to seek care for diabetes than for depression, leaving half of the comorbidity unaddressed (11).

In India, home to the second largest population of people with Type 2 diabetes in the world (13), recent epidemiological and qualitative data suggest that the illness is becoming more prevalent among the middle classes and working poor (15). In tandem, mental healthcare is limited (16). Despite active research and policies aimed at addressing chronic and mental health diseases in India (17), there remains a large gap in knowledge about how these conditions afflict various Indian communities in their everyday lives, especially poor women. Qualitative research on depression and diabetes in India indicates that lower income people experience higher rates of social stress and depression, and poorer access to health care (12). Such research also underscores the powerful role that gendered social roles play in shaping women's mental health and diabetes outcomes (18). For example, gendered behavioral norms orient Indian women strongly toward the care of others, and therefore away from the self-care activities that are usually integral to diabetes management (11). Maintaining these other-care-oriented roles appears to be good for diabetic women's mental, but not physical, health.

The recognition of social forces as part of diabetes and depression etiology in India and other LMICs presents new challenges for public health because it underscores that medicating these complex illnesses does not fully address them. Finding a better public health solution to comorbidities like Type 2 diabetes and depression will likely only occur when we understand the limitations, and harness the power of, cultural beliefs and social conditions to shape behaviors that affect chronic diseases: how people eat, move, and medicate; how economic conditions may function as a barrier to treatment; and how depression may complicate a chronic disease, both socially and physically (7).

The comorbidity between depression and diabetes among women in LMICs is but one example of the ways in which women's non-reproductive health concerns deserve more prominence in global health. It also presents a strong

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case for increased attention to social and psychological determinants of women's health over the life course. The present lack of such perspectives in women's global health may result from limited funding for non-reproductive issues, lack of interest, or may simply be another manifestation of the great information gap between high-income countries and LMICs. Regardless, it should be a priority of future research, programming, and policy.

Focusing on health, not disease

Why should diabetes and depression comorbidity be on the women's health agenda? Depression has only become a major global health concern in the past decade, and has proven very difficult to address, not least because of stigma and limited human resources for mental healthcare. This is especially true for women in LMICs, whose access to mental healthcare may be virtually non-existent, and whose care-seeking behaviors and budgets typically include little, if any, room for mental healthcare. Moreover, most LMICs' health systems are poorly equipped to meet the complex prevention and management challenges associated with chronic conditions like diabetes and mental illnesses because, until very recently, infectious diseases were the dominant population health concerns.

The Movement for Global Mental Health's often-cited slogan, that there is 'no health without mental health' (14), emphasizes the need for integrated mental and physical healthcare systems to combat the next generation of public health problems. This would require an ideological and organizational shift in biomedicine, which has until recently viewed physical and mental health as separate categories of pathology requiring separate treatments, but would likely open up new avenues for cost-effective treatment. The WHO mental health Gap Action Program (mhGAP), for instance, suggests steps by which mental illness diagnosis and treatment can be integrated into primary care settings, and many initiatives are working to actualize this goal in LMICs (e.g. PRIME: http://www.prime.uct.ac.za/). With relatively little additional investment, basic mental healthcare could also be integrated into existing diabetes care guidelines. Such an approach is particularly important for women who face a higher burden of social problems and mental illness, which influence diabetes self-care and health outcomes. Yet, until a more integrative approach is adopted within clinics and public health agendas, healthcare silos will dominate global health dialogues, funding structures, and disease-focused (as opposed to *health*-focused) campaigns.

As the co-occurrence of mental and physical health problems gains recognition in the public health agenda, a more nuanced understanding of sociocultural influences on women's lifetime health is crucial. This is particularly important in LMIC settings where women face not only great social disadvantage but also an increasing burden of mental and physical health problems. A life course perspective requires acknowledging that women's mental and physical health are closely linked with cultural beliefs, social experiences (both past and present), and economic conditions over time. It also recognizes that women's health status shapes their social and economic conditions, for better or worse. Strategic points of intervention can improve women's social and emotional well-being across decades, which could then empower them to identify and care for their own health problems more effectively. In this way, integrating a social and psychological approach into health agendas, from the clinical to the policy level, can make a big impact.

Main findings

- Moving beyond disease-focused silos in public health requires that we attend to the plurality of experiences that shape women's health from social determinants of depression, such as gendered subjugation within the home and public sphere, to the structural determinants of obesity and diabetes, such as poor access to health foods and health care.
- Complexities demonstrated by the comorbidity of depression and type 2 diabetes illustrate the need for a life course perspective in women's health; social and economic factors serve as both causes and consequences of these co-conditions.
- The recognition of social forces as part of diabetes and depression aetiology in low- and middle-income countries presents new challenges for public health because it underscores that medicating these complex illnesses does not fully address them; this requires that we understand the limitations, and harness the power of, cultural beliefs and social conditions to shape behaviors that affect chronic diseases.

Key messages for action

- Integrating a social and psychological approach into health agendas, from the clinical to the policy level, can make a big impact.
- Strategic points of intervention can improve women's social and emotional well being across the life course, which could then empower them to identify and care for their own health problems more effectively.
- With relatively little additional investment, basic mental healthcare (as illustrated in the WHO mental health Gap Action Program (mhGAP)) can be integrated into existing diabetes care guidelines; such an approach is particularly important for women who face a higher burden of social problems and mental illness, which influence diabetes self-care and health outcomes.

Conflict of interest and funding

No conflict of interests declared.

References

1. Knaul FM, Frenk J. Strengthening health systems to address New Challenge Diseases (NCDs). HSPH News. Fall 2011.
2. Lynch J, Smith G. A life course approach to chronic disease epidemiology. Annu Rev Public Health 2005; 26: 1–35.
3. Worthman C, Kohrt B. Receding horizons of health: biocultural approaches to public health paradoxes. Soc Sci Med 2005; 61: 861–78.
4. Patel V, Kleinman A. Poverty and common mental disorders in developing countries. Bull World Health Organ 2003; 81: 609e–15.
5. Murray CJL, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012; 380: 2197–223.
6. Leone T, Coast E, Narayanan S, Aikins A. Diabetes and depression comorbidity and socioeconomic status in low and middle income countries (LMICs): a mapping of the evidence. Global Health 2012; 8: 39–49.
7. Popkin BM, Adair LS, Ng SW. Global nutrition transition and the pandemic of obesity in developing countries. Nutr Rev 2012; 70: 3–21.
8. Golden S, Lazo M, Carnethon M, Bertoni A, Schreiner P, Roux A, et al. Examining a bidirectional association between depressive symptoms and diabetes. JAMA 2008; 299: 2751–9.
9. Musselman D, Betan E, Larsen H, Phillips L. Relationship of depression to diabetes types 1 and 2: epidemiology, biology, and treatment. Biol Psychiatry 2003; 54: 317–29.
10. Mendenhall E. Syndemic suffering: social distress, depression, and diabetes among Mexican immigrant women. Walnut Creek, CA: Left Coast Press; 2012.
11. Weaver LJ. When family comes first: diabetes, social roles, and coping among women in North India. Atlanta, GA: Emory University; 2013.
12. Mendenhall E, Shivashankar R, Tandon N, Ali MK, Narayan KMV, Prabhakaran D. Stress and diabetes in socioeconomic context: a qualitative study of urban Indians. Soc Sci Med 2012; 75: 2522–9.
13. International Diabetes Federation. IDF diabetes atlas. Brussels, Belgium: IDF; 2011.
14. Prince M, Patel V, Saxena S, Maj M, Maselko J, Phillips MR, et al. No health without mental health. Lancet 2007; 370: 859–77.
15. Deepa M, Anjana R, Manjula D, Narayan K, Mohan V. Convergence of prevalence rates of diabetes and cardiometabolic risk factors in middle and low income groups in urban India: 10-year follow-up of the Chennai Urban Population Study. J Diabetes Sci Technol 2011; 5: 918–27.
16. Patel V. The future of psychiatry in low- and middle-income countries. Psychol Med 2009; 39: 1759–62.
17. Patel V, Chatterji S, Chisholm D, Ebrahim S, Golapakrishna G, Mathers C, et al. Chronic diseases and injuries in India. Lancet 2011; 377: 413–28.
18. Weaver LJ, Hadley C. Social pathways in the comorbidity between Type 2 diabetes and mental health: concerns in a pilot study of urban middle- and upper-class Indian women. Ethos 2011; 39: 211–25.

Contact: globalhealthTA@med.cornell.edu
Website: https://international.weill.cornell.edu/
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Speaker: Grace Sun, M.D.
Date: February 22, 2021
Time: 1:00pm - 2:00pm
Title: Global Blindness

Zoom info: https://weillcornell.zoom.us/j/95082030968 **Meeting ID**: 950 8203 0968 **Passcode**: 586713

Summary: Focus on identify the leading causes of global blindness, potential treatments and interventions to ameliorate the burden of global blindness and skills to perform a basic eye exam in under-resourced communities'

Suggested Readings:

Tanzania Fact Sheet

Global Data on Visual Impairments, World Health Organization

Woodward, R., Mgaya, E., Mwanansao, C., Peck, R.N., Wu, A. and Sun, G. (2020), Retinopathy in adults with hypertension and diabetes mellitus in Western Tanzania: a cross-sectional study. Trop Med Int Health, 25: 1214-1225. https://doi.org/10.1111/tmi.13463

Case Study:

Weill Cornell Ophthalmology's efforts in Tanzania

Tanzania Fact Sheet

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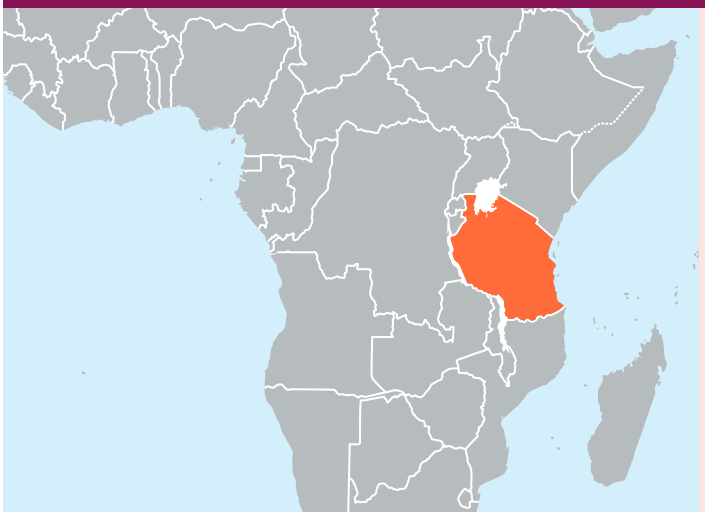
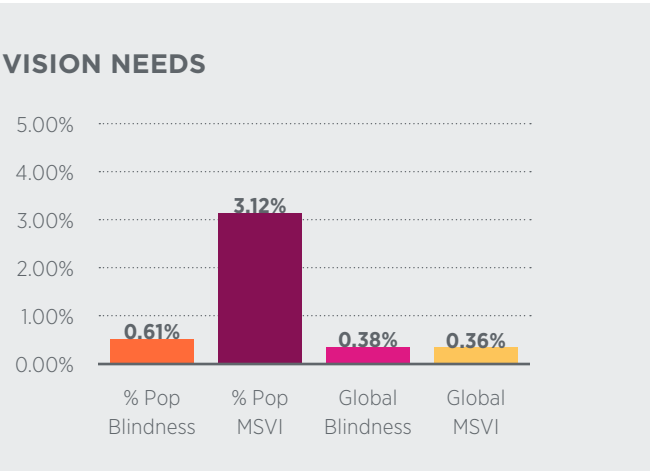


Country Overview

- Located in Eastern Sub-Saharan Africa
- The Republic of Tanzania spans 945,087 square kilometers (364,900 square miles)
- Population: 53.47 million people
- 2016 Human Development Index Ranking: 165 of 188 countries[1]

Scope of Eye Care Needs[2]

- 0.61% of Tanzania's population is blind (136K), as compared to 0.15% in the United States
- 3.12% of the population has moderate to severe vision impairment or MSVI (779k), as compared to 1.25% in the United States
- 0.38% (136,523/36M) of global blindness
- 0.36% (779,643/217M) of global MSVI



Nationwide Eye Care Response

Sub-Saharan Africa's median Cataract Surgical Rate (CSR) is 488 – one third of the global average and 1/13th of the average for high-income countries. Seva works to improve these rates through our hospital management systems and training support in Tanzania, focusing on improvement in the following Global Action Plan indicators for universal eye health.

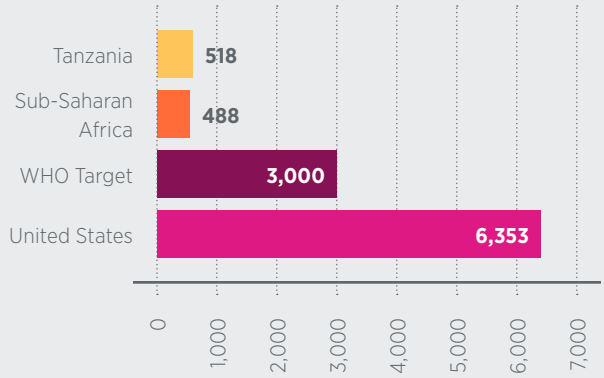
- Tanzania's CSR was 518 surgeries per million in 2010, as compared to the US CSR of 6,353
- 0.8 ophthalmologists per million people in Tanzania (40/50.64M as of 2013 (US = 60 per million people)
- 5.7 optometrists per million people as of 2012 (280)
- 8.8 AOPs per million people (405 in 2011)

1 2016 UNDP Human Development Report: http://hdr.undp.org/en/2016-report

2 Unless otherwise noted, all statistics provided by IAPD Vision Atlas Global Vision Database.

TANZANIA FACT SHEET

CATARACT SURGICAL RATE PER MILLION PEOPLE



SIGHT SERVICES

0.8
Ophthalmologists per million people

5.7
Optometrists per million people

8.8
Ophthalmic personnel per million people

= 1 million people

Seva's Approach in Tanzania

Seva partners with the Kilimanjaro Centre for Community Ophthalmology (KCCO) to reduce blindness in Tanzania. Established in 2001 in response to the VISION 2020 initiative, KCCO is the largest organization in Africa dedicated to reducing blindness through community ophthalmology training. With Seva's support in hospital management systems and training, KCCO partners with local governmental hospitals to train community health workers, conduct outreach trips to rural communities without regular access to eye care, provide clinical training for ophthalmologists and cataract surgeons, and providing funds for medical treatments for those who cannot afford them. In Tanzania, Seva's Global Sight Initiative supports three regional hospitals to bring quality eye care to as many people as possible: Benjamin Mkapa Hospital, Dodoma; Bugando Regional Hospital, Mwanza; and Singida Regional Hospital.

Since partnership began in 2011, Seva has supported three clinics. In 2017 alone, over 10,000 patients were seen and 1,382 surgeries conducted.

Resources:

Seva in Tanzania

Program Videos

KCCO Website

IMPACT (FY17-18)

3	401
Clinics	Surgeries

SPOTLIGHT ON BUILDING CAPACITY

Tanzania's central Singida region is served by only one ophthalmologist for over 1.3 million people. Dr. Ng'hungu Kuzenza works tirelessly to treat eye injuries, remove cataracts, and save the eyesight of people in need. With Seva's support in achieving sustainable management systems, Dr. Kuzenza was able to increase his office hours from four to 12 months per year. Seva helped him to increase the number of surgeries from 563 in 2015 to 940 surgeries in 2016, bringing vision and hope to 67% more patients. With Seva's support, Dr. Kuzenza and KCCO are also developing a robust outreach program to allow patients who cannot afford the journey to the hospital to access eye screenings and other treatments.

WHO/NMH/PBD/12.01

GLOBAL DATA ON VISUAL IMPAIRMENTS 2010

World Health Organization

Correspondence to: Silvio P. Mariotti, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland.

FOREWORD

Estimating the global magnitude of blindness and visual impairments is part of the core functions of WHO and since 1995 the Prevention of Blindness team has been issuing regular updates of the estimates.

The estimates, which are provided for the 6 WHO regions offer a tool to monitor the global trend of avoidable blindness and to identify any significant changes in the distribution in the six regions and in the attributed causes .

From the prevalence and the causes of the impairment the need of assessments, the interventions or norms can be defined; plans of action can be developed or monitored.

The data indicate that visual impairment and blindness are lower than in past estimates , with different distribution in WHO regions, and with significant changes in the causes.

INTRODUCTION

In order to set policies and priorities and to evaluate global eye health, it is essential to have up to date information on prevalence and on causes of visual impairment. As it previously did in 1995, 2002 and 2004 (1-3) the WHO Prevention of Blindness and Deafness Programme has carried out a systematic search and review of all available data to obtain a global estimate of visual impairment for 2010. Estimates of visual impairment have been derived at global level and in the six WHO Regions. The major causes of visual impairment and of blindness have been determined. These estimates provide essential information for the prevention of visual impairment and the improvement of eye health globally.

METHODS

Definitions

The definitions of visual impairment used for the estimates in this study follow the categories of the International Classification of Diseases Update and Revision 2006 that defines impairment according to presenting vision (http://www.who.int/classifications/icd/2006updates.pdf).

Visual impairment comprises categories 1 to 5, blindness, categories 3 to 5. The two categories of moderate and severe visual impairment (<6/18 $\geq$ 6/60 and <6/60 $\geq$3/60) are combined in this study (<6/18 $\geq$ 3/60) and they are referred to as "low vision".

Population estimates and WHO Regions

Population size and structure are based on the current population tabulation of WHO according to *World Population Prospects: the 2008 Revision,* from the United Nations Population Division (4).

The estimates are reported for the 6 WHO regions (http://www.who.int/about/regions/en/index.html).

Socio-economic data

Sources of the indicators used are the Human Development Report 2009 from the United Nations Development Programme (5), the World Bank Development Indicators 2009 (6), the Organization for Economic Co-operation and Development Policy Briefs 2009 (7), data from the United Nations Economic and Social Commission for Asia and the Pacific (8), the World Health Statistics 2009 (9) and governmental statistical data.

Sources of epidemiological data and inclusion criteria

Inclusion criteria have been discussed previously (2,3,10): the studies have to be population based, representative of the country and of the area sampled, with sample size adequate to the population sampled (from 1200 to 46000), sufficient response rate (80% or higher), reporting data for persons, with definitions of visual impairment in agreement with the ones for this study.

Medline was searched for published data with no language restriction (search terms: Visual Impairment, Blindness, Prevalence, country and continent names; last search on June 30th, 2010); studies were searched in the WHO regional databases (www.who.int/library/databases/en); unpublished data available to WHO/PBD were also used if satisfying the inclusion criteria.

Estimates of prevalence

The prevalence of visual impairment and blindness were determined for the 6 WHO regions for three age groups: 0 to 14 years, 15 to 49 years and 50 years and older, non disaggregated by gender. These age groups are consistent with the available data sources and with the grouping used in WHO for similar estimates of prevalence. Smaller age groups were not considered since data given in the studies are adjusted by sample composition only for larger age groups and smaller age groups would have much higher uncertainties. Gender stratification was not attempted given the inconsistencies of the data within Regions and countries, the uncertainties in the gender stratification could lead to even higher uncertainties at global level.

Estimates of prevalence for the age group 0 to14 and 15 to 49 years were calculated applying to the actual population size and structure the prevalence from the most recent estimates by WHO (2,3) that were considered still valid. The regional prevalence was obtained from population based studies from countries with data and imputed estimates for countries missing data. The imputation process was based on a model that utilized three parameters, GDP per capita in 2007 measured in Purchasing Power Parity (PPP) (6) , World Bank classifi-

Correspondence to: Silvio P. Mariotti, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland.

cation of Economies (Low Income, Lower Middle Income, Upper Middle Income, High Income) (6) and prevalence of blindness in the age group 50 years and older, chosen because of the many studies available, a consequence of the prevailing use of rapid assessment survey protocols focused on this age group. Since prevalence of blindness and visual impairment were strongly correlated with each other, only prevalence of blindness was selected as the parameter. The correlation between PPP and prevalence of blindness was consistently strong in all regions, with coefficients >0.8, other socio-economic (5,7,8) or health indicators (9) were tested and showed only weak correlations (0.5 or less). In each WHO region the countries were clustered into ranges of PPP and World Bank Classification of Economies (6). A weighted prevalence of visual impairment and blindness was calculated for countries with data within a PPP cluster and imputed to the other countries in the same cluster. A discussion of methods for missing data can be found in reference 11.

Estimates of causes of visual impairment

For the age groups 0 to 14 and 15 to 49 years the causes of visual impairment are based on previous estimates (2,3) For the age group 50 years and older the causes were calculated using the causal attribution provided by the studies that were used to estimated the prevalence. Each cause was calculated as an average percentage of the total causes at regional level first and then at global level, by including all the regional values.

Error analysis

Since only simple imputation using deductive methods was used and no regression analysis was conducted, the known errors on the regional estimates come from the reported uncertainties of the studies, which for the age group 50 years and older are around 10%, for the other ages around 20%.

Additional uncertainties are due to data imputation: these can be assumed to be lower in regions with more numerous studies.

RESULTS

Data sources

53 surveys from the 39 countries, listed in Table 1, met the inclusion criteria for this study: details are found in Annex 1 and 2. The majority of the studies, 38, took place between 2005 and 2008, 15 between 2001 and 2004;. the largest majority were rapid assessments of cataract surgical services or of avoidable blindness (12, 13), a minority were national studies for all ages, some were targeting specific age groups or settings.

Other studies not satisfying fully the inclusion criteria provided supporting evidence for the estimates developed by the model.

WHO Region	Countries with studies
African Region	Botswana, Cameroon, Eritrea, Ethiopia, Gambia, Ghana, Kenya, Mali, Nigeria, Rwanda, Uganda, United Republic Of Tanzania
Region of the Americas	Argentina, Brasil, Chile, Cuba, Dominican Republic, Guatemala, Mexico, Paraguay, Peru, Venezuela
Eastern Mediterranean Region	Islamic Republic of Iran, Oman, Pakistan, Qatar
European Region	Russian Federation, Turkmenistan
South-East Asian Region	Bangladesh, Democratic Republic of Timor-Leste, India, Indonesia, Myanmar, Nepal
Western Pacific Region	Cambodia, China, Papua New Guinea, Philippines, Viet Nam

Model of visual impairment in the six WHO Regions

Visual impairment was estimated in each WHO Region with a model built using prevalence of blindness and countries' economic status from available data as described in Methods.

The African Region comprises 46 countries of which 40 are classified by the World Bank either as Low Income (LI) or Lower Middle Income (LMI) within a narrow range of PPP, representing 93.2 % of the population in the Region. Five countries are classified as Upper Middle Income (UMI) and one as High Income (HI) representing 6.8 % of the region population. 19 surveys from 12 countries, all classified as LI or LMI, were available for inclusion in the model for the region. Given the similar economic status of these countries they were considered as a single cluster of PPP. The weighted prevalence of visual impairment and blindness from the 19 surveys was imputed to the whole Region.

In the Region of the Americas the 36 countries were divided into three clusters of PPP corresponding to the World Bank classifications: LMI (10 countries), UMI (20 countries) , HI (6 countries). Data were available from three countries in the LMI cluster, and seven in the UMI cluster. The combined population in the 10 countries with available data in the LMI and UMI clusters represented 80% of the total population in these 30 countries. The weighted average of the prevalence of visual impairment and blindness was derived separately in the two clusters and imputed to the other countries in the

Correspondence to: Silvio P. Mariotti, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland.

same cluster. Recent data satisfying the inclusion criteria for this study for the HI cluster were not available: prevalence was derived from previous WHO estimates (2,3).

The 21 countries in the Eastern Mediterranean Region were sorted into two clusters of PPP. The first included 13 countries classified as LI and LMI, the second 8 countries classified as UMI and HI. Data from three countries in the LI/LMI cluster and from one in the UMI/ HI cluster were available for estimates.

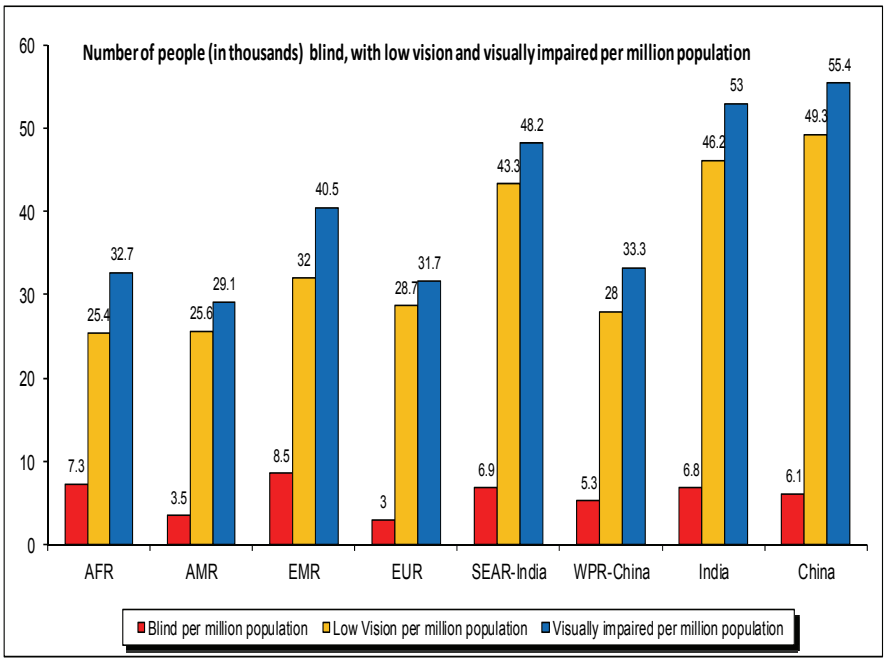
In the European Region three economic clusters were defined, one including 25 HI countries, a second, 11 UMI countries and the third, 14 LMI and 3 LI countries. Data were available from one country each in the UMI and in the LMI /LI clusters. The data from a single country were imputed to the UMI cluster and analogously data from a single country to the LMI/ LI cluster. Recent data for this study were not available for the HI cluster and previous WHO estimates were used (2,3).

The estimates for the South-East Asian Region were derived for India and for the other countries in the Region separately. The prevalence for India was derived from 3 recent surveys (see Annex 1 and 2). The other 10 countries in the Region are classified either as LMI or LI and given the similarity of PPP were all included in one single cluster. Data were available from 5 of the 10 countries comprising almost 80% of the population in the region (India excluded). The weighted prevalence estimated from the data in the five countries was imputed to the whole cluster.

The estimates for China were derived separately from the other countries in the Western Pacific Region and were based on recent surveys conducted in the rural areas combined with data from urban settings (see Annex 1 and 2). The other countries in the Region were sorted into 3 clusters: the first included 7 countries classified as HI and one as UMI ; the second included all 15 Pacific Islands with 14 countries classified as LMI and one UMI ; the third comprised 4 countries, 2 classified as LI and 2 as LMI. For the first cluster prevalence was derived from the previous estimates (2,3). Data from one country were used for the second cluster and data from 3 countries for the third cluster (see Annex 1 and 2).

Global Prevalence of Visual Impairment

The estimated number of people visually impaired in the world is 285 million, 39 million blind and 246 million having low vision; 65 % of people visually impaired and 82% of all blind are 50 years and older (Table 2). The distribution of people visually impaired in the six WHO Regions is shown in Table 3 with the percentage of the global impairment shown in parentheses. Figure 1 shows the number of people visually impaired, with low vision and blind per million population in the six WHO Regions and in India and China separately.



Cause of visual impairment

Globally the principal causes of visual impairment are uncorrected refractive errors and cataracts, 43% and 33 % respectively. Other causes are glaucoma, 2%, age related macular degeneration (AMD), diabetic retinopathy, trachoma and corneal opacities, all about 1%. A large proportion of causes, 18%, are undetermined, (Figure 2A).

The causes of blindness are cataract, 51%, glaucoma, 8%, AMD, 5%, childhood blindness and corneal opacities, 4%, uncorrected refractive errors and trachoma, 3%, and diabetic retinopathy 1%, the undetermined causes are 21% (Figure 2 B).

DISCUSSION

This study presents some limitations, the most significant are the following: the surveys in the last 10 years have been mostly Rapid Assessments for ages 50 years and older, and national studies for all ages with or without WHO Eye Survey Protocol have been few. As a consequence data could be limited in representation of countries and of ages. The imputation of prevalence for missing data can give errors that are difficult to estimate: clearly they could be high in regions with sparse data. In the Eastern-Mediterranean Region recent data were unavailable for most of the countries, hence the estimates were in large extent based on surveys from 1993-1998 (2,3) Data from HI countries were also missing or were dated as far back as 15 years. However it must be noted that in HI countries from available information there was no evidence of major changes in prevalence.

The combined effect of these uncertainties is possibly an over or under estimation of visual impairment and blindness of approximately 20%.

The attribution of the causes of visual impairment and blindness is also prone to uncertainty. This is often the instance in surveys carried out in the field with limited diagnostic capacity, but it is particularly true in the case of

Correspondence to: Silvio P. Mariotti, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland.

rapid assessments whose aim is primarily to survey cataract surgical services for ages 40 or 50 years and older. The large percentages of undetermined causes is are also likely to be a reflection of these protocols.

The strengths of the estimates derive firstly from the fact that new data were available to replace previous extrapolations. Furthermore, to estimate the prevalence of visual impairment in countries missing data, a model was used based on the same economic parameters for all countries. This is a new approach in producing estimates of visual impairment. The imputation process via a model is more transparent than using expert assumptions and it provides consistency between countries and regions. It also allows for adjustments and corrections as soon as new information becomes available and it could also be adapted for estimating trends.

Because data available and methods used have changed, it is not possible to draw conclusions from differences in present estimates and previously published estimates. In areas where surveys were repeated with similar protocols for ages 50 years and older a reduction of visual impairment is shown despite the rapid growth of this age group. This decline fits with increased socio-economic development, but it is also the direct consequence of investments made by Governments and of interventions by international partners.

Posterior segment (retinal) diseases are a major cause of visual impairment worldwide, and likely to become more and more important, with the rapid growth of the aging population . The proportion of the total visual impairment and blindness from age related macular degeneration, glaucoma and diabetic retinopathy is currently greater than from infective causes such as trachoma and corneal opacities.

This requires the urgent development of eye care systems that address chronic eye diseases with rehabilitation, education and support services.

CONCLUSION

Monitoring the magnitude of visual impairment is essential for policies aiming at the prevention and elimination of the avoidable causes. The global estimates have significant uncertainties that could be reduced with population based studies from regions with limited or old data and with studies conducted at national level for all ages recording all causes of blindness. Particularly urgent is to determine the extent of posterior segment diseases as causes of visual impairment, since these require the development of eye care systems, including human resources and infrastructures.

REFERENCES

1- Thylefors B, Négrel A-D, Pararajasegaram R, et al. Global data on blindness. Bull World Health Organ 1995;**73**:115-121.

2- Resnikoff S, Pascolini D, Etya'ale D, et al. Global data on visual impairment in the year 2002. Bull World Health Organ 2004;**82**:844-851.

3- Resnikoff S, Pascolini D, Mariotti SP, et al. Global magnitude of visual impairment caused by uncorrected refraction errors in 2004. Bull World Health Organ 2008;**86**:63:70.

4- United Nations, Department of Economic and Social Affairs, Population Division, World population Prospects: the 2008 Revision. New York 2009 (advance Excel tables).

5-United Nations Development Programme. Human Development Report 2009. http://hdr.undp.org/hdr2009. date accessed March 1st, 2010.

6-World Bank. World Bank list of economies (July 2009) http://siteresources.worldbank.org/DATASTATISTICS/Resources/ClASS.xls. date accessed March 15, 2010.

7-Organisation for Economic Co-operation and Development. Policy Briefs available at http://www.oecd.org/publications/Policybriefs. date accessed May 1, 2010.

8- United Nations Economic and Social Commission for Asian and the Pacific. Social Policy and Population Division. http://www.unescap.org/estd/psis/population. date accessed May 15, 2010.

9- World Health Organization. World Health Statistics 2009. Geneva: WHO 2009.

10- Pascolini D, Mariotti SP, Pokharel GP, et al. 2002 Global update of available data on visual impairment: a compilation of population-based prevalence studies. Ophthalmic Epidemiol 2004;**11**:67-115.

11- International Labour Organization Employment Trends Units. Trends Econometric Models: A review of Methodology. 2009 ILO working paper. Geneva.

12- Limburg H, Kumar R, Indrayan A, et al. Rapid assessment of prevalence of cataract blindness at district level. Int J Epidemiol 1997;**26**:0149-54.

13 - Dineen B, Foster A, Faal H. A proposed rapid methodology to assess the prevalence of causes of blindness and visual impairment. Ophthalmic Epidemiol 2006;**13**:31-4.

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Correspondence to: Silvio P. Mariotti, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland.

Table 2. **Global estimate of the number of people visually impaired by age, 2010; for all ages in parenthesis the corresponding prevalence (%).**

Ages (in years)	Population (millions)	Blind (millions)	Low Vision (millions)	Visually Impaired (millions)
0-14	1,848.50	1.421	17.518	18.939
15-49	3548.2	5.784	74.463	80.248
50 and older	1,340.80	32.16	154.043	186.203
all ages	6,737.50	39.365 (0.58)	246.024 (3.65)	285.389 (4.24)

Table 3. **Number of people visually impaired and corresponding percentage of the global impairment by WHO Region and country, 2010**

		Blindness	Low vision	Visual Impairment
WHO Region	Total population (millions)	No. in millions (percentage)	No. in millions (percentage)	No. in millions (percentage)
Afr	804.9 (11.9)	5.888 (15)	20.407 (8.3)	26.295 (9.2)
Amr	915.4 (13.6)	3.211(8)	23.401 (9.5)	26.612 (9.3)
Emr	580.2 (8.6)	4.918 (12.5)	18.581 (7.6)	23.499 (8.2)
Eur	889.2 (13.2)	2.713 (7)	25.502 (10.4)	28.215 (9.9)
Sear (India excluded)	579.1 (8.6)	3.974 (10.1)	23.938 (9.7)	27.913 (9.8)
Wpr (China excluded)	442.3 (6.6)	2.338 (6)	12.386 (5)	14.724 (5.2)
India	1181.4 (17.5)	8.075 (20.5)	54.544 (22.2)	62.619 (21.9)
China	1344.9 (20)	8.248 (20.9)	67.264 (27.3)	75.512 (26.5)
World	6737.5 (100)	39.365 (100)	246.024 (100)	285.389 (100)

Correspondence to: Silvio P. Mariotti, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland.

Fig. 2A

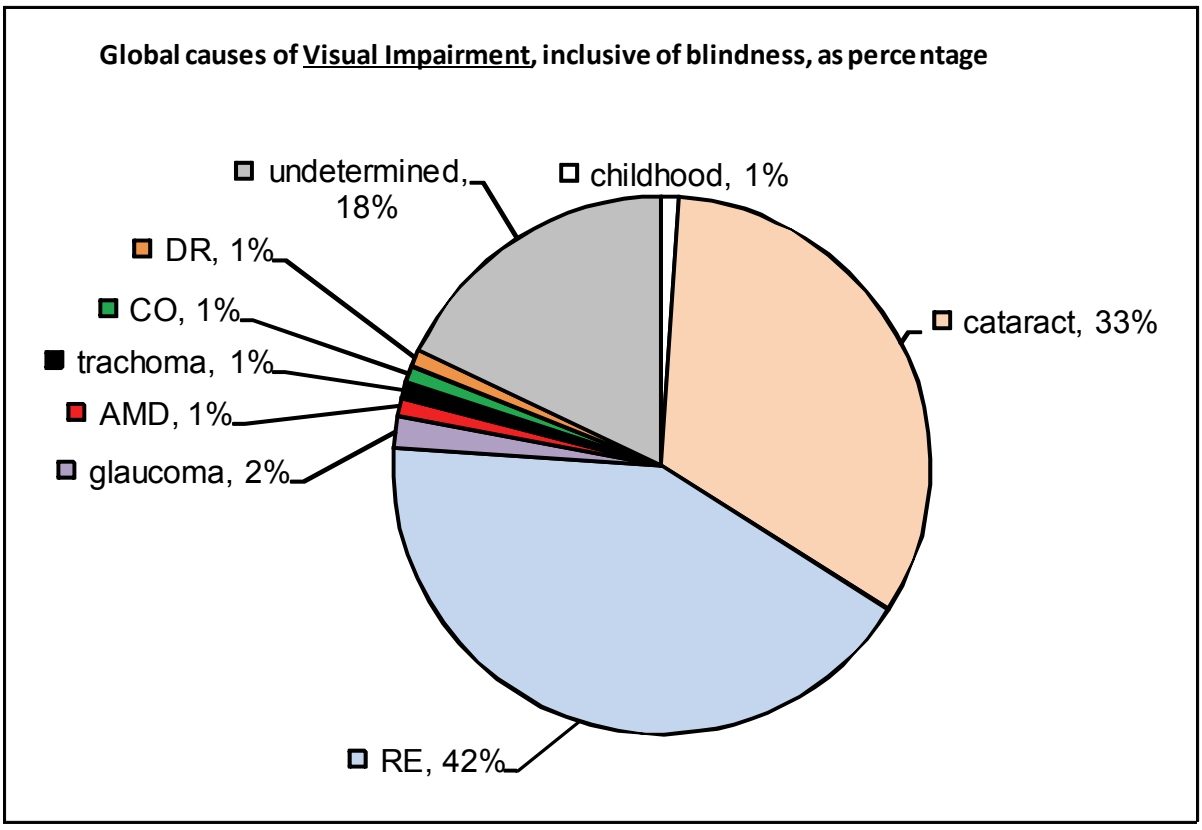
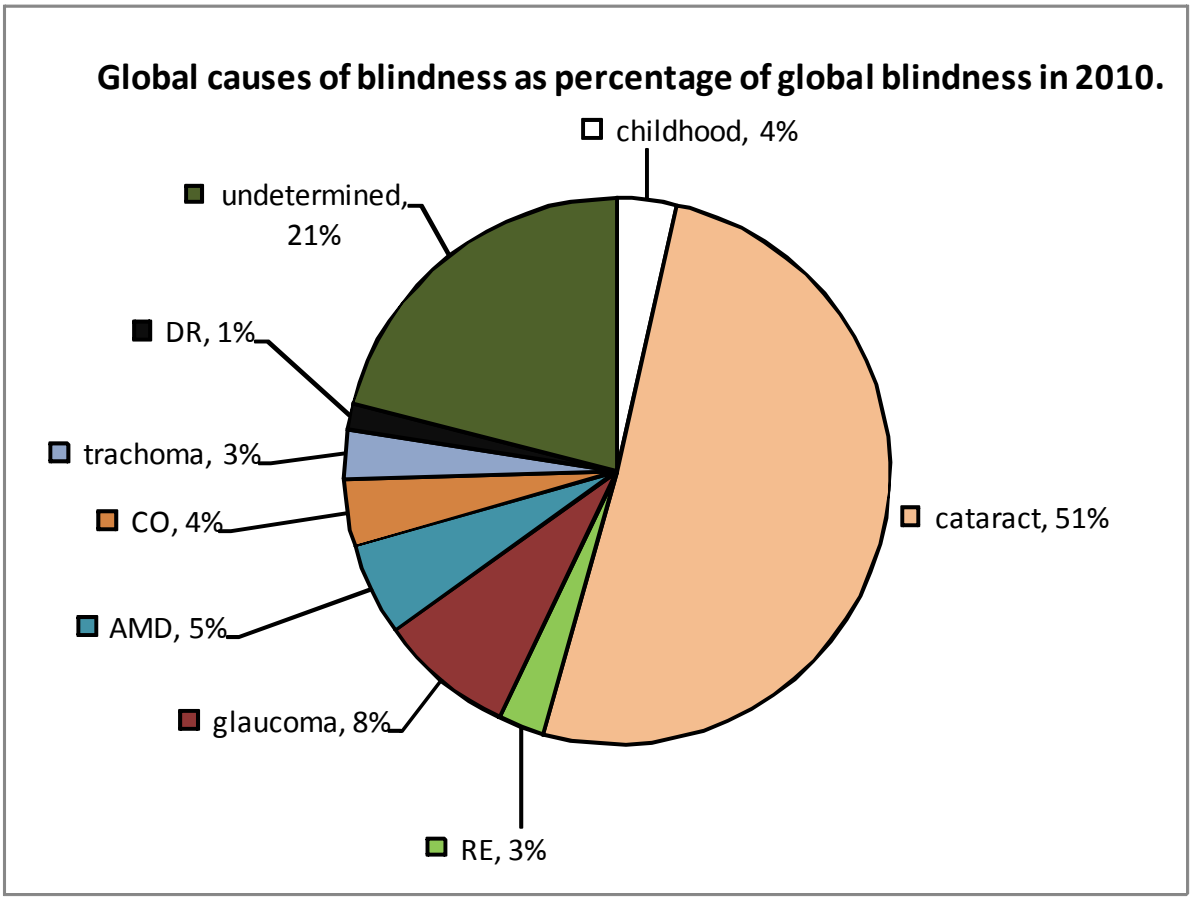


Fig. 2B



Correspondence to: Silvio P. Mariotti, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland.

Annex 1

WHO African Region	date of survey	study population	sample size	age group	reference
Botswana	2006	*national urban/rural and rural*	2127	50 years and older	BWA 1
Cameroon	2006	*subnational urban*	2215	40 years and older	CMR 1
Cameroon	2004	*subnational rural urban*	1787	40 years and older	CMR 2
Eritrea	2008	*national urban and rural*	3163	50 years and older	ERI 1
Ethiopia	2005	*national urban and rural*	25650	all ages	ETH 1
Gambia	2007	*national*	2992	50 years and older	GMB 1
Ghana	2001	*subnational*	2289	40 years and older	GHA 1
Ghana	2005	*subnational rural*	9117	40 years and older	GHA 2
Kenya	2005	*subnational rural*	3475	50 years and older	KEN 1
Kenya	2007	*subnational rural*	3376	50 years and older	KEN 2
Kenya	2007	*subnational urban*	2419	50 years and older	KEN 3
Mali	2008	*subnational*	2438	50 years and older	MLI 1
Nigeria	2008	*national urban and rural*	13593	10 to 15 years 40 years and older	NGA 1
Nigeria	2006	*subnational urban and rural*	2424	50 years and older	NGA 2
Rwanda	2006	*subnational rural*	2006	50 years and older	RWA 1
Uganda	2007	*subnational*	3294	50 years and older	UGA 1
UR Tanzania	2007	*subnational rural*	3202	50 years and older	TZA 1
UR Tanzania	2007	*subnational rural*	3463	50 years and older	TZA 2
UR Tanzania	2007	*subnational urban and rural*	3160	50 years and older	TZA 3

Correspondence to: Silvio P. Mariotti, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland.

WHO Region of the Americas	date of survey	study population	sample size	age group	reference
Argentina	2004	*subnational peri-urban*	4302	50 years and older	ARG 1
Brazil	2004	*subnational urban*	2224	50 years and older	BRA 1
Chile	2006	*subnational urban and rural*	2915	50 years and older	CHL 1
Cuba	2005	*subnational peri-urban*	2716	50 years and older	CUB 1
Dominican Republic	2008	*national urban and rural*	3873	50 years and older	DOM 1
Guatemala	2004	*subnational urban and rural*	4806	50 years and older	GTM 1
Mexico	2006	*subnational rural*	3764	50 years and older	MEX 1
Paraguay	2002	*national urban and rural*	2136	50 years and older	PRY 1
Peru	2002	*subnational rural*	4782	50 years and older	PER 1
Venezuela	2005	*national urban and rural*	3317	50 years and older	VEN 1
WHO Eastern Mediterranean Region	date of survey	*study population*	sample size	age group	reference
Iran (Islamic Republic of)	2005	*subnational urban and rural*	5456	10 years and older	IRN 1
Oman	2005	*national urban and rural*	2339	40 year and older	OMN 1
Pakistan	2004	*national urban and rural*	16507	30 years and older	PAK 1
Qatar	2008	*urban peri-urban*	2433	50 years and older	QAT 1
WHO European Region	date of survey	*study population*	sample size	age group	reference
Russian Federation	2008	*subnational peri-urban*	3837	50 years and older	RUS 1
Turkmenistan	2001	*subnational urban/rural*	6011	50 years and older	TKM 1

Correspondence to: Silvio P. Mariotti, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland.

WHO South-East Asian Region	date of survey	*study population*	sample size	age group	reference
Bangladesh	2005	*subnational rural*	4868	50 years and older	BGD 1
Democratic Republic of Timor Lester	2005	*subnational urban and rural*	1414	40 years and older	TLS 1
India	2007	*national urban and rural*	40447	50 years and older	IND 1
India	2003	*subnational urban and rural*	7084	50 years and older	IND 2
India	2006	*subnational urban and rural*	13016	5 to 15 years 50 years and older	IND 3
Indonesia	2004	*subnational rural*	2629	50 years and older	IDN 1
Myanmar	2005	*subnational rural*	2076	40 years and older	MMR 1
Myanmar	2003	*subnational rural*	2885	50 years and older	MMR 2
Myanmar	2003	*subnational rural*	2990	50 years and older	MMR 3
Nepal	2002	*subnational rural*	5002	45 years and older	NPL 1
Nepal	2005	*subnational rural*	5138	50 years and older	NPL 2
WHO Western Pacific Region	date of survey	*study population*	sample size	age group	reference
Cambodia	2007	*national urban and rural*	5902	50 years and older	KHM 1
China	2007	*subnational rural*	45747	50 years and older	CHN 1
China	2003	*subnational urban and peri-urban*	3040	60 years and older	CHN 2
Papua New Guinea	2005	*subnational urban and rural*	1174	50 years and older	PNG 1
Philippines	2006	*subnational urban and rural*	5951	50 years and older	PHL 1

Correspondence to: Silvio P. Mariotti, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland.

WHO Western Pacific Region	date of survey	*study population*	sample size	age group	reference
Viet Nam	2007	*national urban and rural*	28073	50 years and older	VNM 1
Viet Nam	2007	*national urban and rural*	28800	0 to 15 years	VNM 1

Correspondence to: Silvio P. Mariotti, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland.

	WHO African Region
BWA 1	Nikomazana O. National prevalence survey of visual impairment in Botswana. Submitted for MSc Community Eye Health at the London School of Hygiene and Tropical Medicine. London 2006.
CMR 1	Oye JE, Kuper H. Prevalence and causes of blindness and visual impairment in Limbe urban area, South West Province, Cameroon. Br J Ophthalmol 2007;**91**:1435-1439.
CMR 2	Oye JE, Kuper H, Dineen B, et al. Prevalence and causes of blindness and visual impairment in Muyuka: a rural health district in South West Province, Cameroon. Br J Ophthalmol 2006;**90**:538-542.
ERI 1	Mueller A. Rapid assessment of avoidable blindness in Eritrea. 2008; unpublished report. The Fred Hollows Foundation, 1 Mitchell Street, Enfield NSW 2136, Australia
ETH 1	National survey on blindness, low vision and trachoma in Ethiopia.Federal MOH of Ethiopia, The Carter Center, CBM, ITI, ORBIS Int.Ethiopia and LfW, Opthalmol Society of Ethiopia, Ethiopian Public Health Association. Addis Ababa, Ethiopia 2006. Survey report prepared by Yemane Berhane, Alemayehu Worku, Abebe Bejiga.
GMB 1	Department of State for Health and Social Welfare, The Gambia, International Centre for Eye Health, London School of Hygiene and Tropical Medicine, London, UK, Sightsavers International. Rapid assessment of avoidable blindness in The Gambia. 2008. unpublished report.
GHA 1	Guzek JP, Anyomi FK, Fiadoyor S, et al. Prevalence of blindness in people over 40 years in the Volta region of Ghana. Ghana Medical J 2005;**39**:55-62.
GHA 2	Ahorsu F, Hagan M, Wanye S, et al. Prevalence of blindness and visual impairment among people aged 40 years and above in three districts in the Northern Region of Ghana. 2005. unpublished report.
KEN 1	Mathenge W, Kuper H, Limburg H, et al. Rapid assessment of avoidable blindness in Nakuru District, Kenya. Ophthalmology 2007;**114**:599-605.
KEN 2	Karimurio J, Sheila M, Gichangi M, et al. Rapid assessment of cataract surgical services in Embu district, Kenya. East Afr J Ophthalmol 2008;**13**:19-25.
KEN 3	Rapid assessment of avoidable blindness in Kericho, Great Rift Valley, Kenya. 2007; unpublished report from P. Huguet.
MLI 1	Traoré L, Oyé J. Appréciation rapide de la cécité évitable dans la région de Koulikoro au Mali en 2008. personal communication.
NGA 1	Kyari F, VSG Murthy, Sivsubramaniam S, et al. Prevalence of blindness and visual impairment in Nigeria: the national blindness and visual impairment survey. Invest Ophthalmol Vis Sci 2009;**50**:2033-2039.
NGA 2	Rabiu MM, Muhammed N. Rapid assessment of cataract surgical services in Birnin-Kebbi Local Government Area of Kebbi State, Nigeria. Ophtahlmic Epidemiology 2008 **15**:359-365.
RWA 1	Mathenge W, Nkurikiye J, Limburg H, et al. Rapid assessment of avoidable blindness in Western Rwanda: blindness in a postconflict setting.PLoS Medicine 2007;**4**:1187-1193.
TZA 1	Rapid assessment of cataract surgical services in Kyela, United Republic of Tanzania. 2007; unpublished report from P. Huguet.
TZA 2	Habiyakire C, Kabona G, Courtright P, et al. Rapid assessment of avoidable blindness and cataract surgical services in Kilimanjaro region Tanzania. Ophthalmic Epidemiology. 2010;**17**:90-94.
TZA 3	Kikira S. Rapid Assessment of avoidable blindness in Zanzibar. Submitted for MSc Community Eye Health at the London School of Hygiene and Tropical Medicine. London 2007.
UGA 1	Rapid assessment of cataract surgical services in Massaka, Uganda. 2007; unpublished report from P. Huguet.

Correspondence to: Silvio P. Mariotti, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland.

	WHO Region of the Americas
ARG 1	Nano MG, Nano HD, Mugica JM, et al. Rapid assessment of visual impairment due to cataract and cataract surgical services in urban Argentina. Ophthalmic Epidemiol 2006;**13**:191-197.
BRA 1	Arieta C. Results of rapid assessment of cataract surgical services in Campinas, Brazil, 2003. University of Campinas Ophthalmic Department. Unpublished report.
CHL 1	Maul E, Barrosa S, Munoz SR, et al. Refractive error study in children: results from La Florida, Chile. Am J Ophthalmol 2000;**129**:445-454.
	Barria F, Silva JC, Limburg H, et al. Analisis de la prevalencia de ceguera y sus causas mediante encuesta rapida de ceguera evitable (RAAB) en la VIII Region Chile. 2007; unpublished report.
CUB 1	Hernandez Silva JR, Rio Torres M, Padilla Gonzalez CM. Resultados del RACSS en Ciudad de La Habana, Cuba, 2005. Rev Cubana Oftalmol 2006;**19**:1-9.
DOM 1	Consejo Nacional para la Prevención de la Ceguera. Encuesta nacional de ciegos. Republica Dominicana 2008. Santo Domingo, Republica Dominicana 2009.
GTM 1	Beltranena F, Casasola K, Silva JC, et al. Cataract blindness in 4 regions of Guatemala. Ophthalmology 2007;**114**:1558-63.
MEX 1	Rapid assessment of avoidable blindness in Nuevo Leon State, Mexico. 2006. unpublished report from Limburg H
PRY 1	Duerksen R, Limburg H, Carron JE, et al. Cataract blindness in Paraguay-results of a national survey. Ophthalmic Epidemiol 2003;**10**:349-357.
PER 1	Aguila LP, Carrion R, Luna W, et al. Ceguera por catarata en personas mayores de 50 anos en una zona semirural del norte del Peru. Pan Am J Public Health 2005;**17**:387-93.
VEN 1	Siso F, Esche G, Limburg H. et al. Test nacional de catarata y servicios quirurgicos "RACSS Rapid assessment of cataract surgical services": primera encuesta nacional. Rev Oftalmol Venez 2005; **61**:112-39.
	WHO Eastern Mediterranean Region
IRN 1	Hossein-Ali Shahriari, Shahrokh Izadi, Mohammad-Reza Rouhani, et al. Prevalence and causes of visual impairment and blindness in Sistan-va-Baluchestan Province, Iran: Zahedan Eye Study. Br J Ophthalmol 2007;**91**:579-584.
OMN 1	Khandekar R, Mohammed AJ, Raisi AA. Prevalence and causes of blindness and low vision; before and five years after Vision 2020 initiatives in Oman: a review. Ophthalmic Epidemiol 2007;**14**:9-15.
PAK 1	Jadoon MZ, Dineen B, Bourne RRA, et al. on behalf of the Pakistan National Eye Survey Study Group. Invest Ophthalmol Vis Sci 2006;**47**:4749-4755.
QAT 1	Al Gamra H, Al Mansouri F, Khandekar R, et al. Prevalence and causes of blindness, low vision and status of cataract in 50 years and older citizen of Qatar-a community based survey. Ophthalmic Epidemiol 2010;**17**:292-300.
	WHO European Region
RUS 1	Branchevskiy S. Rapid assessment of avoidable blindness in Samara. 2009; personal communication.
TKM 1	Amansakhatov S, Volokhovskaya Z P, Afanasyeva A N, et al. Cataract blindness in Turkmenistan: results of a national survey. Br J Ophthalmol 2002;**86**:1207-1210.

Correspondence to: Silvio P. Mariotti, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland.

	WHO South-East Asian Region
BGD 1	Wadud Z, Kuper H, Polack S, et al. Rapid assessment of cataract surgical services in Sathkhira District, Bangladesh. Br J Ophthalmol 2006;**90**:1225-1229.
TLS 1	Ramke J, Palagyi A, Naduvilath T, et al. Prevalence and causes of blindness and low vision in Timor-Leste. Br J Ophthalmol 2007;**91**:1117-1121.
IND 1	Neena J, Rachel J, Praveen V, et al. for the RAAB India Study Group. Rapid Assessment of Avoidable Blindness in India. Plos One, 2008,**3**:e2867.
IND 2	National Programme for the Control of Blindness. Rapid assessment of blindness in North Eastern States of India 2003. Ophthalmology/ Blindness Control Section, Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India, New Delhi, 110011 India.
IND 3	National Programme for the Control of Blindness. Survey of childhood blindness and visual impairment (Gujarat and Wes Bengal). Rapid assessment of blindness in 50+ population (Bharuch, Gujarat). 2006. Ophthalmology/ Blindness Control Section, Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India, New Delhi, 110011 India.
IDN 1	Rapid assessment of cataract surgical services in Lombok, Indonesia. 2004; unpublished report from P. Huguet.
MMR 1	Casson RJ, Newland HS, Muecke J, et al. Prevalence and causes of viusal impairment in rural Myanmar: the Meiktila Eye Study. Ophthalmology 2007;**114**:2302-8
MMR 2	Limburg H, Maung N, Khin Aye Soe, et al. Study report on rapid assessment of cataract surgical services in Hpaan District, Union of Myanmar. Ministry of Health, Department of Health, Trachoma Control and Prevention of Blindness Programme. 2001.
MMR 3	Limburg H, Maung N, Khin Aye Soe, et al. Study report on rapid assessment of cataract surgical services in Rakhine District, Union of Myanmar. Ministry of Health, Department of Health, Trachoma Control and Prevention of Blindness Programme. 2001.
NPL 1	Sapkota YD, Pokharel GP, Nirmalan PK, et al. Prevalence of blindness and cataract surgery in Gandaki Zone, Nepal. Br J Ophthalmol 2006;**90**:411-416.
NPL 2	Sherchan A, Kandel RP, Sharma MK,et al. Blindness prevalence and cataract surgical coverage in Lumbini Zone and Chetwan District of Nepal. Br J Ophthalmol 2010;**94**:161-166.

	WHO Western Pacific Region
KHM 1	Rapid assessment of avoidable blindness program in Cambodia. 2007. unpublished report (contact: Dr. Do Seiha)
CHN 1	Zhao J, Ellwein LB, Cui H, et al. Prevalence of vision impairment in older adults in rural China: the China Nine-Province Survey. Ophthalmology 2010; **117:**409-416.
CHN 2	Li L, Guan H, Xun P, et al. Prevalence and causes of visual impairment among the elderly in Nantong, China. Eye, 2008; **22**:1069-75.
PNG 1	Garap NJ, Sheeladevi S, Shamanna BR, et al. Blindness and vision impairment in the elderly of Papua New Guinea. Clin Experiment Ophthalmol 2006;**34**:335-341.
PHL 1	Eusebio C, Kuper H, Polack S, et al. Rapid assessment of avoidable blindness in Negros Island and Antique Dstrict, Philippines. Br J Ophthalmol 2007,**91**:1588-1592.
VNM 1	Limburg H. Viet Nam National Institute of Ophthalmology, Hanoi, Viet Nam. Results of Rapid Assessment for Avoidable Blindness in 16 provinces of Viet Nam. 2008, unpublished report**.**

Correspondence to: Silvio P. Mariotti, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland.

Correspondence to: Silvio P. Mariotti, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland.

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Retinopathy in adults with hypertension and diabetes mellitus in Western Tanzania: a cross-sectional study

Richmond Woodward[1] Evarista Mgaya[2] Christopher Mwanansao[2] Robert N. Peck[3 4 5] Alan Wu[6] and Grace Sun[7]

1 *Department of Ophthalmology, Duke University, Durham, NC, USA*
2 *Department of Ophthalmology, Bugando Medical Center, Mwanza, Tanzania*
3 *Center for Global Health, Weill Cornell Medical College, New York, NY, USA*
4 *Department of Medicine, Weill Bugando School of Medicine, Mwanza, Tanzania*
5 *Mwanza Interventions Trial Unit, Mwanza, Tanzania*
6 *Division of Biostatistics and Epidemiology, Department of Healthcare Policy Research, Weill Cornell Medicine, New York, NY, USA*
7 *Department of Ophthalmology, Weill Cornell Medical College, New York, NY, USA*

Abstract

OBJECTIVE Little is known about the retinal manifestations of arterial hypertension (HTN) and diabetes mellitus (DM) in Western Tanzania and how to maximise the utilisation of scarce eye health resources. To address this, we determined the prevalence of hypertensive and diabetic retinopathy (DR), associated risk factors and relevant patient knowledge.

METHODS Adults with HTN or DM attending outpatient clinics at Bugando Medical Center (BMC) from June to August 2017 were enrolled. Fundus photographs were obtained, and data were collected on blood pressure (BP), body mass index (BMI), blood sugar, visual acuity (VA) and responses to questions about the effects of HTN and DM on the eye.

RESULTS A total of 180 persons were screened. When only individuals with DR were considered, bivariate regression found systolic BP was significantly associated with severity of DR ($P = 0.034$). Receiver operating characteristic (ROC) curve analysis using the maximum Youden index revealed the optimum cut-off using duration of DM to predict any DR was 8 years (AUC = 0.75, 95% CI 0.65 0.85). Fewer persons with HTN were aware of the effect of high BP on the eye (61.6%) than persons with DM who were aware of the effect of high blood sugar on the eye (74.4%) ($P = 0.048$).

CONCLUSION Efforts should be made to vigorously treat HTN among adults with DM and refer adults with duration of DM of 8 years or more for a dilated retinal examination. Additional efforts should be made to promote awareness of the sight threatening potential of HTN in resource-limited settings.

keywords diabetic retinopathy, hypertensive retinopathy, screening, prevalence, Tanzania, Africa

Sustainable Development Goals SDGs): SDG 3 (good health and well-being), SDG 17 (partnerships for the goals)

Introduction

Non-communicable diseases, including HTN and DM, are emerging as leading causes of death and disability on the African continent. In the last 10 years, the age standardised mean systolic BP has risen in east, west, central and southern Africa more than any other region of the world [1]. The burden of HTN is a particular concern in Tanzania, and data on the prevalence of the sequelae of HTN are limited [2 4].

The number of adults (20 79 years) with DM globally is projected to rise from 463 million to 700 million people by the year 2045, with the highest percentage increase to occur in low-income/lower middle-income countries [5, 6]. Along with the rise in the prevalence of DM is a rise in vison loss due to the sequela of diabetic eye disease, in particular DR [5].

Although some published data exist on the prevalence of DR and associated risk factors in the Kilimanjaro region of Tanzania [7, 8], data are lacking in other regions. Data are available for awareness of Type 2 DM in the adult population of Mwanza city [9], and for awareness of DR among adults with DM attending diabetes clinics in various regions of Tanzania [10]. However, data are lacking on possible associations between patient awareness of DM and prevalence of DR.

Bugando Medical Center (BMC) is a tertiary care hospital in Mwanza serving over 13 million people living in the Lake zone of northwest Tanzania. At the time of this study, there were only two Tanzanian ophthalmologists in the region. BMC has partnered with Weill Cornell to address the increasing burden of eye disease in the Lake zone by combining the expertise of ophthalmologists at both centres to carry out a cross-sectional study of people identified with either DM or HTN attending outpatient clinics at BMC. Together, we sought to determine the hospital-based prevalence of hypertensive and diabetic retinopathy, associated risk factors and awareness about the effect of high BP and high blood sugar on the eye. We aimed to describe clinical parameters that can identify people most likely to have retinopathy and to identify gaps in knowledge among people with DM or HTN that can be addressed, all with the goal of improving patient care.

Methods

Between 14th June and 4th August 2017, BMC conducted a pilot project to screen all adults (over 18 years of age) attending the BMC HTN or DM clinics for retinopathy. The goal of the pilot was to determine the feasibility and possible benefit of a universal screening approach in Tanzanian adults attending HTN and DM clinics. Arterial HTN was defined as a BP of >140/90 on two consecutive clinic visits. DM was defined as fasting blood sugar concentration levels 126 mg/dL (7.0 mmol/L) or random blood sugar concentration levels 200 mg/dL (11.1 mmol/L) on two consecutive clinic visits. Those consenting had one to three 45-degree fundus photographs taken of each eye with a Topcon NW300 nonmydriatic camera (Topcon Medical, Oakland, NJ) without using dilating drops. The images were stored on a password protected laptop with an encrypted hard drive.

Data were collected on BP, BMI, blood sugar and VA. Blood pressure was taken in the right arm with an Omron (Omron Healthcare Co. Ltd; Kyoto, Japan) M6 portable digital BP device that measured systolic and diastolic BP. The cuff was placed on the bare arm, while subjects were seated with their feet on the floor, and BP was measured after subjects were quiet for 3 5 min. A single reading was taken. An extra-large cuff with an integrated aneroid was available to measure BP of individuals with an arm larger than the applicable circumference of the digital device. Blood sugar levels were measured from a fingerstick whole blood sample and measured using Contour glucose test strips and a Contour point-of-care blood glucose meter (Bayer Healthcare LLC; Sunnyvale, CA). Distance VA was measured with a multi-letter Snellen eye chart with subjects positioned 6 metres from the chart. Corrected VA was measured in each eye. For the purpose of analysis, the VA of the best eye was used. Visual impairment was defined as VA less than 6/18 in the better eye.

Demographic information and clinical history were obtained by questionnaire. To assess awareness of the effect of high BP and high blood sugar on the eye, an investigator administered a questionnaire with targeted knowledge questions (Appendix 2).

Comprehensive ophthalmologists at BMC trained in the diagnosis of diabetic and hypertensive retinopathy during their four-year ophthalmology training performed the grading of retina photographs. All ophthalmologists were masked to subjects' diagnosis and history. Ten per cent of the retina photographs were randomly selected to be interpreted by a second reader from the Weill Cornell Department of Ophthalmology (New York, NY, USA) for quality control. The inter-rater agreement was 100% for all grades of DR and maculopathy, and for Grade 3 and 4 hypertensive retinopathy. Per cent agreement including all seven categories measured was 93.9% (263/280). Results for DR and maculopathy were graded based on the minimum data set recommended by the English and Wales National Screening Committee (Appendix 1, 7). Results for hypertensive retinopathy were graded according to modified Scheie's criteria (Appendix 1, 11).

Statistical analysis

Data were entered into an Excel spread sheet and analysed, including graphical output, using R version 3.6.3. The eye having the more advanced diabetic or hypertensive retinopathy was used for the analysis. Characteristics of the study population were described using absolute numbers with percentages for categorical variables. Welch's two-sample *t*-test, one-way ANOVA, chi-squared test (with Yates correction), Fisher's exact test and bivariate regression were used to investigate the relationship between retinopathy outcome and clinical data, demographic factors, and responses to knowledge questions. Bivariate tables were created to summarise independently associated factors with retinopathy outcome. A P value of 0.05 was considered statistically significant. Receiver operating curves and two-sample test of proportions were used to assess viability of selected clinical variables as potential discriminants of retinopathy outcomes.

Ethics

Ethical approval was obtained from the Weill Cornell Medical College Institutional Review Board and from the ethics committees of BMC and the National Institute of

Medical Research in Tanzania. Written informed consent was obtained from all study participants.

Results

During the pilot study period, 185 adults were seen in the DM and HTN clinics. Of these, 180 agreed to undergo screening. Common reasons for refusal to participate included concerns about the duration of time needed to complete clinical data collection and respond to the questionnaires. Of the 180 participants enrolled, 6 (3.3%) had images that were ungradable due to media opacity. A total of 174 people had their fundus images graded for hypertensive and diabetic retinopathy. The distribution of outpatient clinics varied, with 83 (47.7%) participants attending HTN clinic, 24 (13.8%) attending DM clinic and 67 (38.5%) attending with both DM and HTN clinics. Participants were most frequently employed as farmers, and the highest educational level obtained among most participants was primary school (Table 1).

For participants with HTN, the prevalence of any hypertensive retinopathy was 37.3% (95% CI 29.6 45.1%) with Grade I, II, III and IV hypertensive retinopathy having a prevalence of 12.0% (95% CI 6.8 17.2%), 14.0% (95% CI 8.4 19.6%), 8.7% (95% CI 4.2 13.2%) and 2.7% (95% CI 0.1 5.2%), respectively (Table 2a).

For participants with DM, the overall prevalence of any DR was 42.9% (95% CI 32.7-53.0%) with background diabetic retinopathy (BDR), pre-proliferative diabetic retinopathy (PPDR) and proliferative diabetic retinopathy (PDR) having a prevalence of 24.2% (95% CI 15.4 33.0%), 13.2% (95% CI 6.2 20.1%) and 5.5% (95% CI 0.8 10.2%), respectively. The overall prevalence of diabetic maculopathy was 26.5% (95% CI 17.0 36.0%), and prevalence of referable maculopathy/clinically significant macular oedema (CSME) was 22.9% (95% CI 13.9 31.9%) (Table 2b). Fundus images where haziness due to media opacity interfered with the view of the macula were considered ungradable for maculopathy. All participants with any maculopathy also had findings of DR such that 22 patients (24.2% of all adults with DM) had both DR and maculopathy.

Factors associated with hypertensive retinopathy

The characteristics and questionnaire results of participants with HTN with and without any hypertensive

Table 1 Participant characteristics by condition

Characteristic			All (n = 174)	
Proportion (%) or mean (SD)	HTN*,* (n = 150)	Diabetes*,* (n = 91)		n
Gender				172
Female	84 (56.0%)	57 (62.6%)	102 (59.3%)	
Male	64 (42.7%)	34 (37.4%)	70 (40.7%)	
Age	62.3 (10.7)	59.2 (11.4)	60.6 (11.5)	173
Vision				174
No visual impairment	98 (65.3%)	62 (68.1%)	116 (66.7%)	
Visual impairment	52 (34.7%)	29 (31.9%)	58 (33.3%)	
Duration of disease in years	9.5 (8.8)	9.3 (7.6)	n/a	
Clinic blood glucose in mmol/L	8.0 (3.9)	9.7 (4.1)	8.4 (4.0)	128
Body Mass Index (BMI) in kg/m^2	27.41 (5.4)	27.2 (5.4)	27.1 (5.5)	169
Clinic blood pressure in mmHg				171
Systolic	159.8 (27.0)	151.0 (28.8)	155.5 (28.4)	
Diastolic	87.1 (15.7)	83.2 (12.9)	86.4 (15.5)	
Employment				171
Farmer	54 (36.7%)	34 (38.2%)	62 (36.2%)	
Govt, Small business	20 (13.6%)	12 (13.5%)	27 (15.8%)	
Homemaker	22 (15.0%)	10 (11.2%)	24 (14.0%)	
Day labour, Informal	24 (16.3%)	18 (20.2%)	26 (15.2%)	
Student, Unemployed, Other	27 (18.4%)	15 (16.8%)	32 (18.7%)	
Education				167
None, primary	80 (55.5%)	46 (52.9%)	92 (55.1%)	
Secondary, vocational	42 (29.2%)	27 (31.0%)	49 (29.3%)	
University	22 (15.3%)	14 (16.1%)	26 (15.6%)	

*Including participants with both HTN and DM.

Table 2 Prevalence and grade of (a) hypertensive retinopathy among participants with HTN (n = 150) (b) Prevalence and grade of diabetic retinopathy and maculopathy among participants with DM (n = 91)*

(a)

Hypertensive retinopathy	of subjects	As per cent of subjects with HTN	95% CI
Gr 1	18	12.0	6.8 17.2%
Gr 2	21	14.0	8.4 19.6%
Gr 3	13	8.7	4.2 13.2%
Gr 4	4	2.7	0.1 5.2%
Gr 0 (None)	94	62.7	54.9 70.4%
Total HTN retinopathy	56	37.3% = Prevalence HTN Retinopathy	95% CI 29.6 45.1%

(b)

Diabetic Retinopathy	of subjects	As per cent of subjects with DM	95% CI
BDR (Gr 1)	22	24.2%	15.4 33.0%
PPDR (Gr 2)	12	13.2%	6.2 20.1%
PDR (Gr 3)	5	5.5 %	0.8 10.2%
None	52	57.1%	47 67.3%
Total DR	39	42.9% = Prevalence Diabetic Retinopathy	95% CI 32.7 53.0%
Diabetic Maculopathy	**of subjects**	**As per cent of subjects with DM**	**95% CI**
Non-referable	3	3.6%	0 7.6%
Referable (CSME)	19	22.9%	13.9 31.9%
None	61	73.5%	64 83%
Total Diabetic Maculopathy	22	26.5% = Prevalence Diabetic Maculopathy	95% CI 17.0 36.0%
Ungradable for Maculopathy	8		

*Participants classified by the eye with the more advanced disease.

retinopathy are shown in Table 3. Systolic and diastolic BP were strongly associated with any hypertensive retinopathy by bivariate analysis, P = 0.001 and P = 0.001, respectively (Table 3). We explored the relationship between systolic BP and hypertensive retinopathy. Receiver operating characteristic (ROC) curve analysis using the Youden index and the area under the ROC curve (AUC) revealed the optimum cut-off using systolic BP for detecting any hypertensive retinopathy was 154 mm Hg (AUC = 0.66, 95% CI 0.57 0.75, Table 5). The proportion of participants with systolic BP greater than or equal to 155 mm Hg and any hypertensive retinopathy (48.2%) was significantly greater than the proportion of participants with systolic BP less than 155 mm Hg and any hypertensive retinopathy (23.1%) (P = 0.0017, Figure 1).

When participants with HTN were asked 'Can high blood pressure make vision worse?', 85 (61.6 %) responded 'yes' and 53 (38.4%) responded 'no' or 'unsure'. Awareness of the effect of high BP on the eye was not associated with the presence of any hypertensive retinopathy (Table 3).

Factors associated with diabetic retinopathy and maculopathy

The characteristics and questionnaire results of individuals with DM with and without any DR are shown in Table 4. Duration of DM was significantly associated with both any DR (P < 0.001) and any maculopathy (P = 0.002) (Table 4). We explored the relationship between the duration of DM and any DR. ROC curve analysis using the Youden index revealed the optimum cut-off using duration of DM for detecting any DR was 8 years (AUC = 0.75, 95% CI 0.65 0.85, Table 5). The proportion of participants with duration of DM greater than or equal to 8 years and any DR (62.5%) was greater than the proportion of participants with duration of DM <8 years and any DR (19.5%) (P 0.0001, Figure 2).

We also explored the relationship between systolic blood pressure and DR. When only participants with DM and any DR are considered, in a bivariate regression, we found systolic BP was significantly associated with the severity (grade) of DR (P = 0.034). ROC curve analysis

Table 3 Factors associated with hypertensive retinopathy in outpatients with hypertension (n = 150)

Characteristic Proportion (%) or mean (SD)	Hypertensive retinopathy (n = 56)	No hypertensive retinopathy (n = 94)	P-overall*
Gender			
Female	30 (54.5%)	54 (58.1%)	0.806
Male	25 (45.5%)	39 (41.9%)	
Age	61.0 (11.2)	63.0 (10.5)	0.288
Vision			0.975
No visual impairment	36 (64.3%)	62 (66.0%)	
Visual impairment	20 (35.7%)	32 (34.0%)	
Duration hypertension in years	9.0 (8.1)	9.8 (9.3)	0.595
Clinic blood glucose in mmol/L	7.4 (3.7)	8.3 (4.1)	0.282
Body Mass Index (BMI) in kg/m^2	27.1 (5.5)	27.6 (5.3)	0.557
Clinic Blood pressure in mm Hg			
Systolic	169 (24.8)	154 (26.8)	0.001
Diastolic	94.2 (18.7)	84.2 (12.3)	0.001
Employment			0.544
Farmer	16 (29.6%)	38 (40.9%)	
Govt, small business	8 (14.8%)	12 (12.9%)	
Homemaker	8 (14.8%)	14 (15.1%)	
Day labour, informal	12 (22.2%)	12 (12.9%)	
Student, unemployed, other	10 (18.5%)	17 (18.3%)	
Education			0.349
None or primary	29 (53.7%)	51 (56.7%)	
Secondary or vocational	19 (35.2%)	23 (25.6%)	
University	6 (11.1%)	16 (17.8%)	
Knowledge Question 1†			0.840
No	6 (11.8%)	8 (9.2%)	
Unsure	15 (29.4%)	24 (27.6%)	
Yes	30 (58.8%)	55 (63.2%)	

**P*-values calculated via ANOVA, Kruskall Wallis or chi-squared (or Fisher's) depending on whether the row variable is continuous normal, continuous non-normal or categorical.
†Appendix 2.

using the Youden index revealed the optimum cut-off using systolic BP for detecting any DR was 149.5 mm Hg (AUC = 0.64, 95% CI 0.54 0.74. Table 5). The proportion of participants with systolic BP greater than or equal to 150 mm Hg and any DR (56.2%) was greater than the proportion of participants with systolic BP less than 150 mm Hg and any DR (29.3%) (P = 0.0106, Figure 3).

When participants with DM were asked 'Can high blood sugar make vision worse?', 64 (74.4 %) responded 'yes' and 22 (25.6%) responded 'no' or 'unsure'. Awareness of the effect of high blood sugar on the eye was not associated with the presence of any DR (Table 4).

Factors associated with comorbid hypertension and diabetes mellitus

The characteristics of individuals diagnosed with both HTN and DM are shown in Table 6. Among individuals identified with both HTN and DM, duration of DM was significantly associated with any DR (P = 0.004) and any maculopathy (P = 0.015) by bivariate analysis. Among individuals identified with both HTN and DM, diastolic BP (P = 0.004) and younger age (P = 0.014) was significantly associated with any hypertensive retinopathy by bivariate analysis (Table 6).

Discussion

This is the first study of the prevalence of diabetic retinopathy, clinically significant macular oedema, hypertensive retinopathy and associated risk factors among persons with HTN and DM in Western Tanzania. The results of our investigation highlight the high disease burden Western Tanzania faces from DR, CSME and hypertensive retinopathy and provides data to plan screening services and health education for people with DM and/or HTN in the Lake zone.

The prevalence of any DR in our data set (42.9%) is higher than that observed at entry into a DR screening

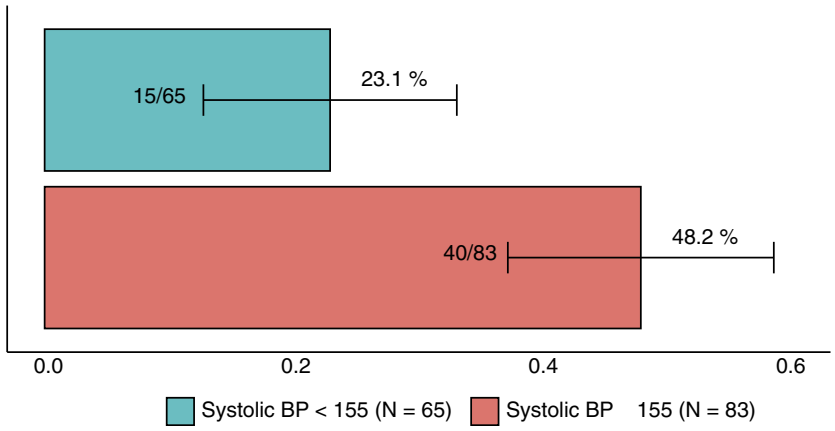

Figure 1 Proportion with any hypertensive retinopathy by systolic BP cut-off

Table 4 Factors associated with Diabetic Retinopathy (n = 91) and Maculopathy* (n = 83) in outpatients with diabetes mellitus

Characteristic Proportion (%) or mean (SD)	Diabetic Retinopathy n = 52	No Diabetic Retinopathy n = 39	P-overall†	Maculopathy n = 22	No Maculopathy n = 61	P-overall†
Gender			1.000			0.712
Female	24 (61.5%)	33 (63.5%)		15 (68.2%)	37 (60.7%)	
Male	15 (38.5%)	19 (36.5%)		7 (31.8)	24 (39.3%)	
Age	58.7 (9.0)	59.5 (13.1)	0.744	60.0 (7.6)	58.8 (12.5)	0.620
Vision			0.974			0.636
No visual impairment	26 (66.7%)	36 (69.2%)		14 (63.6)	44 (72.1)	
Visual impairment	13 (33.3%)	16 (30.8%)		8 (36.4)	17 (27.9)	
Duration of diabetes in years	12.8 (7.8)	6.7 (6.4)	<0.001	14.0 (8.0)	7.5 (6.7)	0.002
Clinic blood glucose in mmol/L	9.9 (4.3)	9.5 (4.0)	0.686	10.5 (5.1)	9.4 (3.9)	0.391
Body Mass Index (BMI) in kg/m^2	26.8 (4.8)	27.5 (5.8)	0.561	26.6 (5.6)	27.0 (5.1)	0.759
Clinic Blood pressure, mm Hg						
Systolic	157 (26.5)	147 (30)	0.095	159 (21.8)	149 (31.4)	0.118
Diastolic	83.8 (11.9)	82.8 (13.8)	0.727	85.0(11.8)	83.0 (13.9)	0.515
Employment			0.508			0.697
Farmer	13 (35.1%)	21 (40.4%)		7 (33.3%)	23 (38.3%)	
Govt, small business	6 (16.2%)	6 (11.5%)		3 (14.3%)	8 (13.3%)	
Homemaker	6 (16.2%)	4 (7.7%)		3 (14.3%)	5 (8.3%)	
Day labour, informal	8 (21.6%)	10 (19.2%)		6 (28.6%)	12 (20.0%)	
Student, Unemployed, Other	4 (10.8%)	11 (21.1%)		2 (9.5%)	12 (20.0%)	
Education			0.187			0.174
None or primary	22 (57.9%)	24 (49.0%)		12 (54.5%)	28 (48.3%)	
Secondary or vocational	13 (34.2%)	14 (28.6%)		9 (40.9%)	17 (29.3%)	
University	3 (7.9%)	11 (22.4%)		1 (4.5%)	13 (22.4%)	
Knowledge question 2‡			0.140			0.049
No	4 (11.1%)	3 (8.3%)		4 (18.2%)	3 (5.4%)	
Unsure	3 (8.3%)	12 (24.0%)		1 (4.6%)	13 (23.2%)	
Yes	29 (80.6%)	35 (70.0%)		17 (77.3%)	40 (71.4%)	

*Those ungradable for maculopathy were removed.
†P-values calculated via ANOVA, Kruskall Wallis or chi-squared (or Fisher's) depending on whether the row variable is continuous normal, continuous non-normal or categorical.
‡Appendix 2.

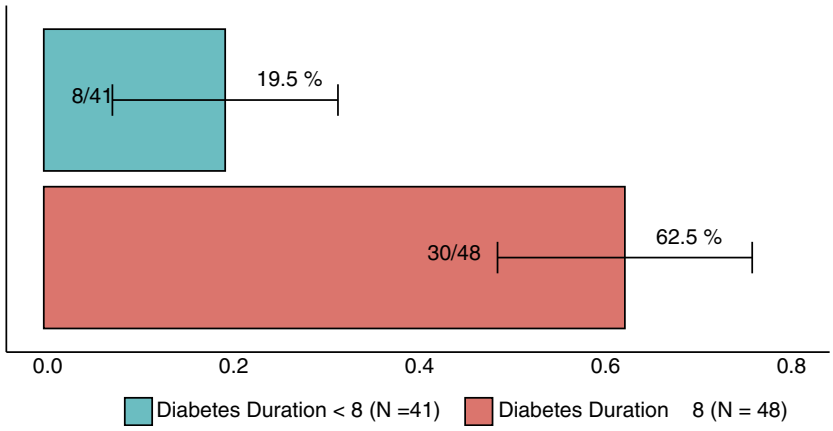

Figure 2 Proportion with any diabetic retinopathy by duration of DM cut-off

programme in the Kilimanjaro region of Tanzania (27.9%) [7]. This may reflect selection bias due to patients attending a tertiary care centre clinic having a greater burden of disease. However, our observed prevalence of DR and maculopathy (42.9% and 26.5%, respectively) is similar to that found in a household-based study in the Kilimanjaro region of Tanzania (48.6% and 25.7%, respectively) [8] suggesting our prevalence results may be generalisable to the population of adults living with DM in Tanzania.

The high prevalence of DR among outpatients attending clinics at BMC will be a heavy burden for the few ophthalmologists in Western Tanzania, especially in light of the expected rise in the prevalence of DM in SSA [5, 6]. The human resources for eye health, including the number of ophthalmologists, in SSA lag behind that of high resource regions [12]. In addition, the ophthalmic practitioner to population ratio is concentrated in large cities in SSA at the expense of those needing services in rural areas [12].

Our results showing a strong association between duration of DM and any DR suggests duration of DM is a reasonable predictor variable for detecting DR by retinal examination and might allow for determining a cut-off for referral that maximises benefits for patients living in a resource-poor setting. The AUC statistic derived from our ROC curve analysis using duration of DM to detect any DR indicates 8 years duration of DM provides acceptable discrimination between those with and without DR [13, 14]. Our goal is to maximally utilise resources spent performing retinal examinations on patients with DM to ensure that those with DR can receive diagnosis and treatment at minimal cost. Thus, referring adults with DM in Western Tanzania with duration of DM of at least 8 years to an ophthalmologist may be a reasonable strategy to increase efficiency of DR screening given the severe resource limitations and high cost for patients.

The finding that systolic BP was positively associated with the severity or grade of DR among participants with DM is consistent with the United Kingdom Prospective Diabetes Study (UKPDS), where tight blood pressure control in patients with type 2 DM reduced the rate of progression of DR by 34% [15]. In another study of 544 high-risk type 2 diabetes patients, high BP was a predictor for progression of DR [16]. This suggests vigorous efforts should be made to identify and treat HTN among all adults with DM in Western TZ. While the AUC statistic for the prediction of any DR from systolic BP is not as high as the AUC statistic for duration of DM, the relationship between systolic BP and any DR is worthy of further investigation given resource limitations.

Our results demonstrate a strong association between systolic BP and any hypertensive retinopathy. The AUC statistic for the prediction of any hypertensive retinopathy from systolic BP indicates systolic BP has discriminatory ability for detecting any hypertensive retinopathy. However, the AUC value falls under the range generally acceptable for screening purposes [14]. When the systolic BP cut-off determined by ROC curve analysis is rounded from 154 to 155 mg Hg, the proportion of participants with any hypertensive retinopathy remains significantly greater for participants with systolic BP equal to or >155 mm Hg compared to <155 mm Hg. This suggests additional investigation of systolic BP to guide referral of patients with HTN to an ophthalmologist is needed.

Duration of HTN was not associated with hypertensive retinopathy. This may be due to the observation that patterns of retinal vascular changes vary with both current

Table 5 Optimal screening cut-offs based on the maximal Youden index and associated measures of performance

Condition (screening parameter)	Value	95% confidence interval
Diabetes (Duration Diabetes)		
Optimal cut point (years)	8.0	
Area under ROC curve (AUC)	0.75	0.65 0.85
Sensitivity (%)	78.9	82.7 90.4
Specificity (%)	64.7	50.1 77.6
Positive predictive value (%)	62.5	47.7 80.8
Negative predictive value (%)	80.5	64.9 88.6
Diagnostic likelihood ratio ( )	2.24	1.49 3.36
Diagnostic likelihood ratio ( )	0.33	0.17 0.62
Diabetes (Systolic Blood Pressure)		
Optimal cut point (mm Hg)	149.5	
Area under ROC curve (AUC)	0.64	0.54 0.74
Sensitivity (%)	69.2	52.4 83.0
Specificity (%)	58.0	43.2 71.8
Positive predictive value (%)	56.2	41.2 70.5
Negative predictive value (%)	70.7	54.5 83.9
Diagnostic likelihood ratio ( )	1.65	1.12 2.43
Diagnostic likelihood ratio ( )	0.53	0.31 0.90
Hypertension (Systolic Blood Pressure)		
Optimal cut point (mm Hg)	154	
Area under ROC curve (AUC)	0.66	0.57 0.75
Sensitivity (%)	74.5	61 85.3
Specificity (%)	53.8	43 4.2
Positive predictive value (%)	48.8	38.3 65.4
Negative predictive value (%)	78.1	78.1 65.6
Diagnostic likelihood ratio ( )	1.61	1.23 2.11
Diagnostic likelihood ratio ( )	0.47	0.29 0.77

and past BP levels [17] and makes it even more vital that people with HTN in Western Tanzania be promptly diagnosed and treated to prevent damage to the retina. This is especially important as Tanzania transitions from a rural to urban society [18, 19] given the higher prevalence of HTN in urban versus rural areas [20].

Age was negatively associated with hypertensive retinopathy among individuals with both HTN and DM, with younger age being a risk factor for developing HTN retinopathy. A possible explanation is that early in the course of HTN, the vascular system has not developed compensatory mechanisms, leading to retina damage [21]. Elevated diastolic BP rather than systolic BP was a risk factor associated with hypertensive retinopathy in individuals with comorbid HTN and DM by bivariate analysis. This finding may be explained by the observation that among local factors affecting the retina, retinal diastolic arterial pressure rises before retinal changes appear and that retinal diastolic retinobrachial ratio is more significant than retinal systolic retinobrachial ratio for the development of hypertensive retinopathy [22].

Our questionnaire results for the effect of high BP on the eye suggest awareness of the complications of hypertensive eye disease could be improved among adults with HTN. Nearly, 40% of participants with HTN were not aware that HTN could cause eye disease. In low resource settings, the perceived severity of medical problems is the most important predictor for healthcare-seeking behaviour [23] and poor knowledge is associated with not seeking care for chronic medical conditions [24]. Thus, a lack of understanding of hypertensive eye disease is a potential barrier for individuals with HTN who need treatment and can be addressed with education programmes.

In conclusion, our findings show a readily obtainable historical parameter can identify adults with DM in

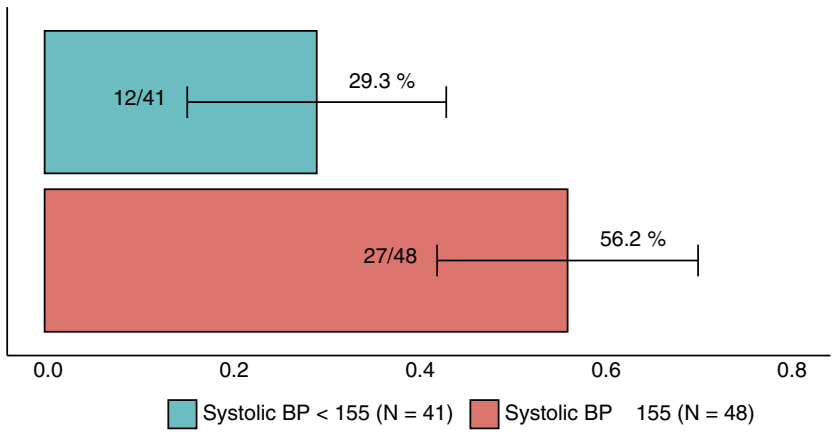

Figure 3 Proportion with any diabetic retinopathy by systolic BP cut-off

Table 6 Factors associated with Hypertensive Retinopathy, Diabetic Retinopathy and Maculopathy in outpatients with both hypertension and diabetes mellitus ($n = 67$)

Characteristic	HTN retinopathy $n = 21$	No HTN retinopathy $n = 46$	*P*-overall*	Diabetic Retinopathy $n = 31$	No diabetic retinopathy $n = 36$	*P*-overall*	Maculopathy $n = 18$	No maculopathy $n = 44$	*P*-overall*
Gender			1.000			1.000			0.552
Female	12 (57.1%)	27 (58.7%)		18 (58.1%)	21 (58.3%)		12 (66.7%)	24 (54.5%)	
Male	9 (42.9%)	19 (41.3%)		13 (41.9%)	15 (41.7%)		6 (33.3%)	20 (45.5%)	
Age	58.5 (6.9)	64.0 (10.4)	0.014	61.0 (6.1)	63.3 (12.0)	0.323	61.2 (6.6)	62.5 (10.5)	0.560
Vision			1.000			0.942			0.812
No impairment	14 (66.7%)	30 (65.2%)		21 (67.7%)	23 (63.9%)		11 (61.1%)	30 (68.2%)	
Impairment	7 (33.3%)	16 (34.8%)		10 (32.3%)	13 (36.1%)		7 (38.9%)	14 (31.8%)	
Duration HTN	8.2 (6.1)	10.8 (9.7)	0.197	12.2 (9.7)	8.4 (7.8)	0.115	10.1 (8.0)	9.78 (8.8)	0.887
Duration DM	11.0 (8.3)	9.4 (8.1)	0.460	13.0 (8.3)	7.2 (7.1)	0.004	13.9 (8.2)	8.10 (7.2)	0.015
Clinic blood glucose	9.0 (4.1)	9.6 (4.3)	0.563	9.6 (4.4)	9.3 (4.4)	0.779	10.4 (5.4)	9.19 (3.8)	0.404
BMI	27.8 (4.8)	27.9 (5.3)	0.922	27.4 (4.5)	28.3 (5.6)	0.448	27.6 (5.5)	27.5 (4.8)	0.972
Blood pressure									
Systolic	166 (17.6)	157 (29.6)	0.122	163 (24.8)	156 (28.3)	0.323	163 (21.7)	159 (28.9)	0.587
Diastolic	92.2 (11.4)	82.5 (12.9)	0.004	84.9 (11.9)	85.9 (14.3)	0.762	86.4 (12.3)	85.6 (13.9)	0.816

**P*-values calculated via ANOVA, Kruskall Wallis or chi-squared (or Fisher's) depending on whether the row variable is continuous normal, continuous non-normal or categorical.

Western Tanzania most likely to have DR and benefit from a retina examination. In particular, referring adults with DM for 8 or more years to an ophthalmologist for a dilated eye examination can allow those with the highest likelihood of DR to be screened. Our findings suggest utilisation of scarce ophthalmic resources may also benefit from further study of systolic BP cut-offs for detecting DR in adults with DM. In addition, efforts should be made to maximise the treatment of HTN among all adults with DM given our results showing the severity of DR is associated with systolic BP and the finding that all subjects with the most severe form of DR, PDR, were diagnosed with both HTN and DM. Our results also suggest further study of the relationship between systolic BP and hypertensive retinopathy may allow for determining an optimal systolic BP cut-off for referring adults with HTN for a retina examination. The feasibility of integrating programmes to promote awareness of the effect of high BP on the eye into community medical clinics should also be explored.

Acknowledgements

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References

1. Guwatudde D, Nankya-Mutyoba J, Kalyesubula LC *et al.* The burden of hypertension in Sub-Saharan Africa: a four-country cross sectional study. *BMC Public Health* 2015: **15**:1211.
2. Jones R, Putnam HWI, Philippin H *et al.* Retinal imaging to identify target organ damage in older Africans: a pilot study. *J Clin Hypertens* 2018: **20**: 1296 1301.
3. Putnam H, Jones R, Rogathi J *et al.* Hypertension in a resource-limited setting: Is it associated with end organ damage in older adults in rural Tanzania? *J Clin Hypertens* 2018: **20**: 217 224.
4. Chillo P, Ismail A, Sanyiwa A, Ruggajo P, Kamuhaba A. Hypertensive retinopathy and associated factors among non-diabetic chronic kidney disease patients seen at a tertiary hospital in Tanzania: a cross-sectional study. *Int J Nephrol Renovasc Dis* 2019: **12**: 79 86.
5. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care* 2004: **27**: 1047 1053.
6. International Diabetes Federation. IDF Diabetes Atlas [Internet], 9th edn. Brussels (Belgium); 2019. (Available from: http://www.diabetesatlas.org).
7. Cleland CR, Burton MJ, Hall C *et al.* Diabetic retinopathy in Tanzania: prevalence and risk factors at entry into a regional screening programme. *Trop Med Int Health* 2016: **21**: 417 426.
8. Stanifer JW, Cleland CR, Makuka GJ *et al.* Prevalence, risk factors, and complications of diabetes in the Kilimanjaro region: a population-based study from Tanzania. *PLoS One* 2016: **11**: e0164428.
9. Ruhembe CC, Mosha TC, Nyaruhucha CN. Prevalence and awareness of type 2 diabetes mellitus among adult population in Mwanza city, Tanzania. *Tanzan J Health Res* 2014: **16**: 89 97.
10. Mafwiri MM, Mwakyusa N, Shilio B, Lutale JK. Health education and awareness about diabetic retinopathy among patients attending diabetic clinics in tertiary and regional hospitals in Tanzania. *J Ophthalmol Eastern Central Southern Africa* 2016: **20**: 44 51.
11. Bowling B, Kanski JJ. *Kanski's clinical ophthalmology: A systematic approach* (8th edn), Elsevier: Amsterdam, 2016.
12. Palmer JJ, Chinanayi F, Gilbert A *et al.* Mapping human resources for eye health in 21 countries of sub-Saharan Africa: current progress towards VISION 2020. *Hum Resour Health* 2014: **12**: 44.
13. Hosmer DW, Lemeshow S. *Applied Logistic Regression* (2nd edn). New York, NY: John Wiley and Sons, 2000.
14. Mandrekar J. Receiver operating characteristic curve in diagnostic test assessment. *J Thorac Oncol* 2010: **5**: 1315 1316.
15. UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group. *BMJ* 1998: **317**: 703 713.
16. Cardoso CRL, Leite NC, Dib E, Salles GF. Predictors of development and progression of retinopathy in patients with type 2 diabetes: importance of blood pressure parameters. *Sci Rep* 2017: **7**: 4867.
17. Bhargava M, Wong T. Current concepts in hypertensive retinopathy. *Retinal Physician* 2013: **10**: 43 45.
18. UNICEF [Internet]. Cities and children: the challenge of urbanization in Tanzania; 2012. (Available from: https://www.unicef.org/infobycountry/files/Cities_and_Children_-_FINAL.pdf)
19. National Bureau of Statistics and Office of Chief Government Statistician. United Republic of Tanzania, Migration and Urbanization Report [Internet]; 2015. Vol IV. (Available from: http://nbs.go.tz/nbs/takwimu/census2012/MigrationandUrbanisationMonograph.pdf).
20. Mosha NR, Mahande M, Juma A *et al.* Prevalence, awareness and factors associated with hypertension in

North West Tanzania. *Glob Health Action* 2017: **10**: 1321279.
21. Henderson AD, Biousse V, Newman NJ, Lamirel C, Wright DW, Bruce BB. Grade III or grade IV hypertensive retinopathy with severely elevated blood pressure. *West J Emerg Med* 2012: **13**: 529 534.
22. Lal SK, Jain IS, Gupta SD, Wahi PL. Role of local factors in hypertensive retinopathy. *Indian J Ophthalmol* 1974: 221 225.
23. Kanungo S, Bhowmik K, Mahapatra T, Mahapatra S, Bhadra UK, Sarkar K. Perceived morbidity, healthcare-seeking behavior and their determinants in a poor-resource setting: observation from India. *PLoS One* 2015: **10**: e0125865.
24. Habtu Y, Yohannes S, Laelago T. Health seeking behavior and its determinants for cervical cancer among women of childbearing age in Hossana Town, Hadiya zone, Southern Ethiopia: community based cross sectional study. *BMC Cancer* 2018: **18**: 298.

Appendix 1
Grading schemes

Table A1 The grading scheme used for diabetic retinopathy based on the minimum data set recommended by the English and Wales National Screening Committee [7]

Retinopathy		
Level 0	None	
Level 1	Background	Microanuerysm(s)
		Retinal haemorrhage(s)
		Exudate(s)
Level 2	Pre-proliferative	Venous beading
		Venous loop or reduplication
		Multiple deep round or blot haemorrhages
		Intraretinal microvascular abnormality (IRMA)
Level 3	Proliferative	New vessels on the disc (NVD)
		New vessels elsewhere
		Pre-retinal or vitreous haemorrhage
		Pre-retinal fibrosis
Maculopathy		
No maculopathy		Does not meet any criteria for maculopathy
Non-referable maculopathy		Any microaneurysm or haemorrhage within 1 disc diameter (DD) of fovea
Referable maculopathy		Any exudate within 1 DD of the centre of the fovea

Table A2 The grading scheme used for hypertensive retinopathy based on the modified Scheie classification [11]

Retinopathy	
Grade 0	None
Grade I	Mild arteriolar attenuation
Grade II	AV nicking
	Copper wiring
Grade III	Grade 2 plus:
	Retinal haem
	Cotton wool spots
	Exudate
Grade IV	Grade 3 plus:
	Optic nerve swelling
	Silver wiring

Appendix 2

Table A1 Knowledge and Awareness questionnaire instructions

Question 1: Effects of hypertension on the eye
Instructions: Now I am going to ask you a question about what you know about high blood pressure and the eyes. Please answer the best you can, if you don't know the answer it is fine to say that.
Question: Can high blood pressure make vision worse?
Possible responses: yes, no, unsure
Question 2: Effects of diabetes mellitus on the eye
Instructions: Now I am going to ask you a question about what you know about high blood sugar and the eyes. Please answer the best you can, if you don't know the answer it is fine to say that.
Question: Can high blood sugar make vision worse?
Possible responses: yes, no, unsure

Corresponding Author **Richmond Woodward**, Department of Ophthalmology, Duke University, Durham, NC 27710, USA. E-mail: richmond.woodward@duke.edu

Speaker: Lucy Bruell and Randi Diamond, M.D.
Date: March 1, 2021
Time: 5:00pm – 6:00pm
Title: Palliative Care

Zoom info: https://weillcornell.zoom.us/j/94030989169 **Meeting ID**: 940 3098 9169 **Passcode**: 546727

Summary: Oli Otya? Life and Loss in Rural Uganda is the story of a team of nurses from a small hospital and volunteer doctors from the U.S. who care for villagers with life -threatening illnesses. The film follows the palliative care team as they travel to the villages to bring medical supplies, pain medicine, compassion, and spiritual support to patients in their homes. The session will feature a panel discussion with the filmmaker and the medical team featured in the documentary about the challenges they encountered in practicing palliative care in rural Uganda.

Suggested Readings:

https://www.oliotyafilm.com/screening/weill-cornell-screening-march-01-2021/
PW: CornellMAR012021#

Knaul, F. M., Farmer, P. E., Krakauer, E. L., De Lima, L., Bhadelia, A., Jiang Kwete, X., Zimmerman, C. (2018). Alleviating the access Abyss in palliative care and pain RELIEF—AN imperative of universal health coverage: The Lancet Commission report. The Lancet, 391(10128), 1391-1454. https://doi.org/10.1016/s0140-6736(17)32513-8

Lynch, T., Connor, S., & Clark, D. (2013). Mapping levels of palliative care development: A global update. Journal of Pain and Symptom Management, 45(6), 1094-1106. https://doi.org/10.1016/j.jpainsymman.2012.05.011

Alleviating the access abyss in palliative care and pain relief—an imperative of universal health coverage: the *Lancet* Commission report

Felicia Marie Knaul, Paul E Farmer, Eric L Krakauer*, Liliana De Lima, Afsan Bhadelia, Xiaoxiao Jiang Kwete, Héctor Arreola-Ornelas, Octavio Gómez-Dantés, Natalia M Rodriguez, George A O Alleyne, Stephen R Connor, David J Hunter, Diederik Lohman, Lukas Radbruch, María del Rocío Sáenz Madrigal, Rifat Atun†, Kathleen M Foley†, Julio Frenk†, Dean T Jamison†, M R Rajagopal†, on behalf of the* Lancet *Commission on Palliative Care and Pain Relief Study Group‡*

Executive Summary

> In agonising, crippling pain from lung cancer, Mr S came to the palliative care service in Calicut, Kerala, from an adjoining district a couple of hours away by bus. His body language revealed the depth of the suffering.
>
> We put Mr S on morphine, among other things. A couple of hours later, he surveyed himself with disbelief. He had neither hoped nor conceived of the possibility that this kind of relief was possible.
>
> Mr S returned the next month. Yet, common tragedy befell patient and caregivers in the form of a stock-out of morphine.
>
> Mr S told us with outward calm, "I shall come again next Wednesday. I will bring a piece of rope with me. If the tablets are still not here, I am going to hang myself from that tree". He pointed to the window. I believed he meant what he said.
>
> Stock-outs are no longer a problem for palliative care in Kerala, but throughout most of the rest of India, and indeed our world, we find near total lack of access to morphine to alleviate pain and suffering.
>
> *Dr M R Rajagopal, personal testimony*

Poor people in all parts of the world live and die with little or no palliative care or pain relief. Staring into this access abyss, one sees the depth of extreme suffering in the cruel face of poverty and inequity.

The abyss is broad and deep, mirroring relative and absolute health and social deprivation. Of the 298·5 metric tonnes of morphine-equivalent opioids distributed in the world per year (average distribution in 2010–13), only 0·1 metric tonne is distributed to low-income countries.[1] The amount of morphine-equivalent opioids distributed in Haiti is 5 mg per patient in need of palliative care per year, which means that more than 99% of need goes unmet. By contrast, the annual distribution of morphine is 55 000 mg per patient in need of palliative care in the USA and more than 68 000 mg per patient in need of palliative care in Canada—much more than is needed to meet all palliative care and other medical needs for opioids on the basis of estimates of the Commission (figure 1).

The fact that access to such an inexpensive, essential, and effective intervention is denied to most patients in low-income and middle-income countries (LMICs) and in particular to poor people—including many poor or otherwise vulnerable people in high-income countries—is a medical, public health, and moral failing and a travesty of justice. Unlike so many other priorities in global health, affordability is not the greatest barrier to access, and equity-enhancing, efficiency-oriented, cost-saving interventions exist.

The global health community has the responsibility and the opportunity to close the access abyss in the relief of pain and other types of suffering at end-of-life and throughout the life course, caused by life-limiting and life-threatening health conditions. However, unlike many other essential health interventions already identified as priorities, the need for palliative care and pain relief has been largely ignored, even for the most vulnerable populations, including children with terminal illnesses and those living through humanitarian crises, and even in the Sustainable Development Goals (SDGs).[2] Yet palliative care and pain relief are essential elements of universal health coverage (UHC).

Several barriers explain this neglect: the focus of existing measures of health outcomes—major drivers of policy and investment—on extending life and productivity with little weight given to health interventions that alleviate pain or increase dignity at the end of life;[3] opiophobia, which refers to prejudice and misinformation about the appropriate medical use of opioids;[4–6] the focus, in medicine, on cure and extending life and a concomitant neglect of caregiving and quality of life near death;[7,8] limitations on patient advocacy due to the seriousness of illnesses; the focus on preventing non-medical use of internationally controlled substances without balancing the human right to access medicines to relieve pain;[9–12] and the global neglect of non-communicable diseases, which account for much of the need for palliative care.[13]

Global health is devoid of the investments, interventions, and indicators that are essential to ensure universal access to safe, secure, and dignified care at the end of life or to the palliation of pain and suffering. With this Report, we aim to remedy these limitations by: (1) quantifying the heavy burden of serious health-related suffering (SHS) associated with a need for palliative care and pain relief (section 1); (2) identifying and costing an Essential Package Of Palliative Care And Pain Relief Health Services (the Essential Package) that would alleviate this burden (section 2); (3) measuring the unmet need for one of the most essential components of the

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See **Comment** page 1338

*Equal contributors

†Senior authors

‡Study group members are listed at end of this Report

Department of Public Health Sciences, Leonard M Miller School of Medicine (Prof F M Knaul PhD, Prof J Frenk MD), **Institute for Advanced Study of the Americas** (Prof F M Knaul, A Bhadelia PhD, X Jiang Kwete MD, H Arreola-Ornelas MSc, N M Rodriguez PhD), **Sylvester Comprehensive Cancer Center** Prof F M Knaul), **and School of Business Administration** (Prof J Frenk), **University of Miami, Coral Gables, FL, USA; Tómatelo a Pecho, A.C., Mexico City, Mexico** (Prof F M Knaul, H Arreola-Ornelas); **Fundación Mexicana para la Salud, AC, Mexico City, Mexico** (Prof F M Knaul, H Arreola-Ornelas); **Harvard Medical School, Boston, MA, USA** (Prof P E Farmer MD, E L Krakauer MD, Prof R Atun FRCP); **Massachusetts General Hospital, Boston, MA, USA** (E L Krakauer); **World Health Organization, Geneva, Switzerland** (E L Krakauer); **International Association for Hospice and Palliative Care, Houston, TX, USA** (L De Lima MHA, Prof L Radbruch MD); **Department of Global Health and Population** (A Bhadelia, X Jiang Kwete, Prof R Atun), **Department of**

Health Policy and Management (Prof R Atun), **Department of Epidemiology** (Prof D J Hunter MBBS) **and Department of Nutrition** (Prof D J Hunter), **Harvard TH Chan School of Public Health, Boston, MA, USA; National Institute of Public Health, Morelos, Mexico** (Prof O Gómez-Dantés MD); **Pan American Health Organization, Regional Office of WHO, Washington, DC, USA** (Prof G O A Alleyne MD); **Worldwide Hospice Palliative Care Alliance, London, UK** (S R Connor PhD); **Nuffield Department of Population Health, University of Oxford, Oxford, UK** (Prof D J Hunter); **Health and Human Rights Division, Human Rights Watch, Maplewood, NJ, USA** (D Lohman MA); **Department of Palliative Medicine, University Hospital Bonn, Germany** (Prof L Radbruch); **The Malteser Hospital, Bonn, Germany** (Prof L Radbruch); **Costa Rican Social Security Fund, San José, Costa Rica** (M del Rocío Sáenz Madrigal MD); **Weill Cornell Medical College, New York City, NY, USA** (Prof K M Foley MD); **University of California, San Francisco, CA, USA** (Prof D T Jamison PhD); **and Trivandrum Institute of Palliative Sciences, WHO Collaborating Centre for Training and Policy on Access to Pain Relief, Pallium India, Kerala, India** (M R Rajagopal MD)

Correspondence to: Prof Felicia Marie Knaul, Institute for Advanced Study of the Americas, University of Miami, Miami, FL 33146, USA **fknaul@miami.edu**

For **WHO's 2015 Global Health Estimates** see http://www.who.int/healthinfo/global_burden_disease/en

For **additional online material** see http://www.miami.edu/lancet

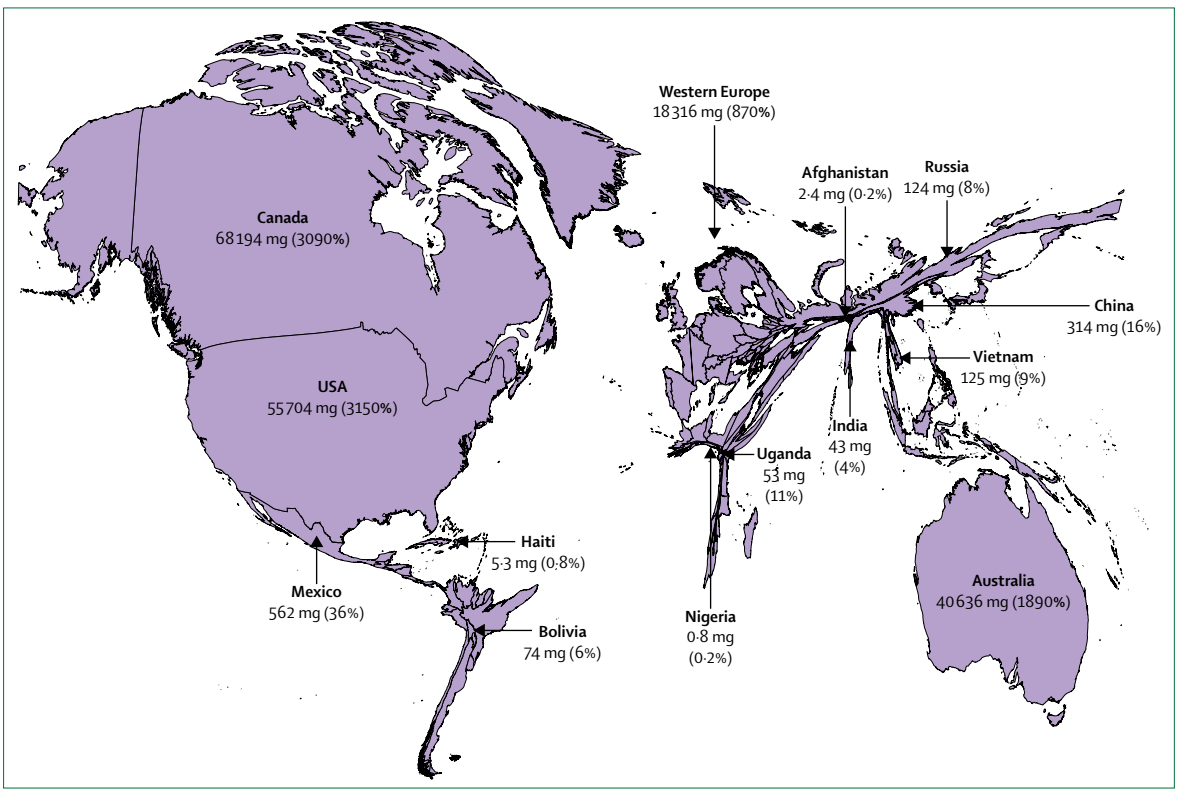

***Figure 1*: Distributed opioid morphine-equivalent (morphine in mg/patient in need of palliative care, average 2010–13), and estimated percentage of need that is met for the health conditions most associated with serious health-related suffering**
Source: International Narcotics Control Board and WHO Global Health Estimates, 2015. See additional online material for methods.

package—inexpensive, immediate-release oral and injectable morphine (section 2); and (4) outlining national and global health-systems strategies to expand access[14] to palliative care and pain relief as an integral facet of UHC by applying a balanced approach that ensures adequate attention to both the medical needs of all patients and the risk of non-medical use (section 3).[12] Our findings and recommendations are summarised in five key messages (panel 1).

Alleviating SHS is a global health and equity imperative

The Commission developed a new conceptual framework for measuring the global burden of SHS. Suffering is health-related when it is associated with illness or injury of any kind. Suffering is serious when it cannot be relieved without medical intervention and when it compromises physical, social or emotional functioning. Palliative care should be focused on relieving the SHS that is associated with life-limiting or life-threatening conditions or the end of life. We analysed the 20 health conditions and 15 symptoms typically associated with these health conditions that cause most of the burden of SHS. We undertook this far-reaching analysis of health conditions because we recognise and uphold the importance of including previously neglected diseases within the realm of palliative care.

More than 25·5 million people who died in 2015—45% of the 56·2 million deaths recorded worldwide—experienced SHS. Of those, more than 80% of the people who died with SHS in 2015 were from developing regions, and the vast majority lack access to palliative care and pain relief.

Every year almost 2·5 million children die with SHS and more than 98% of these children are from developing regions. In high-income countries, children account for less than 1% of all deaths associated with SHS, whereas in low-income countries, children account for more than 30% of all deaths associated with SHS. Yet we also estimate that in low-income countries at least 93% of child deaths associated with SHS are avoidable.

Including both those who die in a given year and the many who live with life-threatening or life-limiting health conditions, we estimate that more than 61 million people are affected by SHS. More than 80% of these patients live in LMICs where palliative care and pain relief is scarce or non-existent.

The annual burden measured in days of physical and psychological SHS is huge—more than 6 billion days, or up to 21 billion days worldwide, depending on symptom overlap. Although HIV and cancer rank highest overall among conditions accounting for both number of people who experience SHS and the total days with SHS, even in

LMICs a number of other chronic and non-communicable diseases rank among the top 10 conditions, including cerebrovascular disease, dementia, lung disease, liver disease, non-ischaemic heart disease, and injuries. As populations age and undergo epidemiological transition, SHS for these complex diseases will become more common relative to acute, preventable illness.

However, infection and poverty-associated health conditions continue to affect people in LMICs, and more than half of the SHS burden in terms of number of patients is associated with avoidable, premature deaths. For example, more than 95% of deaths associated with tuberculosis are avoidable. Palliative care cannot be a substitute for improved access to the public health interventions and treatments that could have prevented much of the SHS and premature deaths in the first place.

A lowest-cost Essential Package can alleviate most SHS

The Commission's expert panel of palliative care providers determined that much of the SHS burden could be alleviated with health services that can be made accessible to poor people living in all parts of the world. We developed an Essential Package that is the minimum a health system, however resource-constrained, should make universally accessible (panel 2).

The Essential Package is lowest cost by design (section 2), yet universal access to this Essential Package will rely on additional investment that would equate to a high proportion of health expenditure in low-income countries, especially with the additional cost of ensuring safe supply chains and training. With budget constraints, this will mean trade-offs against other health-system priorities, and we propose a framework for measuring the value to patients and families of alleviating SHS that would complement existing metrics like quality-adjusted life-years (QALYs) and enable balanced decision making.[18] We also present mechanisms for accessing lowest prices through collective action, adopting human resource models based on competencies to lower cost, and extending coverage through more efficient delivery models. We highlight the opportunities for cost-saving by reducing end-of-life hospital admissions, reducing the risk of impoverishment, and adopting the diagonal approach.[19–24] For example, access to best international prices would reduce overall costs of the Essential Package for low-income countries by about 25%. Prices paid by countries for medicines, especially injectable morphine, vary enormously; for example, the overall medicine cost of the Essential Package in Rwanda, using reported country prices (additional online material), is nearly three times that using lowest reported international prices, whereas for injectable morphine, the difference in price is almost six fold.

Although a rigorous cost-effectiveness analysis was beyond the scope of this report, we compared the costs of the Essential Package to estimates of UHC packages.

***Panel 1*: Global access to palliative care and pain relief: five key messages**

The findings and evidence presented by the Commission demonstrate that:

1. Alleviation of the burden of pain, suffering, and severe distress associated with life-threatening or life-limiting health conditions and with end of life is a global health and equity imperative. Most high-income countries have responded with effective interventions, yet the needs of poor people have been neglected, and people living in low-income and middle-income countries (LMICs) have little or no access to pain relief or palliative care.
2. An affordable, Essential Package of palliative care and pain relief interventions can ameliorate a large part of the preventable burden of serious health-related suffering (SHS), and this package can be made universally accessible to remedy the abyss in access to care.
3. LMICs have enormous but unrealised opportunities to improve the welfare of poor people at modest cost. Publicly financing and fully integrating the Essential Package into national health systems as part of universal health coverage, using cost-effective models that can be applied in all countries, offers a solution.
4. International collective action is necessary to ensure that all people, including poor people, have access to palliative care and pain relief for life-threatening and life-limiting health conditions and end-of-life care. A well functioning and balanced global system must both prevent non-medical use and misuse of medicines and ensure effective access to essential medicines for palliative care, including opioids for pain relief.
5. Effective policy making requires better evidence and priority-setting tools to adequately measure the global need for palliative care, implement policies and programmes, and monitor progress toward alleviating the burden of pain and other types of SHS.

Our Essential Package follows the most recent Disease Control Priorities methods[25] and is one of the least costly of the components that form the essential UHC package. For low-income countries, the Essential Package costs, at lowest reported international medicine prices, about US$2·16 per capita per year, which is about 2–3% of the cost of the essential UHC package. In lower-middle-income countries, the cost is $0·78 (0·6% of the cost of the essential UHC package).

One of our most emphatic recommendations is that immediate-release morphine be made available in both oral and injectable formulations in the appropriate and neccesary dose for any patient with moderate-to-severe pain or terminal dyspnoea that cannot be relieved adequately by other means. The enormous gap between need and availability of opioid analgesics is growing and is increasingly skewed against people living in poverty. However, we estimate that the cost of meeting the global shortfall of about 48·5 metric tonnes of morphine-equivalent opioids is about $145 million per year if all countries had access to the lowest retail prices paid by some high-income countries, which is a fourth of the projected cost at current region-specific reported prices. The shortfall in LMICs accounts for more than 99% of this, and the cost to cover this unmet need in LMICs at lowest retail prices is only 0·009% of LMIC health expenditure in 2015. For low-income countries, the cost of meeting the shortfall in morphine is

Panel 2: An Essential Package Of Palliative Care And Pain Relief Health Services

The Essential Package contains the inputs for safe and effective provision of essential palliative care and pain relief interventions to alleviate physical and psychological symptoms, including the medicines and equipment that can be safely prescribed or administered in a primary care setting. The list of essential medicines in the Essential Package is based on WHO's list of essential medicines,[15] and considers the medicines, doses, and administration routes for palliative care for both adults and children.

The Essential Package is designed to be lowest cost by including only off-patent formulations, frugal innovation for needed equipment, and a staffing model based on competencies rather than professions. Tasks often undertaken by specialised medical personnel in high-income countries can be performed by other specialised and general practitioners and nurses or by community health workers empowered with the necessary training and medical supervision to participate effectively in the delivery of palliative care and pain treatment at all levels of care, from the hospital to the home.[16,17]

With the key exception of morphine, the medicines in the Essential Package are available in most countries even if supply is limited. For morphine, an essential palliative care medicine, assuring safety and accessibility is complex. Ensuring a balance between appropriate medical access to controlled medicines and the prevention of their diversion and non-medical use is crucial, and the Commission not only designed appropriate human resource models but also the strategies to provide the complementary policy and stewardship to expand access to an Essential Package that includes morphine.[12]

The health services of the Essential Package must be complemented by interventions for the relief of social and spiritual suffering to preserve the dignity of patients, facilitate access to health interventions, and prevent financial hardship and impoverishment. Yet, these social supports are neither part of the remit of health ministries nor should they be financed from a health budget.

Antipoverty and social development policies, publicly funded safety nets, programmes, and ministries must give special attention to ensure that families do not sacrifice their basic needs in desperate attempts to care for loved ones. These persons with life-limiting or life-threatening health conditions and their families should be mainstreamed into existing social support and social welfare programmes, yet they are often ignored, excluded, or marginalised, preventing them from being effectively integrated into these programmes.

Medicines

- Amitriptyline
- Bisacodyl (Senna)
- Dexamethasone
- Diazepam
- Diphenhydramine (chlorpheniramine, cyclizine, or dimenhydrinate)
- Fluconazole
- Fluoxetine or other selective serotonin-reuptake inhibitors (sertraline and citalopram)
- Furosemide
- Hyoscine butylbromide
- Haloperidol
- Ibuprofen (naproxen, diclofenac, or meloxicam)
- Lactulose (sorbitol or polyethylene glycol)
- Loperamide
- Metoclopramide
- Metronidazole
- Morphine (oral immediate-release and injectable)
- Naloxone parenteral
- Omeprazole
- Ondansetron
- Paracetamol
- Petroleum jelly

Medical equipment

- Pressure-reducing mattress
- Nasogastric drainage or feeding tube
- Urinary catheters
- Opioid lock box
- Flashlight with rechargeable battery (if no access to electricity)
- Adult diapers (or cotton and plastic, if in extreme poverty)
- Oxygen

Human resources (varies by referral, provincial or district hospital, community health center, or home

- Doctors (specialty and general, depending on level of care)
- Nurses (specialty and general)
- Social workers and counsellors
- Psychiatrist, psychologist, or counsellor (depending on level of care)
- Physical therapist
- Pharmacist
- Community health workers
- Clinical support staff (diagnostic imaging, laboratory technician, nutritionist)
- Non-clinical support staff (administration, cleaning)

Additional detail is provided in the additional online material.

$69 million per year, compared with $13 million per year at lowest retail prices.

The cost to cover morphine-equivalent pain treatment for all children younger than 15 years with SHS in low-income countries is $1 million per year. This is a pittance compared with the $100 billion a year the world's governments spend on enforcing global prohibition of drug use.[26]

Integration of palliative care and pain relief interventions, beginning with the Essential Package, will strengthen national health systems to meet the SDGs

By definition, palliative care is a core component of UHC and a key element of quality health care.[27–29] Yet in most parts of the world, the definition has not been translated into practice.

Countries cannot meet SDG Target 3.8 on UHC without including palliative care and pain relief, and the Commission calls on all countries to ensure universal access, with financial risk protection, to the Essential Package by 2030.[2] As posited by previous *Lancet* Commissions,[30] a model of progressive universalism should be applied, and middle-income countries in particular should strive to have the Essential Package in place before 2030 and to expand the Essential Package to include palliative surgery and slow-release, off-patent morphine formulations, radiation, and chemotherapy.

The benefits of universal access to palliative care and pain relief spill into other parts of a health system and contribute to the quality of care. Systemic integration of palliative care and pain relief is a quintessential example of the diagonal approach[24,31,32] because the implementation of these interventions will strengthen the overall performance of health systems. Findings from an extended cost-effectiveness analysis undertaken for the Commission suggest that universal, public financing of the Essential Package can reduce risk of catastrophic health-care expenditures, a main cause of impoverishment in LMICs.[33,34] Finally, in an extensive review of literature about the introduction of palliative care and data analysis from Mexico, we found important, potential cost-saving in LMICs by reducing end-of-life hospital admissions.[19–23,35]

Health-system functions of stewardship, financing, delivery, and resource generation[36] must be strengthened to expand access to palliative care and pain relief in the context of UHC. For stewardship, the Commission stresses that each country should: (1) design and implement legal and regulatory guidelines that include the safe management of opioid analgesics and other controlled medicines without creating unnecessary barriers for patients, covering all service providers who participate in palliative care and pain treatment, and restricting the influence of for-profit companies on the marketing of opioid medications; (2) encourage priority-setting public education and awareness-building campaigns, and incorporate the alleviation of SHS into the national health agenda; (3) develop and implement comprehensive palliative care and pain treatment and management guidelines and national plans; and (4) convene and coordinate the multisectoral actors and entities that engage in palliative care and pain relief through ministries of health.

Public financing for palliative care and pain relief is crucial, and the Essential Package must be integrated into all existing national insurance and social security programmes and included in systemic health reforms. The Commission recommends that governments allocate public or publicly mandated resources to cover the Essential Package, especially for poor people, and establish mechanisms to expand funding to extend the package of covered services.

The Essential Package must be anchored in clinical guidelines and referral systems to ensure safe and effective delivery at all levels of care. In primary care, this relies on nurses, general practitioners, community health workers, efficient referral systems, and extensive use of appropriate communication technologies (eg, mobile phones). Palliative care must become a recognised, licensed medical specialty in every country, and all licensed general practitioners who provide palliative care should have training to achieve basic competencies.[37,38]

Each country must design and implement an accountability framework that includes monitoring and evaluation of legislative provisions, policies, interventions, and programmes. Progress on health and on human rights can be monitored with explicit outcomes scales and benchmarks, using an appropriate set of metrics that extend beyond mortality and morbidity. Effective management relies on data monitoring and indicators of palliative care and pain relief that are embedded in national and subnational health information systems. Civil society and academia should be part of performance assessment and accountability initiatives, and data and results must be publicly available.

We advocate for countries to establish interdisciplinary, interinstitutional, multistakeholder committees that can eventually be formally associated with their ministries of health. These should include the diverse participants who have historically been or could in the future be involved in policy making and delivery of palliative care and pain relief, such as parliamentarians, lawmakers, representatives of faith-based organisations and other not-for-profit civil society organisations, and the for-profit private sector.[39] As with previous *Lancet* Commissions,[40] our Report can serve as impetus, and this Commission as an example, for developing these national committees or commissions.

The appropriate response to the global burden of untreated SHS is to expand access to effective palliative care and pain relief alongside the expansion of other components of UHC. Health systems need to be strengthened through the integration of palliative care alongside prevention, early detection, treatment, and rehabilitation strategies to ensure that all patients have access to effective, efficient, and responsive care strategies and full information. This will ensure that an effective response to suffering is at the core of a people-centred approach to health systems.

Effective global collective action is needed to expand access to palliative care and pain relief

To achieve universal access to palliative care and pain relief, global health institutions must become adept at promoting and facilitating effective action by countries. Activities should be focused on four core functions: (1) international stewardship; (2) production of global public goods, especially knowledge-related goods; (3) management of externalities; and (4) mobilisation of global solidarity and convening.[41]

The 2014 World Health Assembly (WHA) Resolution 67.19[42] gives WHO the mandate and mission to become the leading global steward for achieving universal access to palliative care as part of UHC. By voting for the Resolution, countries publicly attested to their intention to implement the recommendations targeted at member states. However, the translation of commitment into progress is weakened by the absence of an accountability framework.[43] The Commission calls for WHO to develop and implement a formal accountability mechanism tied to the Resolution that includes specific indicators, associated targets, and recommendations for corrective action. Lessons from the AIDS response are testatment to the salience of these global systems.[39]

Stewardship of palliative care must be intersectoral and interinstitutional, especially because of the role of the UN Office on Drugs and Crime and the International Narcotics Control Board (INCB).[42] The *Lancet* Commission on Essential Medicines put forward proposals for action,[44] and we strongly support these recommendations and suggest working jointly to ensure access to medicines for pain relief.

Knowledge exchange is crucial to effective investment in change and is needed to assist countries to effectively adapt and adopt systemic innovations. We recommend that both global and regional actors invest in evidence to facilitate corrective policies and ensure effective progress. Of highest importance are: the indicators, measures, and metrics for routine data collection and reporting in palliative care; the design of clinical guidelines; and training material, including standardised, global, online curricula. Much of this work should be done by international agencies such as WHO, but international civil society organisations and academics also have a role.

For the management of externalities through global collective action, the Commission focused on the limitation of access to controlled medicines for pain relief, especially in LMICs. Global entities and countries must maximise access to morphine for medical and scientific use while minimising the risk of diversion and non-medical use. Countries have considerable leeway in applying the principals of international law and treaties to adapt to local situations in ways that promote balance.[12] Countries that report high consumption of opioids and little or no non-medical use must disseminate lessons learned and best practices. In most LMICs, unduly restrictive laws and regulations hinder the availability of and access to opioids for people with legitimate needs. Yet there is reason to assume that the diversion and non-medical use of drugs is not a function of increasing medical access in LMICs, but rather a consequence of inadequate safeguards to minimise such diversion in certain high-income countries.[45,46]

The Commission found substantial potential savings if countries could access best-case international medicine prices, evidencing the need for global collective action to aggregate demand, better understand the market and supply, and support LMICs with information and negotiating capacity to secure stable, lowest prices. We advocate for establishing global or regional purchasing and procurement funds and financing entities to facilitate access to the medicines outlined in the Essential Package, especially immediate-release oral morphine. To secure best quality and price, and to provide technical assistance to countries in establishing safe and effective supply chains, the Commission calls on the World Bank, regional development banks, WHO, and the The Global Fund to Fight AIDS, Tuberculosis and Malaria to establish financing platforms to link to the provision of other medicines for treatment of chronic and non-communicable diseases. The pharmaceutical industry must be called upon to participate in making these off-patent medicines accessible and affordable.

Children in need of palliative care face tremendous barriers to access, and removing these barriers must become a priority. The absolute number of children in need of palliative care is relatively small, so the cost of providing them with the Essential Package is very low. The Commission advocates that the World Bank, as a leading global development financing facility with expertise in innovative financing, be called upon to develop and manage a fund with a strong focus on low-income countries where even the Essential Package is likely to be price-prohibitive and supply channels are least developed.

The relief of SHS has not been prioritised in humanitarian disasters, and even the most basic inputs such as morphine are often inadequate or entirely unavailable. Global humanitarian assistance organisations must include palliative care and pain relief medicines and experts in all responses to natural disasters or disasters caused by human beings. The Commission calls upon WHO to work with international humanitarian assistance agencies to develop funding, delivery, and accountability mechanisms that ensure access to palliative care and pain relief.

Effective national and global policy making must be evidence-based, and this requires a rigorous, vigorous, and substantive research agenda

The research agenda must provide the key knowledge for closing the access abyss and the tools to both set and monitor global and national priorities and progress on

palliative care and pain relief. The Commission sets forth the elements of an agenda that emphasises the need to develop strong metrics and data to monitor progress and implement research around SHS.

This research and dissemination agenda will demand resources. Very few foundations and donors prioritise work on palliative care and pain relief in LMICs; most of those that previously provided support have now closed their programmes.[47] To support these research endeavours, the Commission calls on non-governmental and governmental research funding agencies and foundations to incorporate palliative care and pain relief into their priorities in health and social development. Although this funding can be triggered by researchers, to date only a small group of palliative care specialists have prioritised international work, and the issue has been largely ignored by experts working on specific health conditions associated with SHS, many of which are neglected non-communicable diseases.[13]

Afterlife of the Commission: advocacy, accountability, and analysis

The Commission should provide a platform to push for progress and ensure accountability. We have engaged with civil society to enable the Commission's evolution into a working group of leaders from global, national, and regional palliative care advocacy institutions. The mandate of the working group is to: develop monitoring frameworks and public accountability tools, including indicators and targets that can be adapted and adopted by both countries and global governance institutions; support national commissions through training and capacity building; catalyse national planning for palliative care and pain relief; encourage the production and dissemination of knowledge from implementation and health-systems research, especially in LMICs; and forge linkages between the palliative care community and the non-communicable diseases movement.[48]

The working group will report periodically on progress in implementing the recommendations of the Commission and on the degree of uptake by national and global stewards. This work is aligned with previous and planned initiatives of three global non-governmental organisations (International Association for Hospice and Palliative Care, International Children's Palliative Care Network, and Worldwide Hospice Palliative Care Alliance), each of which is committed to facilitating the work of this group in collaboration with regional and national civil society representing Africa, Asia, eastern Europe, Latin America, and the Caribbean.

Introduction

> From that moment commenced the shrieking fit which lasted for three days, and was so terrible that it was impossible to hear it without horror even through two doors.
>
> *Leo Tolstoy, The Death of Ivan Ilyich, 1886*

Imagine your final months, weeks, and days of life. Like most, you probably hope to be free of pain. Consider, however, a scenario in which you and those who hold you dear face those painful days with no access to the palliative care that could alleviate your suffering: Tolstoy's Ivan Ilyich bereft of even opium to calm the fear and agony. Unimaginable? Yet this is the reality for most people. With few exceptions, poor people throughout the world live and die with little or no access to pain relief or any other type of palliative care.

Access to palliative care and pain relief is a health, equity, and human rights imperative that has been largely ignored in the goal to achieve UHC. Indeed, our Commission[49] found no other important health intervention as lacking or inequitably distributed as pain relief, the pillar of palliative care. The global health community has the responsibility and the opportunity to close this access abyss by providing universal access to an affordable package of palliative care services that can alleviate the remediable suffering associated with life-threatening and life-limiting health conditions.

The access abyss is both relative and absolute. Of the 298·5 metric tonnes of morphine-equivalent opioids distributed in the world each year (an average from 2010–13), 287·7 metric tonnes are distributed to high-income countries, and this distribution is dramatically skewed to a few countries. Only 0·1 metric tonnes—0·03% of the total amount—are distributed to low-income countries. In the poorest decile of countries, a patient with life-threatening or life-limiting health conditions has access to only 10 mg morphine-equivalent opioids per year. Our estimates show that this amount is sufficient to meet less than 2% of palliative care needs and an even smaller proportion of the total medical need for pain relief medicines. In the world's wealthiest decile of countries, each patient in need of palliative care has access to more than 47 000 mg morphine-equivalent opioids per year, which is much more than is needed to meet all palliative care and other medical needs for opioids if all patients in these countries were to have appropriate and necessary access to these essential medicines. The fact that most patients, poor patients in particular—including many poor people in high-income countries—are denied access to such an inexpensive and powerful intervention is a medical, public health, and moral failing.

Although many other inequities have been identified as health-care priorities, injustice in access to palliative care and pain relief has been largely ignored, even for children and people at the end of life. This is particularly surprising because we find that most of the burden of SHS, can be alleviated with effective, low-cost interventions contained in an Essential Package that can be made accessible to people living in poverty anywhere in the world.

Current needs for palliative care and pain relief are large and will grow. According to the Commission's

estimates of the need for palliative care throughout the life course and at the end of life, more than 25·5 million people who died in 2015 (45% of the 56·2 million reported deaths worldwide) would have benefited from palliative care. More than 35·5 million people who did not die in 2015 also experienced SHS, and although they did not die from their health conditions, they should have received palliative care or treatment for pain and other types of suffering. More than 80% of these people live in LMICs where access to basic palliative care and medicine-based pain relief is extremely limited or non-existent.

With populations ageing, the number of frail elderly people increasing, and chronic diseases and non-communicable diseases becoming increasingly common, the need for palliative care will grow.[50,51] Between 2015 and 2050, the population of persons aged 60 years or older is projected to more than double, and the number of people aged 80 years or older is projected to more than triple.[52] Between 2015 and 2030, the fastest population growth is expected in Latin America, the Caribbean, Asia, and Africa.[52] In 2015, non-communicable diseases accounted for 60% of the global disease burden (in disability-adjusted life-years), compared with 43% in 1990. More than 70% of deaths in 2015 were attributable to non-communicable diseases, and more than 75% of these deaths occurred in LMICs.[53] Non-communicable diseases such as cancer, dementia, cerebrovascular disease, and lung disease cause a large proportion of SHS, and they are expected to cause increasing SHS as LMICs undergo epidemiological transition.

The global movement to achieve UHC, an SDG3 target[54] that focuses on ensuring healthy lives and wellbeing for all people and at all ages, provides new opportunities to expand access to palliative care at a time when need is increasing rapidly.[2,55] Yet the interest, investment, and indicators needed to guarantee universal access to safe, secure, and dignified care until death, and to ensure palliation of pain and suffering throughout life, are grossly inadequate. Policy makers and providers do not prioritise palliative care, and efforts to promote human development, reduce poverty, and strengthen health systems are stymied, which in turn reduces the capacity of countries to achieve SDG3.[2]

To remedy this vacuum in global health and close the access abyss in palliative care and pain relief, the Commission dedicated itself to estimating the burden of SHS, identifying the basic interventions needed in an Essential Package to remedy this burden, demonstrating the inequity of access to pain relief, and outlining national and global health-system strategies for providing universal access to this Essential Package.

Barriers to increased access to palliative care and pain relief

Achieving effective access to palliative care and pain relief is not only a function of the affordability and availability of health services and technologies.[14] Why have maintaining dignity and security at the end of life and alleviating extreme pain and suffering not become health priorities?

First, existing measures of health outcomes—major drivers of policy and investment—focus on extending healthy life and productivity. Health interventions that relieve pain and suffering but do not extend life have not been effectively integrated into these outcome measures.[56,57]

To this we add opiophobia, the prejudice and mis-information surrounding the appropriate medical use of opioids in the context of a balanced approach that reduces risks of non-medical use.[4,5,11] A prevalent but unwarranted fear of non-medical use and addiction to opioids and opioid-induced side-effects, both among health-care providers and regulators and among patients and their families, has led to insufficient medical use. Unbalanced laws and excessive regulation perpetuate a negative feedback loop of poor access that mainly affects poor people. This leads to underestimates of needs, which in turn affects the amounts of opioids that are produced or imported for medical use in a country.[12]

Efforts to prevent non-medical use of internationally controlled substances, such as morphine and other opioid analgesics, have overshadowed and crippled access to opioids for palliative care. These efforts have focused on preventing diversion and non-medical use rather than ensuring access by people with legitimate health needs.[9–12] Even the SDGs reflect this skew toward preventing non-medical use. SDG Target 3.5 makes an explicit call for strengthened "prevention and treatment of substance abuse, including narcotic drug abuse" yet there is no specific mention of palliative care or pain relief in any target or in any part of the SDGs.[54]

Activism by people living with diseases and health conditions who need palliative care and pain relief should be key, as it was to the global AIDS response,[39] yet there are unique barriers. First, many patients with life-threatening and life-limiting health conditions are very weak, and many do not survive. Second, advocacy tends to be disease-specific and focuses on cure and prevention, shying away from the difficult topic of death. Finally, pain relief has been overshadowed by advocacy efforts around substance control.

Lack of attention to palliative care is also the result of developments in the science of medicine. In much of medical history, the palliation of suffering was the core of medicine and was practised by all doctors, largely because so few effective interventions were available to cure patients. As medical science evolved, doctors were increasingly able to focus on preventing or curing diseases, injuries, and illnesses, marginalising the work of palliating suffering and maximising dignity at the end of life.[7,8] By contrast, from the late 1800s to the last decades of the 20th century, the principles of palliative medicine and the institutional settings for providing terminal care were created, and palliative care developed into a specialised field of medicine (panel 3).

Panel 3: A history of palliative care

Modern palliative care emerged in the 1960s and 1970s, though with much earlier roots. In the 19th century, doctors devised the principles of palliative medicine, showing the value of new pain-relieving medicines and technologies and mapping the challenges of caring for those with advanced disease at a time when society became concerned about the process of dying. Notable was Munk's 1887 treatise on easeful death, in which he described practical, spiritual, and medical end-of-life support.[58]

In parallel, specialised institutional care for dying people in hospices began in several countries, including France, Great Britain, India, South Africa, the USA, and Zimbabwe. Although limited in scale, their philosophy of care inspired others.

Among them was Cicely Saunders who launched a movement in the 1960s for care of the dying, incorporating new knowledge and methods. Her concept of total pain with physical, social, psychological, and spiritual dimensions, revolutionised thinking and practice.[59] She offered a positive, imaginative alternative to medicine's despairing rejection of dying patients and sought to ensure pain relief, maintain dignity, and enhance remaining life, however short. Her approach was embodied in St. Christopher's Hospice, founded in 1967 as the first modern hospice to include research and training facilities. Its influence quickly spread worldwide.

To gain traction in the world of medicine, these protagonists moved from activism to a concerted body of knowledge and practice. Management of cancer pain proved key. Early studies explored and reconsidered prevailing orthodoxies. New competence emerged in use of morphine and other medicines, reinforced by clinical research, which fuelled investment and growth in services.[60]

Balfour Mount is credited with coining palliative care,[61] a term adopted in the 1970s that came to signify the transfer of hospice principles into wider settings within the health-care system, including acute care hospitals, primary care, and homes. Specialist journals were created to disseminate research and clinical practice, and national and international associations were formed. A new field of research was created.

Formal recognition of palliative medicine as a specialty began in the UK in 1987, and extended to other countries and to nursing.[62] WHO had a major role in 1986 when it acknowledged the under-treatment of cancer pain as a public health problem and published the revolutionary Pain Relief Ladder[63] with simple recommendations to treat pain in three steps: mild, moderate, and severe. Recognising the need for a comprehensive approach to palliative care, WHO published a definition of palliative care in 1990[64] and emphasised the importance of symptom management and pain relief. In a 2002 revision, WHO extended their definition of palliative care beyond cancer.[65]

The field of palliative care was now poised for a global role, and huge levels of unmet need were identified. Palliative care was drawn increasingly to a public health framework of appropriate policies, services, and interventions, together with suitable quality assurance and evaluation.[66] Full recognition of the opportunities and challenges came with the World Health Assembly Resolution of 2014 calling all governments to integrate plans for palliative care into their national heath policies.[42]

Definition of palliative care

The Commission worked with WHO's definition of UHC, which calls for all people to have access to the promotive, preventive, curative, rehabilitative, and palliative health services they need, of sufficient quality to be effective, while also guaranteeing that the use of these services does not expose them or their families to financial hardship.[67] This definition includes palliative care as a core component of UHC.[42]

Thus, by definition, no health system can achieve UHC without guaranteeing universal access to at least a minimum package of palliative care services.[68] Yet the expansion of access to palliative care can proceed alongside or precede expansion of coverage of other services. In line with the thesis of progressive universalism and pro-poor health-care strategies,[30] the provision of basic palliative care does not require the achievement of UHC. The rollout of the Essential Package can and should proceed as part of the extension of the most basic aspects of coverage of other health-care components.[69] Covering palliative care is also part of guaranteeing financial protection, a fulcrum of UHC, that frees low-income families from choosing between witnessing a loved one's suffering or incurring impoverishing and catastrophic health spending and foregoing basic needs that drives them further into poverty.

Efforts to provide universal access to palliative care can never excuse the failure to provide other components of UHC. No health system can claim to meet the health-care needs of its citizens if it focuses on palliation and neglects prevention services, disease management, or treatment. This is a crucial caveat. Too many people living in poverty die prematurely because of inadequate access to prevention, early diagnosis, and timely and effective treatment of health conditions. The Commission analysed avoidable mortality to demonstrate this association empirically.

WHO's definition of palliative care is the Commission's starting-point: "an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial, and spiritual".[67] Yet WHO's definition dates to 2002 and has limitations, and the Commission recommends that the definition be reviewed and revised

to encompass health-system advances and low-income settings where medical professionals often have the difficult task of caring for patients without necessary medicines, equipment, or training.

Building on findings described in the scientific literature and WHO's definition of palliative care, the Commission recommends a definition that explicitly rejects any time or prognostic limitation on access to palliative care, includes complex chronic or acute, life-threatening, or life-limiting health conditions, and considers all levels of the health-care system from primary to specialised care and all settings where palliative care can be delivered.[70] Thus, the Commission treats palliative care as an essential component of comprehensive care for persons with complex chronic or acute, life-threatening, or life-limiting health conditions that should be practised by all health-care and social care providers and by palliative care specialists, and that can be provided in any health-care setting, including patients' own homes.[71]

The definition of children's palliative care shares all elements of palliative care for adults and also emphasises the continuing physical, emotional, and cognitive development that defines medical and social needs of children, including their entitlement to education and play, their understanding of disease and death, the role of the family and home as the centre of care, and the necessary link between the paediatrician and the palliative care professional.[70] Although the Commission did not undertake a separate analysis for children, we recognise and emphasise these distinctions throughout the report.

We emphasise and agree with the models that incorporate palliative care as a core component of disease management, integrated from point of diagnosis of a life-threatening or life-limiting health condition, growing in importance as part of comprehensive treatment or end-of-life care, and culminating with bereavement care.[72] The Commission dedicated itself to measuring both decedent and non-decedent burden of SHS because of our conviction that palliative care is not restricted to end of life. Yet the process of disease and pathways of care are complex, making these calculations difficult. Although widely disseminated models depict a single, linear trajectory from diagnosis to the end of life (figure 2A),[74,75] patients move in and out of palliative care depending on disease trajectory around cure, survivorship, and end of life. There is no standard, and the trajectories vary by disease and point in the life cycle of the patient (figure 2B).[74,76,77]

Integration of palliative care for certain health conditions, such as chronic obstructive pulmonary disease, is challenging because it is not easy to identify advanced stage and the ensuing limited prognosis, and the time during the disease trajectory when patients would benefit from palliative care or from a realignment towards palliative care from treatment goals is often missed. Integrating palliative care into a health system and expanding coverage in ways that do not prevent patients from accessing curative care should allow for flexibility and fluid integration of disease management and palliative care from the point of diagnosis. Indeed, for patients and families to accept palliative care early on, they must be assured and reassured that acceptance does not mean foregoing disease-modifying treatment.[78]

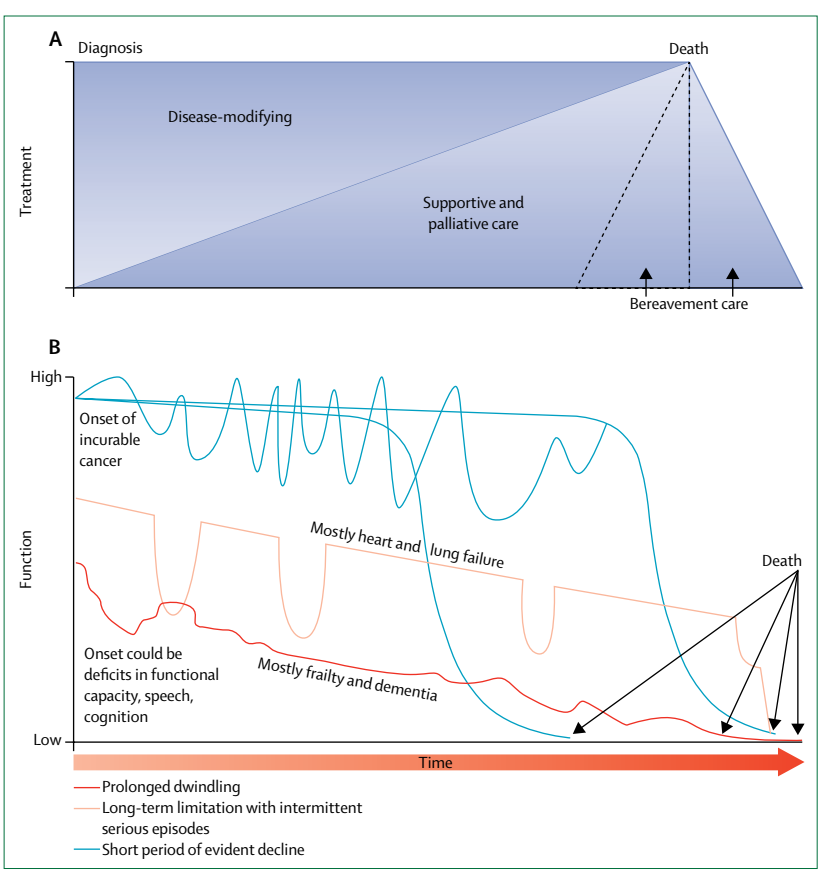

***Figure 2*: Integrating palliative care across illness trajectories**
(A) Palliative care continuum from diagnosis to end of life. (B) Typical functional status trajectorieis of people with progressive chronic illness. Each line in the figure depicts a possible disease trajectory. The blue lines, for example, represent patients with cancers. For example, a patient with pancreatic cancer, with few treatment options and a low 1 year survival rate[16] is represented by the short blue line. The wavy line is more typical of a patient with metastatic cancer who can move between treatment and palliative care, with relatively high functional status, and eventually die of the disease. Source: WHO (1990),[73] Lynn and Adamson (2003).[74]

Scope of the report

Anchored in this definition and model of palliative care, the Commission deliberated at length to define its scope of work and specify the diseases, health conditions, and associated categories of suffering to be analysed. The Commission thoroughly debated, without reaching full consensus, the complex issue of the role of palliative care and the overlap between palliative care and pain treatment and management.

The Commission developed the concept of SHS to describe suffering that compromises physical, social, or emotional functioning, cannot be relieved without medical intervention, and is typically greatly ameliorated

by palliative care and pain relief. The Commission agreed to include within the scope of health-focused palliative care: (1) all health conditions associated with end-of-life; and (2) chronic or acute, life-threatening or life-limiting health conditions, diseases, and injuries. The Commission decided not to focus on acute or chronic health conditions that are not life-threatening or life-limiting, including chronic, non-malignant pain. The scope of the Report is summarised in figure 3.

The Commission insists, however, that SHS of any kind cannot go untreated and that all medical personnel, doctors especially, must be sensitised to respond to the best of their professional capacity. Where health-care resources are inadequate, health conditions that would and should not be serious or life-threatening become so and require palliative care. Particularly in resource-constrained countries and outside large cities where specialty care is unavailable, primary care clinicians must deal with a challenging range of patient needs because specialty medical care, of almost any kind, is often unavailable. The expansion of access to palliative care, and especially pain treatment, will therefore help cover a broad range of SHS.

An overlap in the diseases and symptoms that characterise health conditions that do require palliative care and those that do not, often complicates efforts to clearly differentiate policies and health interventions. Whereas the interventions and policies that we consider in our Report are specific to palliative care, they can often be effectively adapted to cover other realms of patient need, especially pain relief.

Palliative care should be responsive to suffering of any kind and should seek to prevent and relieve not only physical and psychological suffering but also social and spiritual suffering of patients and their families.[67] The Commission decided to focus on physical and psychological suffering because this can be most readily addressed by a health system and because of the empirical and conceptual challenges of measuring spiritual and social hardship. Although remediation of social and spiritual suffering is not the primary role of the health-care system, they are integral interventions of palliative care.[79,80] Social suffering might prevent the delivery of effective palliative care health services, and the Commission has developed recommendations for delivery and financing of these by other social sectors.[81] Patients and families often insist on and need a response to alleviate their spiritual suffering, and with appropriate training and compassion, palliative care professionals can be responsive. While remaining cognisant of the need to respond to social and spiritual suffering, we focused the empirical analysis on SHS and the associated physical and psychological symptoms that can be remediated by an Essential Package within the rubric of a health system.

Although we identified and analysed a range of symptoms, the Commission devoted particular attention

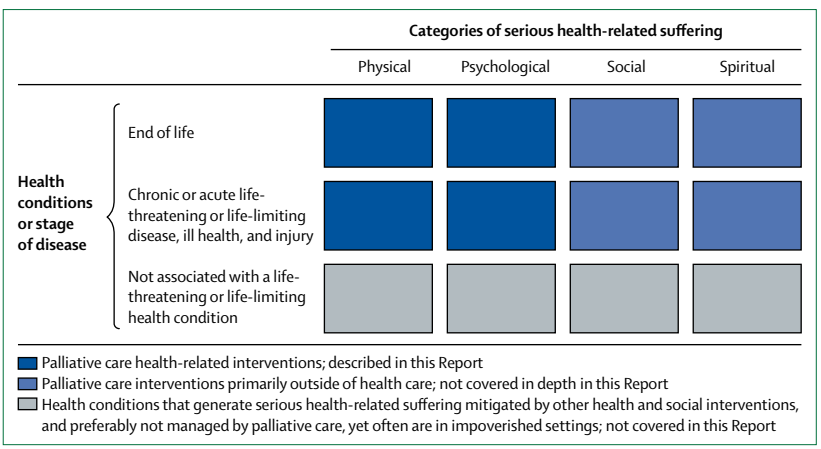

Figure 3: **Serious health-related suffering, palliative care, and scope of this Report**

to the lack of access to pain relief associated with end-of-life care and life-threatening and life-limiting health conditions because pain treatment is essential to palliative care, and lack of access is emblematic of the worst inequities in access to health care. We uphold that access to medicines for the relief of pain is a human right[82–85] and strongly advocate for immediate-release oral morphine to be accessible in LMICs by prescription for patients with medical needs at all levels of the health system, including primary care.

We also recognise that non-medical use of opioids is a real and serious threat. The struggle between addressing the burden of suffering from pain and mitigating the harms that result from non-medical use of opioids is an intersection of two public health priorities.[86] Yet we uphold that there be no confusion with the basic objective of health, rights, and justice of ensuring access to palliative care and pain relief for all, including poor people. In keeping with international agreements and WHO recommendations, we promote and propose applying a balanced approach between maximising access to opioids for rational medical use and minimising risk of diversion and illicit use, and we emphasise this in our national and global health-system analysis and recommendations throughout the Report.[5,6,12] The world needs such a balanced approach because both aims are essential elements of a high quality, just, effective, systemic public health strategy for palliative care and pain relief.

Lessons can be learned from the recent and devastating experiences with the opioid crisis in the USA that point to the importance of the balanced approach (panel 4, figure 4). The situation in most LMICs, where there is virtually no access to any kind of effective medicines to relieve moderate or severe pain, is dramatically and substantively different. Nevertheless, the opioid crisis in the USA shows that vigilance is necessary to achieve and maintain balance in each country's opioid policy as access expands.[100] The Commission also examined cases in other high-income and low-income countries where access to

Panel 4: Opioid analgesics in the USA

In many parts of the world, patients with a medical need for opioid analgesics find it almost impossible to access them, yet in the USA, Canada, and many other high-income countries, opioid analgesics are readily available.[87] The USA, however, is an outlier, not only for the availability of opioids but also because of extreme reliance on these medicines for treatment of acute and chronic pain, which might have contributed to their widespread non-medical use.[88,89] Canada has also reported very high levels of consumption and has recently described, on a much smaller scale, a similar situation as the USA.[90]

According to the US Centres for Diseases Control and Prevention, prescription opioid sales in the USA nearly quadrupled from 1999 to 2014.[91] An estimated one out of five patients with non-cancer pain or pain-related diagnoses was prescribed opioids in office-based settings.[92] Although the types of health issues that cause pain and require opioids do not vary much within the USA, opioid prescribing rates by health care providers vary a lot. Health-care providers in the highest prescribing states write almost three times more prescriptions for opioid analgesics than those in the lowest prescribing states.[93]

As prescriptions of opioid analgesics increased in the USA, so did their non-medical use and incidence of accidental overdose.[94] In 2014, about 28 000 deaths—about 60% of all accidental overdose deaths in the country—were associated with the use of prescription or illegal opioids not intended for palliative care.[91] Between 2000 and 2015, opioid-related overdose (both from prescription and illegal opioids) deaths increased 137% (figure 4).[93] Preliminary data from a subset of states in the USA suggests increases of almost 30% in opioid-related deaths from 2015 to 2016 associated with synthetic opioids.[95]

The notable increase in the prescription of opioid analgesics coincides with the introduction in 1996 of OxyContin (a slow-release oxycodone) and intensive marketing of this medicine for chronic pain. This on-patent, expensive formulation became widely used. New research findings showed that opioid analgesics are not appropriate first-line medicines for many forms of non-malignant and chronic pain, yet the increase in levels of prescribing had already occurred. Claims around the safety of these medicines were based on new formulations erroneously assumed to deter non-medical use. Studies have shown a low risk of non-medical use and drug dependence among patients in palliative care.[96–98] Hospital-based prescribing patterns after acute and perioperative pain management that were longer than necessary worsened the situation.[99]

The crisis in the USA provides lessons on the need for maximising the benefits of opioids and minimising the risk of non-medical use as access to opioid analgesics is increased in a step-wise manner in LMICs. Countries should monitor the supply and marketing of opioids and implement strong conflict-of-interest policies to restrict undue influence of all for-profit entities in the tendering, procurement, and marketing of opioid medications and in describing indications for use and prescription of opioid medications. These policies must also guarantee training on safe use of opioid analgesics grounded in evidence-based protocols.[100]

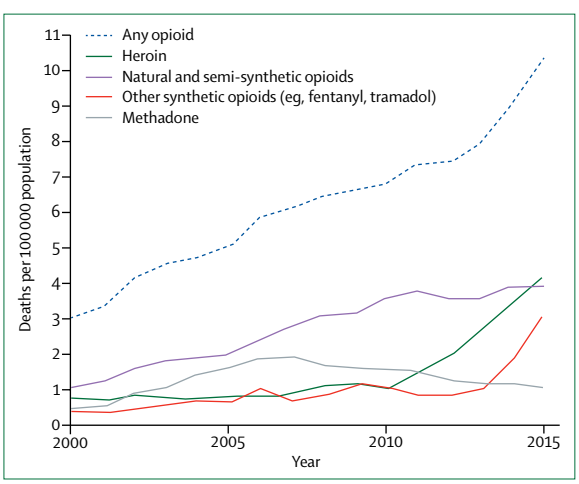

***Figure 4*: Deaths from opioids overdose, by type of opioid, in the USA, 2000–15**
Source: Centers for Disease Control and Prevention, National Center for Health Statistics (Underlying Cause of Death 1999–2015, CDC WONDER Online Database, December, 2016).

palliative care and opioid analgesics is high or has been expanding. We found no evidence that carefully increasing access to oral morphine for medical need, based on our proposed Essential Package, would increase the risk of non-medical use if a balanced approach is implemented. Other high-income countries manage medical access to opioids with a balanced approach and without generating an epidemic of non-medical use, and these experiences provide additional lessons for LMICs.[101] The experiences in Costa Rica, Kerala, and Uganda, although they have not been formally evaluated, also support this conclusion.[96]

The Commission's work distinguishes between the health-care responsibilities associated with specialised palliative care and those that should be covered by other medical specialties and fields. In practice, however, it is not appropriate to implement an either–or model. Our estimates of the SHS burden take into account that much need can and should be managed by doctors whose expertise is not palliative care. Whereas specialised palliative care is sometimes necessary or highly preferred, much of the SHS burden can and should be remedied by other specialists, by generalist doctors and nurses with access to the necessary training, medicines, tools, and appropriate communication technologies, and with support from community health workers trained in palliative care. Hence, the Commission recommends competency-based training in primary palliative care of all general doctors and nurses.[37]

The treatment and management of pain is a particularly important area of overlap with palliative care at all levels of care. Anaesthetists, surgeons, intensivists, or emergency doctors should manage postoperative, treatment-related, and serious acute pain, and pain specialists should manage serious acute pain and chronic, non-malignant pain. Yet in countries where these specialties are not available, it is morally and ethically unacceptable for any health professional to ignore a patient with moderate or severe pain of any kind that can be palliated. We recommend that training in pain treatment and in basic palliative care be a mandatory part of all curricula of health-care professions. General practitioners and nurses with appropriate training should be able to manage both pain that is associated with end-of-life or life-threatening illnesses and other sources of acute and chronic pain.

An example of an area where palliative care is not the recommended area of medicine for providing care is serious psychological suffering. Primary-care-level palliative care can manage many aspects of psychological suffering, but providers cannot be expected or trained to treat severe or chronic psychiatric disorders. Yet these psychiatric disorders generate suffering, and in LMICs, where specialist treatment is rarely accessible, doctors have to respond without specialised training in psychiatry. We do not include this SHS in our analysis, but we do recognise the drain on health-care professionals in low-resource settings and the importance of developing access to mental health professionals to care for patients and guide primary care providers.

In sum, health systems need to be strengthened through the integration of palliative care alongside prevention, early detection, treatment, and rehabilitation strategies to ensure that all patients have access to effective, efficient, and responsive care strategies and full information. The appropriate response to the global burden of untreated SHS is to expand access to effective palliative care and pain relief and to develop other components of UHC. This will ensure that an effective response to suffering is at the core of a people-centred approach to health systems.

Mandate and architecture of the report

The mandate of the Commission was to work across the palliative care and global health communities to measure global divides in access to palliative care and pain relief and to develop systemic solutions that also promote UHC, building on the 2014 WHA Resolution.[42] The idea for the Commission came out of an international workshop organised by the Harvard Global Equity Initiative in April, 2014, under the auspices of the Radcliffe Institute for Advanced Study at Harvard University.[102]

The Commission included 33 commissioners, a Chair, and a co-Chair with expertise in a wide range of key disciplines and occupations, including public health, palliative care specialty medicine, nursing, law, economics, epidemiology, public policy, anthropology, and human rights. The work of the Commission was enhanced by a Scientific Advisory Committee and three Working Groups: Economic Evaluation, Models and Innovations, and Health Systems.

Our first meeting took place in New York, NY, USA, in September, 2014, to establish our mandate and programme of work. This was followed by two in-person meetings, first in Boston, MA, in May, 2015, to review interim findings and further delineate the scope of work, and then in Cuernavaca, Mexico, in August, 2016, to review results and agree on recommendations. Commission members also participated in monthly telephone meetings in 2015–17, and the working groups met several times in 2015 and 2016.

Our research and findings are based on group consultations and deliberations, analysis of publicly available data, new data that were generated and analysed by the Commission, a review of country experiences, and multiple literature searches. All new data and methods are described in detail in the additional online material.

The Economic Evaluation Working Group developed the methodology for measuring the burden of SHS, set forth an essential package of services focused on health, and produced cost estimates. The global burden of SHS is anchored in estimates of the number of patients with SHS and SHS days associated with the health conditions and symptoms that can be ameliorated by palliative care. Our proposed Essential Package is designed to relieve the most common and severe suffering related to illness or injury associated with the burden of SHS, to be cost-effective in LMICs, to help strengthen health systems, and to provide financial risk protection for patients and families. It is the minimum upon which expanded packages must be built in alignment with each country's level of income.

***Panel 5*: Global burden of serious health-related suffering (SHS): key findings**

- More than 61 million people experienced SHS in 2015, including 25·5 million people who died, which is 45% of the 56·2 million reported deaths worldwide
- Considering adults and children separately, almost half of adults (23·1 million) and a third of children aged 15 years or younger (almost 2·5 million) who died in 2015 experienced SHS
- Patients who live with SHS accrue at least 6 billion physical and psychological symptom-days annually and up to 21 billion days summing each symptom; almost 80% of these days are accumulated in low-income and middle-income countries (LMICs)
- In LMICs, of the more than 20 million deaths associated with SHS, a high proportion are caused by diseases and health conditions that could have been prevented or treated; more than 95% of all patients in need of palliative care and pain relief associated with HIV disease, premature birth or birth trauma, tuberculosis, and malnutrition live in LMICs
- More than 98% of children aged 15 years or younger who die with SHS live in LMICs; in high-income countries, children who experience SHS account for less than 1% of all deaths associated with SHS, compared with 12% in LMICs and more than 30% in low-income countries

Panel 6: Measurement of the global burden of serious health-related suffering (SHS)

We identified the 20 health conditions from the 10th edition of the International Classification of Diseases that most commonly result either in death or in suffering that is severe enough to require a palliative care intervention for people of any age. To be included in the burden of SHS, a health condition must be either:

1 a major cause of death (according to WHO's 2015 Global Health Estimates mortality data) that typically causes moderate or severe physical and psychological suffering; or
2 a common cause of moderate or severe physical or psychological suffering associated with a high probability of mortality, especially in low-income and middle-income countries (LMICs), even when curative treatment is attempted (eg, drug-resistant tuberculosis, some haemorrhagic fevers such as Ebola virus disease, and some malignancies), from which the patient can recover (such as serious injury) or that can be controlled for many years (such as HIV disease, some malignant neoplasms, and some musculoskeletal disorders)

The 20 health conditions are: arthrosclerosis; cerebrovascular disease; chronic ischaemic heart diseases; congenital malformations; degeneration of the CNS; dementia; diseases of the liver; haemorrhagic fevers; HIV disease; inflammatory disease of the CNS; injury, poisoning, and external causes; leukaemia; lung diseases; malignant neoplasms (cancers); musculoskeletal disorders; non-ischaemic heart diseases; premature birth and birth trauma; protein energy malnutrition; renal failure; and tuberculosis. This list contains the most common health conditions[113] and includes some health conditions that primarily or exclusively affect children. We produced estimates for all 20 health conditions for decedents. Because death from diabetes mellitus typically occurs suddenly without time to initiate palliative care, we included the specific health conditions resulting from diabetes that often generate a need for palliative care (cerebrovascular disease, renal failure, cardiomyopathy and heart failure, chronic ischaemic heart disease, and atherosclerosis).

Non-decedents are people with SHS related to each of the health conditions who are likely to die of that health condition in the following few years, whose condition could be curable, who could recover although will not be cured, or whose health condition could be controlled for many years. The health conditions for which, given available data and knowledge, we present non-decedent estimates are: congenital anomalies; cerebrovascular diseases; degenerative disease of the CNS; dementia; haemorrhagic fevers; HIV disease; inflammatory disease of the CNS; injury, poisoning, and external causes; malignant neoplasms; musculoskeletal disorder; and tuberculosis. Our mortality data are country-specific and come from the WHO Global Health Estimates for 2015. The 20 health conditions that we include in our data account for 81% of deaths worldwide and 80% of deaths in LMICs, with a slightly lower proportion in low-income countries. For adults, these 20 health conditions account for 84% of total deaths worldwide, and for children younger than 15 years, they account for 60%.

We estimated the proportion of patients with SHS and the duration of symptoms. For each of the relevant health conditions, the panel first estimated the proportion of decedents and non-decedents with SHS. For some health conditions, such as HIV disease and drug-resistant tuberculosis, all decedents require palliative care because of the high prevalence of physical, psychological, and psychosocial suffering associated with dying from these diseases. For other health conditions, the estimate is a fraction of the total number of patients who die from the health condition.

We identified the most common and severe symptoms or types of suffering generated by these health conditions and catagorised them as physical suffering (moderate or severe pain, mild pain, weakness, fatigue, shortness of breath, nausea and vomiting, constipation, diarrhoea, dry mouth, itching, and wounds and bleeding) and psychological suffering (anxiety and worry, depressed mood, delirium or confusion, and dementia referring to disorientation, agitation, or memory loss). Other symptoms were taken into account (eg, insomnia, cough, oedema, hiccups, ascites, and sweating), but because these are less common, often associated with or caused by one of the symptoms listed above, and can usually be managed with the items included in the Essential Package, we decided not to undertake a separate analysis.

We recognise that many patients have multiple health conditions (eg, cancer patients might also have lung or heart disease), so mortality data form the basis of all calculated estimates, and all types of suffering are counted in association with the health condition from which the patient died. For non-decedents, all types of suffering are counted in association with the health condition from which the patient is expected to die or with the health condition that generates the most salient type of suffering (eg, pain in a patient with an injury or burn).

From these data, we produced annual estimates, by health condition and symptom, of the burden of SHS measured by decedents who experience SHS each year, and the number of people living with one of the 20 health conditions (non-decedents) who experience SHS. We sum decedents and non-decedents to arrive at the total number of individuals with SHS per year.

We developed two indicators of the duration of SHS. The first measure, total number of days with any type of suffering, was estimated by summing the duration in days of each symptom.

(Continues on next page)

(Panel 6 continued from previous page)

This is a maximum upper bound in terms of time, and assumes that each day of each type of suffering is distinct. The second measure, number of days with the symptom of longest duration, is the minimum lower bound, and the burden of SHS in days is at least this high. The assumption is that multiple symptoms overlap and that one day with multiple symptoms is the same as a day with a single symptom. We did not attempt to rank the symptoms by intensity or develop a composite measure of health-related suffering. We recommend this as an area for future research.

Additional detail is provided in the additional online material.

The Models and Innovations Working Group identified mainly small-scale projects, programmes, and approaches that offer global lessons for scale-up. In parallel, the Health Systems Working Group reviewed how health systems can integrate palliative care and, through in-depth country cases, identified models and lessons. This research provided guidance on how to integrate the Essential Package into health systems in LMICs as part of UHC, and on important pathways to expand national and global health-system capacity to progress towards the provision of an augmented and eventually ideal package of palliative care interventions.

The report has three sections. In section 1, we present findings from analyses of the SHS burden, in LMICs and worldwide. In section 2, we describe the medicines, equipment, human resources, and interventions that make up the Essential Package, and we present costing data for achieving universal access in LMICs. Because of the importance of pain relief, we analyse need and the severe inequities in the current distribution of opioids for medical use worldwide. Finally, in section 3 we address the national and global health system response required to achieve universal access to palliative care grounded in the proposed Essential Package, given the global burden of SHS. We identify a host of opportunities to increase access through health-system strengthening. The range of possible responses is grouped by health-system function, and we specifically consider stewardship, financing, delivery, resource generation policies, and the role of global actors.

Section 1. Global burden of SHS

The key findings of our analysis are summarised in panel 5.

Framework and methodology

The Commission presents a new conceptual framework for measuring the global burden of SHS. Suffering is health-related when it is associated with illness or injury of any kind. Suffering is serious when it cannot be relieved without medical intervention and when it compromises physical, social, or emotional functioning. Palliative care should be focused on relieving the SHS that is associated with life-limiting or life-threatening health conditions or the end of life.

The burden of SHS is a metric that can be used to measure the effectiveness of palliative care interventions.[68] The results of our analysis, and the supporting empirical work presented in this Report, provide a first approximation of the physical and psychological burden of SHS because we took as our starting point any type of SHS, irrespective of whether the necessary intervention for remediating that suffering has been invented or is available in a given setting.

To date, the existing metrics used by health-system decision makers to prudently allocate scarce resources across competing priorities do not give sufficient weight to the benefits to patients, families, the health system, or economies of alleviating SHS. The symptoms associated with SHS might be additive, compound, or multiplicative components of sequelae that are used as standard measures and components of burden of disease.[103–106] Although palliative care might increase the ability of patients to manage daily activities and occasionally extends life expectancy, palliative care interventions have independent value for patients in relation to SHS.[73,107–111] A complete and robust measure of the burden of disease would account for suffering averted, with an appropriate weighting of duration, intensity, and value to the patient and family. Although challenging to convert into time, the final measure would be akin to a suffering-intensity-adjusted life-year (SALY), against which the efficacy of interventions could be evaluated.

SALYs should first be explored as an adaptation of existing measures of burden of disease. Intense suffering can be described in terms of quality-adjusted life-years (QALYs) as a poor health state for which the associated low quality of life is amenable to improvement through effective palliative care. Incorporating SALYs into QALYs would give a more comprehensive measure for use in economic evaluations when allocating resources across prevention, treatment, and palliation and especially when comparing interventions to alleviate suffering at the end of life, when preserving dignity and providing comfort are crucial, with other types of health interventions.

As a complement to developing SALYs as a measure, we recommend a major initiative to generate data on disease-specific suffering and a clinical focus-group-led analysis to elicit patient preferences and values in relation to suffering and dignity in a variety of cultural contexts, which are important to providing people-centred health care.[112]

Our empirical results constitute a first approximation of burden of SHS. Our goal was accuracy within an order of magnitude rather than a robust set of point estimates. We recognised that measures of duration are even more challenging to develop than measures of patient numbers

	Total deaths (thousands)			Deaths due to health conditions most associated with SHS (thousands)			Deaths associated with SHS								
	All age groups	≥15 years	<15 years	All age groups	≥15 years	<15 years	All age groups		≥15 years			<15 years			
							n	Percentage of total deaths	n	Percentage of total deaths	Percentage of total deaths in age group	n	Percentage of total deaths	Percentage of total deaths in age group
Low-income and middle-income countries	46 410	39 204	7205	37 002	32 732	4269	20 635	44%	18 206	39%	46%	2429	5%	34%
Low income	5458	3336	2122	3625	2459	1166	2150	39%	1490	27%	45%	661	12%	31%
Lower-middle income	21 927	17 719	4208	16 618	14 118	2499	9063	41%	7634	35%	43%	1429	7%	34%
Upper-middle income	19 025	18 150	875	16 759	16 155	604	9422	50%	9083	48%	50%	340	2%	39%
High-income countries	9819	9735	85	8508	8441	67	4919	50%	4880	50%	50%	39	<1%	46%
Total	56 229	48 939	7290	45 510	41 173	4337	25 554	45%	23 086	41%	47%	2468	4%	34%

Table 1: **Mortality associated with serious health-related suffering (SHS), by income region and age groups**

Panel 7: Global burden of serious health-related suffering (SHS) in children

Our data indicate that more than 5·3 million children aged 15 years or younger experience SHS worldwide. These children account for 9% of patients who experience SHS, 5% of total days with SHS days, and 6% of days in pain. In low-income countries, children make up a much larger proportion of patients who experience SHS (21%) and days with SHS (14%) than in high-income countries, where children account for less than 1% of patients with SHS and days with SHS (additional online material).

In the case of children, it is important to consider both the key health conditions associated with paediatric SHS and the age distribution of people affected by SHS for each health condition. Worldwide, the burden of SHS in children is primarily associated with HIV disease (40%), premature birth and birth trauma (20%), and congenital malformations (more than 10%). In low-income countries, more than 50% of the burden of paediatric SHS is associated with HIV disease. Considering the distribution of SHS between adults and children, in low-income and middle-income countries (LMICs), children account for almost 70% of people affected by SHS associated with inflammatory disease of the CNS, about half of people with SHS associated with malnutrition and haemorrhagic fever, and about 10–20% of people with SHS associated with injury, leukaemia, and HIV disease. In low-income countries, children account for substantial proportions of people affected by SHS associated with malnutrition (almost 80%), inflammatory diseases of CNS (almost 75%), haemorrhagic fever (more than 60%), and injuries (more than 30%; additional online material).

Children and their families have specific and intensive palliative care needs that can easily be overlooked because the absolute number of paediatric patients is low compared with adults.[113] The Commission stresses that access to paediatric palliative care is imperative everywhere, including and especially in LMICs because of the concentration of cases.

Although analysing the burden of SHS specific to children was beyond the scope of the Commission, we include children in our estimates both by using all-age mortality data and by including health conditions that are exclusively or primarily paediatric. Our estimates of non-decedent children with SHS are limited. We did not undertake a full analysis of life-threatening and life-limiting health conditions in children, and it was beyond the scope of the Commission to project long-term survivorship. Thus, our estimates of non-decedent children are based on lower bound, conservative estimates.[114] We recommend that future global efforts to develop a metric of SHS especially in primary data collection include a specific focus on children and their needs for palliative care and pain relief.

and that no previous attempts to develop such measures have been made on a global scale. We therefore present two summary indicators, one with a lower and another with an upper bound on duration.

We developed and analysed data on the number of patients with SHS and the number of days of SHS associated with the serious, complex, and life-threatening health conditions that generate most of the global need for palliative care. We estimated the annual SHS burden of decedents and, for a subset of the health conditions, non-decedents. Our framework and calculations go beyond previous work by including 11 physical and four psychological symptoms (panel 6, additional online material).

We identified 20 health conditions and reviewed SHS for each health condition individually for each symptom. Although challenging, this was essential because neither cancer nor HIV are tracer conditions, although they do explain the largest proportion of the SHS burden. We also sought to bring attention to health conditions other than cancer and HIV that have been neglected within palliative care and around which advocacy is generally weak.

Estimates of the global burden of SHS

We estimate that more than 25·5 million of the 56·2 million people who died in 2015, experienced SHS associated with one of the 20 health conditions included in our analysis. About 46·4 million deaths occurred in LMICs, and 20·6 million (45%) of these deaths were associated with SHS. The SHS-associated deaths in LMICs account for 81% of all SHS-associated deaths worldwide.

Almost half of adults who die—23·1 million in 2015—experience SHS (table 1). In the case of children aged 15 years or younger, almost a third of those who die experience SHS, which amounted to 2·5 million children in 2015. Worldwide, considering the 20 health conditions

Panel 8: Previous estimates of the need for palliative care and the burden of serious health-related suffering (SHS)

Our conceptual and measurement framework for quantifying the global burden of SHS builds on earlier work by considering several types of suffering for a series of health conditions. Previous estimates of the need for palliative care focused on cancer and HIV disease, including the Disease Control Priorities (DCP, 2nd edn), and were based on measures of suffering exclusively in terms of pain days at end of life.[115] This provided the foundation for later studies and the work presented in this Report, which extends to a broad range of health conditions.[113,114]

Expert opinion and data from country experiences from several low-income countries suggest that about 80% of people dying from cancer and 50% of people dying from HIV/AIDS experience moderate or severe pain lasting on average 90 days. These proportions were widely applied to develop estimates of the need for pain relief for patients in low-income and middle-income countries (LMICs). The DCP (3rd edn) cancer volume uses these estimates to project that in 2012, about 425 million days of cancer pain could have been relieved with effective access to opioids in LMICs.[116]

In the Global Atlas of Palliative Care at the End of Life,[113] WHO and the Worldwide Hospice Palliative Care Alliance estimated that in 2011, 20·4 million people who died required palliative care. This number is then doubled based on the assumption that about the same number of people need palliative care for reasons other than pain and for longer periods of time, giving a total of 40 million people in need of palliative care every year.[117] This very rough estimate has been widely circulated as the total need for palliative care worldwide.[118]

Panel 9: Caregiver support, bereavement, and complicated grief[119]

There are various concerns related to family caregivers that require specific analysis and intervention. Family caregivers typically provide many hours of care, inside and outside of hospitals and homes, and often accompany the patient to clinic visits. Caregiving might include washing and feeding the patient, purchasing and administering medicines, helping with toileting, and providing emotional support. This caregiving might be required up to 24 h a day and usually creates a major financial risk for families.[120] Caregivers often must withdraw from work, school, or child care. Caregiving can also put the health of the caregiver at risk,[121–123] and family members may experience serious physical, psychological, social or spiritual suffering, and might also need palliative care.[124] The burden of caregiving typically falls on women, including girls, and exacerbates gender inequity.[125,126]

Family caregivers, along with other family members, are at risk for complicated grief after a patient's death.[127] In high-income countries, complicated grief appears to occur in 7% of bereaved persons, although there is little data on the exact number of people per decedent.[128] The Commission was unable to undertake detailed estimates of the suffering and needs of caregivers other than an order-of-magnitude calculation of complicated grief. Assuming that complicated grief is associated with only 7% of deaths, the minimum number of people who suffer complicated grief is 1·8 million, of which more than 80% live in LMICs. If each individual experienced 90 days of complicated grief, this sums to just more than 160 million suffering days per year. This assumes that only one person per family is affected, yet multiple family members are often severely affected.

We believe that complicated grief of a family member should be included as a type of psychological suffering to which palliative care providers should and can often attend and the Essential Package includes one bereavement visit for each death. Palliative care can include providing informal emotional, social, or spiritual support to family members without establishing formal patient–clinician relationships and community health workers can be particularly important providers of emotional and social support to caregivers.

In recognition that caregiving for patients with serious, complex, or life-limiting health problems can cause or exacerbate poverty for the caregiver, we also recommend including family caregivers in social supports as a complement to the Essential Package of palliative care health interventions.

included in our analysis of SHS, adults account for 90% of deaths associated with SHS. Yet the proportion of children who die with SHS as a proportion of overall SHS-related deaths is inversely related to country income. In high-income countries, children who die with SHS account for less than 1% of all deaths, compared with 12% of deaths in LMICs and more than 30% of deaths in low-income countries (panel 7).

Our estimates suggest that in 2015, 35·5 million people experienced SHS although they did not die. Summing decedents and non-decedents, at least 61·1 million people experienced SHS in 2015, and 50·5 million (80%) of these people lived in LMICs.

This estimate of people with SHS exceeds previous estimates[113] of people in need of palliative care by slightly more than 21 million (panel 8). Our calculation of decedents also exceeds previous estimates of 20 million people in need of palliative care by more than 5 million people.[113] Our estimate is higher than previous estimates because we include a broader list of health conditions, consider 15 types of suffering rather than only pain prevalence, and include non-decedents. In the case of children, our estimates of decedents with SHS is also higher than previously estimated (2·5 million deaths compared with 1·2 million deaths),[113] and this is probably also because we consider a broad list of health conditions. Our projection of the total need for palliative care by child decedents and non-decedents is more closely aligned to recent literature. We estimate that more than 5·3 million children aged 15 years or younger lived with SHS in 2015. Data from 2010 and for a larger group of children aged 0–19 years suggests that about 8·1 million lived with SHS.[114]

Summing the duration of all symptoms provides an upper bound estimate of 21·2 billion SHS days per year for all patients worldwide. Using the upper bound estimate, LMICs accrue 16·9 billion SHS days per year, accounting for 80% of total SHS days worldwide. The duration of SHS is much lower when using the lower bound estimate, but more than 6 billion days worldwide is still a considerable amount, of which 5·1 billion days occurred in LMICs. These data do not include the SHS of family members and caregivers (panel 9).

	Rank	Percentage of patients (n=20·6 million)	All symptoms		Physical symptoms		Psychological symptoms	
			Percentage of total number of days (n=9145 million)	Percentage of minimum number of days (n=2473 million)	Percentage of total number of days (n=7193 million)	Percentage of minimum number of days (n=2378 million)	Percentage of total number of days (n=1952 million)	Percentage of minimum number of days (n=1054 million)
Malignant neoplasms	1	26%	47%	45%	50%	46%	36%	36%
Cerebrovascular disease	2	17%	11%	12%	12%	12%	7%	9%
Lung disease	3	11%	9%	11%	8%	11%	12%	12%
Injuries	4	6%	0	1%	0	1%	1%	1%
Tuberculosis	5	6%	6%	6%	4%	4%	10%	9%
Premature birth and trauma	6	5%	0	0	0	0	0	0
HIV	7	5%	12%	8%	11%	8%	12%	12%
Liver disease	8	5%	3%	3%	3%	3%	2%	1%
Non-ischaemic heart disease	9	4%	3%	3%	3%	3%	4%	4%
Dementia	10	3%	4%	4%	3%	3%	10%	10%
All other SHS conditions		11%	5%	8%	5%	8%	6%	6%

Table 2: **Distribution of decedent serious health-related suffering (SHS) in low-income and middle-income countries, by patients and physical and psychological symptom days (ranked by number of patients)**

	Rank	Percentage of patients (n=25·6 million)	All symptoms		Physical symptoms		Psychological symptoms	
			Percentage of total number of days (n=11 902 million)	Percentage of minimum number of days (n=3231 million)	Percentage of total number of days (n=9349 million)	Percentage of minimum number of days (n=3105 million)	Percentage of total number of days (n=2553 million)	Percentage of minimum number of days (n=1376 million)
Malignant neoplasms	1	30%	51%	49%	54%	51%	39%	39%
Cerebrovascular disease	2	16%	10%	10%	11%	11%	6%	8%
Lung disease	3	11%	8%	10%	7%	10%	11%	11%
Injuries	4	6%	0	1%	0	1%	1%	1%
Tuberculosis	5	5%	4%	5%	3%	3%	8%	7%
Dementia	6	5%	6%	6%	4%	4%	13%	13%
Liver disease	7	5%	2%	3%	3%	3%	2%	1%
Premature birth and trauma	8	4%	0	0	0	0	0	0
HIV	9	4%	9%	6%	9%	6%	10%	9%
Non-ischaemic heart disease	10	4%	3%	3%	3%	3%	3%	4%
All other SHS conditions		11%	6%	8%	6%	9%	7%	7%

Table 3: **Distribution of decedent serious health-related suffering (SHS) worldwide, by patients and physical and psychological symptom days (ranked by number of patients)**

Health conditions associated with the burden of SHS

In 2015, LMICs accounted for 84% of the world's population and approximately the same proportion of patients with SHS.[129] For certain health conditions, such as HIV disease, premature birth and birth trauma, tuberculosis, congenital malformations, malnutrition, and inflammatory disease of the CNS, most SHS occurs in LMICs. LMICs have a lower proportion of patients with SHS associated with non-communicable diseases, such as malignant neoplasm and dementia, as compared to worldwide. Injuries account for more than 5% of patients.

In LMICs, the ten health conditions that cause the highest numbers of patients in need of palliative care account for more that 90% of the 20·6 million people who die with SHS (table 2). The same ten health

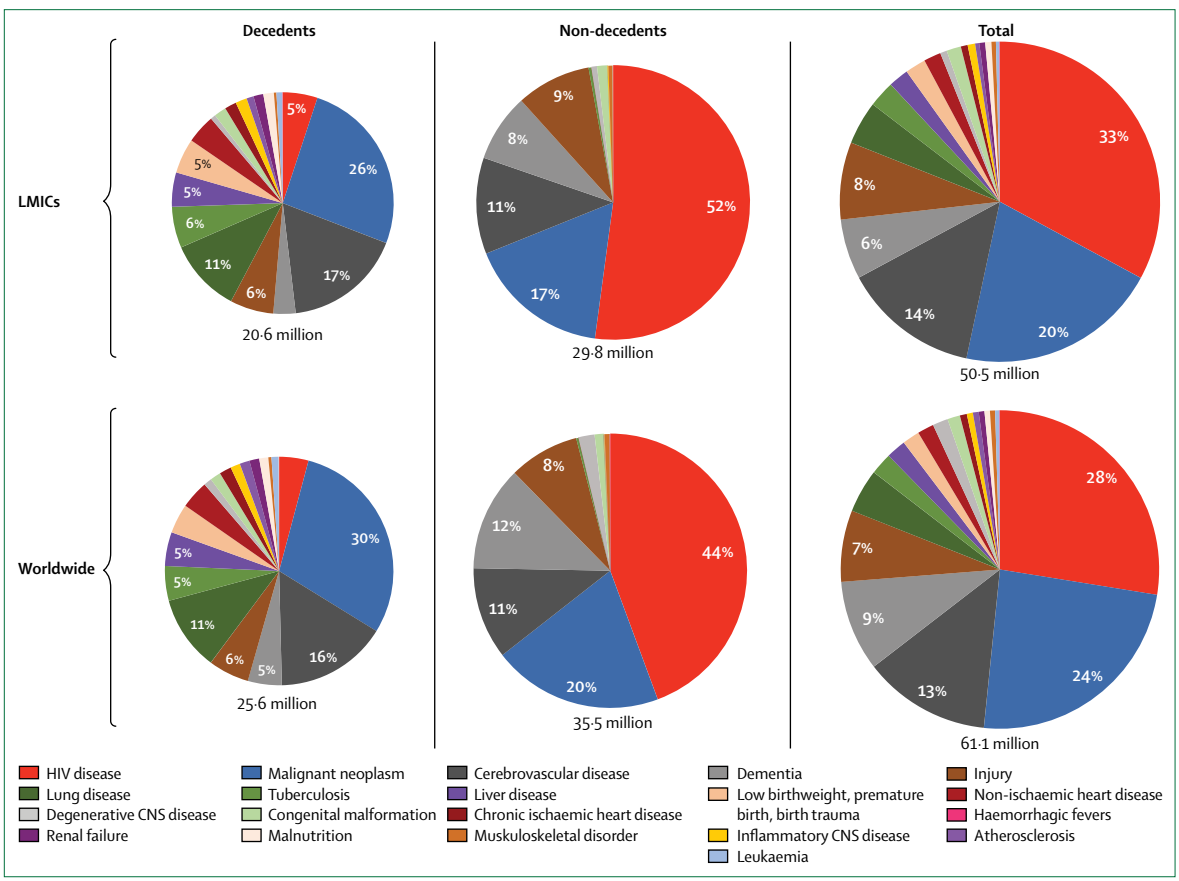

***Figure 5*: Distribution of people in low-income and middle-income countries (LMICs) and worldwide who experienced serious health-related suffering, by health condition, 2015**
Source: WHO Global Health Estimates 2015.

conditions rank similarly worldwide (table 3), but the percentage of patients with dementia is higher and the percentage of patients with HIV is lower than in LMICs because of the high prevalence of dementia in high-income countries and of HIV in LMICs (figure 5).

We also present the burden of SHS in symptom days (figure 6). Decedents with SHS in LMICs accrue a total of 9·1 billion SHS days using the upper bound indicator of the total sum of symptoms, or 2·5 billion days using the lower bound estimate (table 2). Malignant neoplasms account for almost 50% of SHS days using either indicator, followed by HIV, cerebrovascular disease, and lung disease at about 10%. Injuries account for a much larger proportion of patients with SHS than SHS days, whereas the opposite is true for malignant neoplasms and HIV. For physical symptoms, the distributions are very similar, but for psychological symptoms, decedents with malignant neoplasms accrue 36% of SHS days, and decedents with tuberculosis, dementia, HIV, cerebrovascular disease, and lung disease about 10% of SHS days. The ten health conditions that cause the highest numbers of patients in need of palliative care (table 2) account for about 95% of SHS days in LMICs.

> Palliative care is only to provide care for those that are terminally sick to feel comfortable. Because, in most cases, we know that the person is not going to be cured... among those who seek palliative care from our program, 50% of them suffer from some sort of cancer, and nearly 40% of them have suffered from stroke.... a good number of them lose hope of coming back. So, what is important is that you provide care to the person so they feel comfortable at home, and he or she feels that he or she is not alone.[130]
>
> *Quotes from communities in Kerala, India*

Symptoms associated with the global burden of SHS

Physical symptoms account for about 70% of total SHS days by decedents and non-decedents, almost 80% of days for decedents, and 60% of days for non-decedents. The data are similar for LMIC and worldwide. The higher proportion of psychological suffering in non-decedents is because of the high number of people living with dementia (figure 6).

Pain (both chronic, mild pain and moderate to severe pain) is the most common symptom in our data, accounting for more than 20% of total SHS days and almost a third of physical symptom days in LMICs and

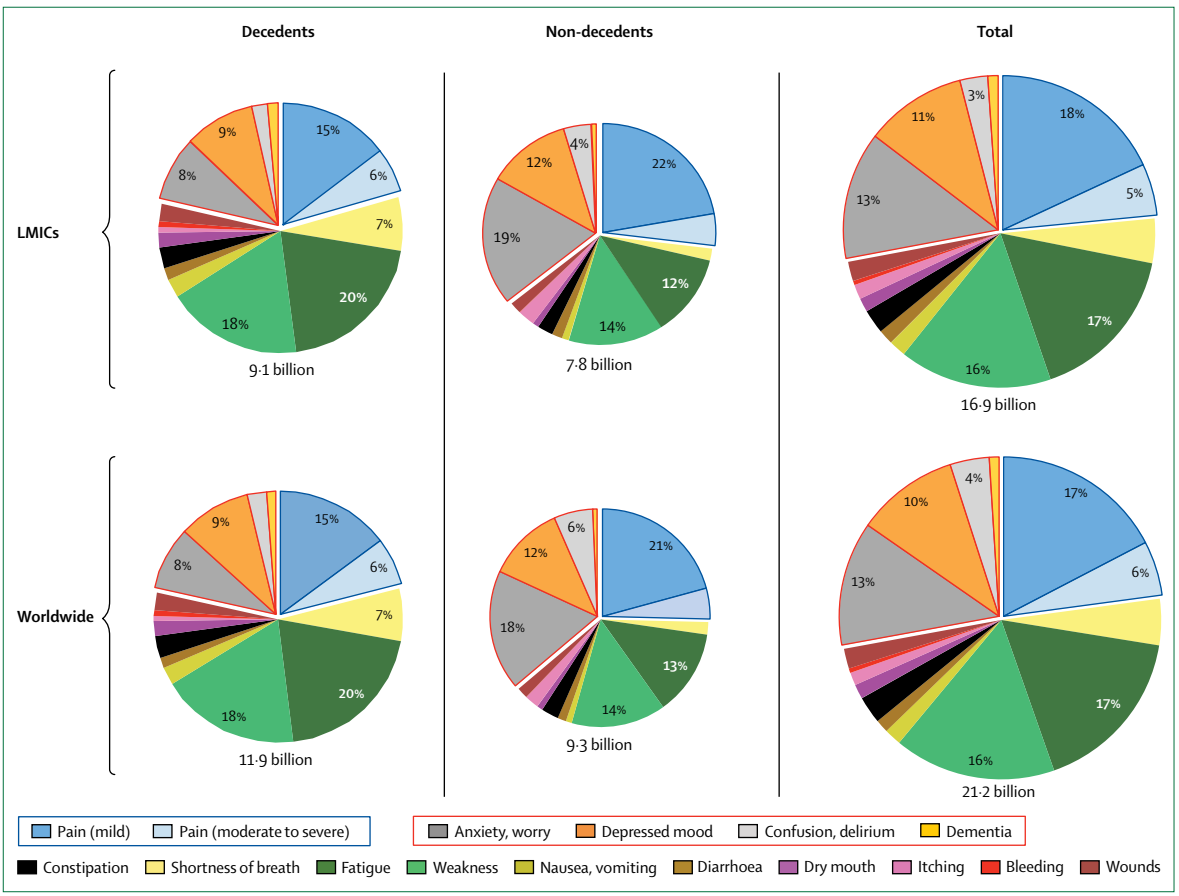

***Figure 6*: Distribution of days that people in low-income and middle-income countries (LMICs) and worldwide experience serious health-related suffering, 2015**
Source: WHO Global Health Estimates 2015.

worldwide, for decedents and non-decedents. Chronic, mild pain is about three times more common than moderate to severe pain. Fatigue and weakness each explain 15–20% of total SHS days in LMICs and worldwide, with lower prevalence among non-decedents. Dyspnoea is most common in decedents and accounts for about 7% of SHS days globally and in LMICs (figure 6).

Anxiety or worry, and depressed mood account for more than half of psychological symptom days for both decedents and non-decedents, both in LMICs and worldwide (figure 6). However, worry and depressed mood explain a larger proportion of SHS days for non-decedents. The estimates are similar in LMICs and worldwide, although they differ between decedents and non-decedents.

The distribution of symptoms is relatively similar across countries, income groups, and decedent versus non-decedent patients, with a few notable exceptions. Non-decedents have more pain and less fatigue and dyspnoea, especially in low-income countries where the proportion of non-decedent patients with HIV disease is high. LMICs account for most (73–94%) of the total symptom days for all symptoms except confusion and delirium, the prevalence of which is much higher in non-decedents in high-income countries where the dementia burden is high.

There is substantial variation in the distribution, by health condition, of the proportion of decedents and non-decedents and of symptoms across SHS days (figure 7; additional online material). Most patients with HIV disease who experience SHS are non-decedents, and pain and anxiety or worry are the most common types of suffering. About half of patients with cancer are non-decedents, and pain, fatigue, and weakness are particularly common. Pain also accounts for substantial proportions of SHS in patients with congenital malformation, musculoskeletal disorder, injury, atherosclerosis, low birthweight and birth trauma, ischaemic heart disease, HIV, and liver diseases. Non-decedents account for most dementia patients with SHS in general, and with confusion or delirium specifically. Dyspnoea is most common in patients with lung disease but also accounts for a large proportion of suffering days in patients with low birthweight and birth trauma (40%), congenital malformation (27%), malnutrition (24%), and non-ischaemic heart disease (20%).

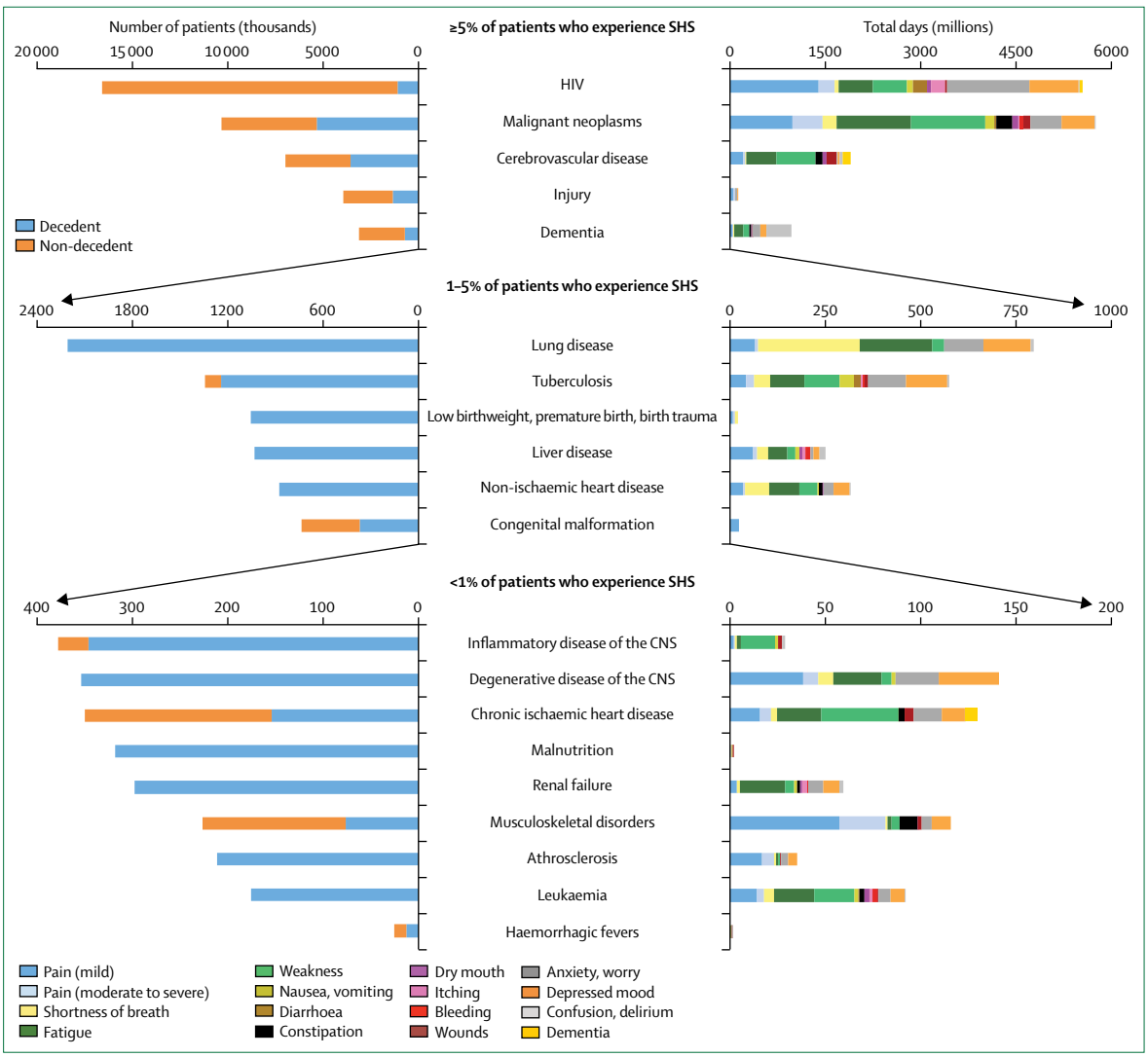

***Figure 7*: Decedents, non-decedents, and days with serious health-related suffering (SHS) in low-income and middle-income countries, by symptom, ordered and grouped by health condition and by total number of patients with each health condition**
The left side of the figure shows the number of decedents and non-decedents who experience SHS. The right side of the figure shows the days of each type of suffering associated with each condition. The health conditions are ranked by the number of people who experience SHS by grouping them into three categories (5% or more, 1–5%, and less than 1%) using a scale specific to each group. Source: WHO Global Health Estimates 2015.

Avoidable mortality and the dynamics of the burden of SHS

The results by health condition and income region are driven largely by the underlying mortality data and show the effect of epidemiological transition on SHS. As the burden of chronic diseases and non-communicable diseases increases in LMICs, SHS related to these health conditions also increases. Yet for health conditions associated with infection, poverty, or other social determinants of health, the SHS burden is high because the health system fails to guarantee access to preventive services or life-saving health interventions and treatment.

Palliative care cannot be a substitute for improving access to the public health interventions and treatment that would prevent suffering and premature death in the first place. Efforts to make palliative care more accessible must rather be accompanied by efforts to make illness prevention, diagnosis, and treatment more accessible and to integrate palliative care into overall health services.

According to our estimates, more than half of SHS in decedents is associated with avoidable, premature deaths. Almost all deaths and palliative care needs in patients with tuberculosis, HIV, inflammatory disease of CNS, low birthweight, or protein malnutrition in LMICs are avoidable. The percentage of avoidable deaths is much lower for chronic diseases and non-communicable diseases such as cancer, dementia, and atherosclerosis (panel 10, table 4).

Panel 10: Avoidable and premature deaths associated with serious health-related suffering (SHS)

The concept of premature death or avoidable mortality has been introduced and applied in previous studies and is defined as the "deaths that should not occur in the presence of effective and timely health care".[131] WHO defines death as premature if it occurs before age 70 years. Estimating the SHS associated with avoidable mortality makes it possible to identify the palliative care need generated by underperforming health systems, which is different from SHS that cannot be prevented but can be remediated.

We defined avoidable mortality as the number of deaths that can be averted if a specified best-case scenario were to occur in a group of countries. We consider in our analysis the median age-specific mortality in each age group of all high-income countries as the best-case scenario. We calculated the number of avoidable deaths from the 20 health conditions included in the analysis of SHS.

We calculated both the number of avoidable deaths from the 20 health conditions and the number of avoidable deaths associated with SHS. The age group of 70 years and older was excluded from the analysis because we assumed that none of these deaths are avoidable. We also calculated avoidable deaths and those associated with SHS in children aged 15 years and younger.

Our data on avoidable deaths from the 20 health conditions (table 4) show that in 2015, avoidable deaths totalled 2·3 million in low-income countries (80% of total deaths from these health conditions), 7·6 million (70%) in lower-middle-income countries, and 3·7 million (48%) in upper-middle-income countries. Infectious diseases and health conditions associated with poverty have the highest percentage of deaths that are avoidable; the percentage is greater than 95% for tuberculosis, HIV, inflammatory diseases of CNS, and malnutrition. The proportion of child deaths that can be considered avoidable is particularly high. This is because, in high-income countries, the survival for children with diseases like cancer is high[132] and the mortality from poverty-associated, preventable health conditions and infections is low. Overall in LMICs, 4·3 million children die from the 20 health conditions, and 3·8 million (88%) of these deaths are avoidable, compared with 1·1 million (93%) children in low-income countries, 2·2 million (89%) children in lower-middle-income countries, and 0·4 million (73%) children in upper-middle-income countries. We also found that for several non-communicable diseases such as cancer, dementia, and atherosclerosis, age-specific mortality rates are lower in many LMICs than in high-income countries, a finding that highlights that LMICs are likely to see increasing demand for palliative care as their burden of non-communicable diseases increases.

Our data on avoidable deaths associated with SHS show that 7·7 million such cases in LMICs are avoidable, which corresponds to 63% of the total, annual number of decedents with SHS. In low-income countries, 1·4 million avoidable deaths are associated with SHS, corresponding to 81% of total deaths, compared with 4·2 million in lower-middle-income countries (69% of total deaths), and 2·0 million in upper-middle-income countries (46% of total deaths). Across health conditions, a substantial proportion of avoidable deaths associated with SHS (10% or more) is from each of cerebrovascular disease, HIV disease, tuberculosis, premature birth and birth trauma, and injury, because the mortality associated with these health conditions while low in wealthy countries is high in poor countries.

The proportion of child decedents with SHS is also substantial. If LMICs were to have the same age-specific mortality as the median mortality of high-income countries, 2·1 million of the 2·4 million child deaths with SHS could be avoided. For low-income countries, more than 90% of child deaths associated with SHS are avoidable, almost 90% are avoidable in lower-middle-income countries, and more than 70% in upper-middle-income countries.

See additional online material for more detailed analysis.

Stronger health systems and more attention to the social determinants of health would prevent many deaths in LMICs, many of which are associated with SHS and generate a need for palliative care. By contrast, the burden of chronic illness and non-communicable diseases will increase as part of epidemiological transition. These diseases will generate a substantial need for palliative care and will, with time, offset and indeed likely exceed any reduction in the number of poor patients needing palliative care associated with infectious diseases and poverty.

Health systems can and should be strengthened through the incorporation of prevention, treatment, survivorship, and palliative care, using integrated care pathways, especially in LMICs (the systemic analogue of the integration pathway for individual patients presented in figure 2B). Integrating palliative care into a health system and expanding coverage should allow for flexibility and fluid integration of disease management and palliative care from the point of diagnosis, in ways that do not prevent patients from accessing treatment or curative care. This is particularly important for health systems in LMICs that need to strive to reduce premature deaths through prevention, early diagnosis, and disease-modifying treatment while increasing access to palliative care for people undergoing treatment and for those who might or will die despite access to both.

Data limitations and considerations

Because of the dearth of reliable empirical data on the types, prevalence, and duration of suffering related to most of the 20 health conditions, we relied heavily on expert opinion. We know of no valid way to rank types

	Total deaths	Avoidable mortality using HIC median* (thousands)	Avoidable mortality using the country income group best case (thousands)	Total deaths with SHS	Avoidable SHS burden (decedents) using HIC median (thousands)	Avoidable SHS burden (decedents) using the income group's best (thousands)
All age groups—LMIC total	21 242	13 558 (64%)	15 285 (72%)	12 233	7656 (63%)	8850 (72%)
Low-income countries	2814	2265 (80%)	1899 (67%)	1699	1383 (81%)	1216 (72%)
Lower-middle-income countries	10 827	7614 (70%)	8273 (76%)	6116	4229 (69%)	4629 (76%)
Upper-middle-income countries	7601	3680 (48%)	5112 (67%)	4417	2043 (46%)	3006 (68%)

HIC=high-income country. LMIC=low-income and middle-income country. *Not counting negative numbers.

Table 4: **Avoidable overall mortality and avoidable deaths associated with serious health-related suffering (SHS) in low-income and middle-income countries (LMICs)**

of suffering by tolerability and did not attempt to do so. We also did not specifically differentiate between children, adolescents, adults, or elderly adults. Social and spiritual suffering are not included in our estimates of the total burden of SHS because resources for primary data collection are limited and no measures exist.

The estimates also have limitations, and we consider them to be first approximations to the burden of SHS. In our data, mortality rates are the only source of variation between populations groups. Furthermore, SHS is not limited to the 20 health conditions we analysed. Although any one of these health conditions is unlikely to individually produce a large amount of days of SHS at a national, regional, or global level, taken together, they would somewhat increase the total burden of SHS. In the case of children, however, the excluded health conditions could be more important. Finally, in the absence of data on prevalence and survivorship for many health conditions, especially in LMICs, we estimated non-decedent SHS only for the health conditions that we believe produce the greatest need for palliative care worldwide, for which data are available, and only for the short term.

The burden of SHS is not completely coincident with the need for palliative care since several health conditions include cases, especially in non-decedents, that are not life-threatening or that can and should be managed by other specialists, such as HIV or intensive care specialists who have been trained in pain treatment. Furthermore, some health conditions should ideally be managed outside the realm of palliative care (eg, injuries and musculoskeletal disorder), and these together account for less than 6% of deaths (1·6 million of the 25·5 million deaths) and 1% of SHS days in 2015. For non-decedents, injuries and musculoskeletal disorders account for 8% of deaths (3·2 million deaths of the 41·1 million deaths) and 2% of SHS days.

For the health conditions for which we were unable to identify estimates of people living with disease (haemorrhagic fever, tetanus, congenital malformations, musculoskeletal disorders, and injuries), we developed estimates of non-decedent need for palliative care as a multiple of number of deaths (additional online material). These five health conditions account for 9% of non-decedent patients (3·6 million of 41·1 million patients) and 2% of non-decedent SHS days.

We analysed the burden of SHS that is not equivalent to the palliative care that is needed or received by the patient. Further analysis should be undertaken on both the total number of days a patient would need palliative care and the total number of days the patient is receiving care. This is especially salient for our analysis of HIV disease. The large number of people living with HIV disease—due, in part, to the success of antiretroviral therapy (ART)—is resulting in a large proportion of the non-decedent and overall SHS, especially in LMICs.[39] However, the palliative care needed by people living with HIV disease, which can often extend life for years, is typically of low intensity, meaning that patients might need palliative care from a nurse or doctor less than once per week or even once per month. Thus, the number of days during which these patients are merely being monitored by a palliative care provider each year might be very high (and similar to the number of SHS days), yet the number of days in which they receive palliative care could be very low and often provided by HIV treatment providers rather than palliative care specialists.

Assessing the need for palliative care by patients living with HIV is complex and evolving with new discoveries, increasing access to treatment in LMICs, and the ageing of these populations. Much of this need can and should be satisfied by low-intensity palliative care provided by primary doctors and HIV specialists with appropriate, competency-based training, rather than by specialist palliative care doctors. Our palliative care expert group considered that, on average, 50% of all people living with HIV have SHS and need palliative care. Among the estimated 36·7 million people living

***Panel 11*: Providing palliative care and pain relief during the Ebola epidemic and the Haiti earthquake: a false dichotomy between survival and comfort during humanitarian emergencies and crises**

The 2014–15 Ebola epidemic and the 2010 Haiti earthquake underscore the importance of palliative care in the response to humanitarian emergencies and crises and the false dichotomy between the need for life-saving treatment and need for palliative care. The Ebola epidemic affected 28 646 people and killed 11 323 people.[144] Despite being an acute humanitarian crisis, this epidemic affected countless communities during the course of 2 years.

The response was defined by severe constraints on human and physical resources, further worsened by fear and by the limitations of personal protective equipment and time spent at the patient's bedside.[145] Clinical symptoms of Ebola include nausea, vomiting, diarrhoea, body aches, and, in late stages, bleeding, respiratory distress, and encephalopathy.[146,147] Palliative therapy focused on management of symptoms such as nausea and vomiting, which not only improve patient comfort but help maintain patient fluid volume and thereby improve chances of survival.[148,149] Opioids such as morphine typically were available only in small amounts in Ebola treatment units or not at all.[150–152]

The non-pharmacological palliative needs (feelings of isolation, fear, and grief) of patients and family members were underreported. People with suspected Ebola virus infection were subject to dehumanising separation from family and friends in west Africa, for instance.[153–155] Psychosocial and spiritual support was integrated in many programmes, but the high number of patients and the limited time health-care workers could spend within treatment units due to Ebola virus status resulted in minimal patient counselling.[156–158]

Patients with Ebola virus disease coped with the loss of their loved ones while facing the disease and fear of death themselves. This double burden was particularly difficult for children who were forced to take on caretaker responsibilities of their younger siblings after having witnessed the death of adults in their families.

Likewise, the 2010 Haiti earthquake highlights the immense immediate need for pain relief during natural disasters. The earthquake caused devastation to health-care infrastructure in both rural and urban areas.[159] Opioid analgesia was needed to treat traumatic wounds and postoperative pain, but the National List of Essential Medicines in Haiti contained only ketamine and inhaled anaesthetic agents.[160] The only readily available pain-control medications were non-steroidal anti-inflammatory agents and pain medications had to be imported into the country via informal supply chains. Some patients had to be transferred to the USA for palliation.

Given the emergency setting and human resource constraints, many people with life-threatening injuries waited for surgeries and had extended periods of acute pain. The need for pain relief stretched beyond the initial trauma in settings where patients needed extended wound care or had secondary infections such as tetanus. In the postoperative setting, inadequate pain relief can keep patients from participating in physical rehabilitation, often leading to increased disability that can prevent them from fully rejoining the workforce.

Similar to what was seen in the Ebola epidemic, the 2010 Haiti earthquake killed or injured 5% of Haiti's population and internally displaced an additional 19%. Mental health support for management of bereavement, both during and in the aftermath of the crisis, was almost non-existent or was imported and not culturally appropriate.[161]

with HIV in 2015, about 19·8 million were diagnosed and receiving ART, 5·9 million were diagnosed and not receiving ART, and 11 million were undiagnosed. Those who were diagnosed, receiving ART or not, are living with a life-threatening and highly stigmatised health condition, and findings from various studies have shown prevalence of reported pain and other symptoms of more than 50% in this population.[133] Although patients with normal CD4 T-cell count who adhere to ART and have undetectable virus load will generally not be at risk for classic, AIDS-related complications, they might be increasingly at risk of chronic comorbidities as they age. The important concept of accelerated ageing with chronic, suppressed HIV (eg, higher incidence of end-organ failure, neurodegenerative disease, and musculoskeletal pain) can have important implications for palliative care.[133] The percentage of people living with HIV who do not know their status is generally decreasing.[134] According to the UNAIDS 2016 report,[134] most undiagnosed cases are in Africa, Asia, and the Pacific, and the percentage of people who do not know they are HIV positive is much higher in LMICs than in high-income countries. Our expert panel felt it necessary to consider, rather than ignore, this extremely vulnerable, often impoverished group of people, most of whom have not been diagnosed because of severe barriers to accessing health care or unwillingness because of stigma, or both, yet still suffer and need palliative care in addition to ART. Findings from a recent systematic review[135] show that most HIV-infected children in sub-Saharan Africa have not been informed of their HIV status. More than 17 million children worldwide have been orphaned because of the AIDS epidemic; every child should have had bereavement support and could suffer from complicated grief.[136]

An additional limitation in our estimates of non-decedents is the potential for double counting of individuals with comorbidities from two or more of the 20 health conditions. We estimate the double count is less than 1 million, especially because many individuals with comorbidities die within a year (eg, patients with HIV and tuberculosis).[137] The exception is HIV and

malignant neoplasms, for which dual diagnosis estimates have been reported up to 6% of HIV patients[138,139] with 1 year survival rates of about 66%.[140,141] Comorbidity, when a person has multiple life-threatening diseases simultaneously, could also exacerbate symptom intensity and intolerability and hence necessitate a different level of palliative care. Comorbidity is an example of why it will be important to measure suffering intensity in ways that are not exclusively time-bound, and we recommend this be a priority for future research on SHS and in developing a metric such as SALYs.

Our calculations do not account for the suffering associated with migration, political violence, armed conflict, climatic and geological catastrophes, or infectious disease epidemics. These can cause suffering of any type and on a massive scale, particularly where health-care systems are weak or dysfunctional. Suffering from these causes typically goes unrelieved in LMICs and might persist for decades and be passed on to the next generation.[142] Furthermore, under these extreme conditions, non-communicable diseases are generally neglected.[143] The Commission calls for palliative care to be an essential component of any response to humanitarian emergencies and crises, including refugee crises (panel 11).[42,71,162–165]

Section 2: An Essential Package with resources and interventions to respond to the burden of SHS

The Commission calls on all countries to ensure universal access to an Essential Package by 2030 to achieve SDG Target 3.8, which calls for UHC with financial risk protection. Ensuring effective access to the Essential Package (panel 2) implies taking a balanced approach to at the same time achieve SDG Target 3.5 on prevention and treatment of substance abuse.[54]

The Essential Package of palliative care health services is intended to guide policy makers in LMICs in choosing interventions across different priorities, given trade-offs and budget constraints, and deciding how these should be financed. It is a complement for other essential packages, not a substitute. Aggregating and integrating all essential packages forms a model essential UHC package.[25]

The Essential Package is focused on LMICs to relieve, in the most cost-effective way, the burden of SHS. It is intended to be provided in the home, at community health centres, and in hospitals and settings that offer more complex care; to help strengthen health systems seeking UHC; and to protect patients and their families from catastrophic health expenditures associated with serious, complex, or life-threatening health problems. No mention is made of infrastructure because no special requirements are needed to provide the Essential Package. The components of the package (panel 2) are mapped onto each health condition, with specific assumptions about dosing and quantities and requirements varying between countries because of the disease burden (additional online material).

This Commission puts forward an Essential Package that is the minimum standard that any health system, however resource-constrained, should make accessible to all patients in need and their families. It includes medicines and equipment as well as the human resources to ensure these are used appropriately and effectively. The package considers the health conditions and symptoms associated with the burden of SHS and was developed in consultation with the Commission's palliative care experts. By including only off-patent medicines, by proposing frugal innovation for necessary equipment, and by outlining staffing models based on competencies rather than professional status, the Essential Package is designed to be lowest cost.

Explicit packages of health services have been developed and used in many countries, and their design and implementation is described in a rich body of literature.[30,36,166–168] These packages have been a fulcrum for a number of successful health reforms by establishing entitlements and anchoring financing in an explicit list of covered services.[36,169–173]

In line with the definition of UHC, for all families that would face financial catastrophe or impoverishment if they were to pay for medical treatment out-of-pocket, we recommend that the Essential Package be covered by dedicated, pro-poor, public, or publicly mandated funding that spans all relevant health conditions and diseases. To ensure coverage for wealthier population groups, and depending on the financing structure of each country's health system, the Essential Package should be integrated into the social security budget, the national health insurance system, and private insurance.

Yet because the Essential Package includes only the most basic of medicines, equipment, and human resources, the provision of this package should not be the final goal of any health system seeking to achieve UHC and effectively meet the palliative care needs of a population. The Essential Package is a base on which to build more extensive and costly packages as budgets expand. Countries should expand and build on the Essential Package in line with population need, cultural norms, human resources, health infrastructure capacity, and financial resources, and they should work to provide a package specific to the needs of children and other especially vulnerable groups.

As posited by the SDGs and previous *Lancet* Commissions,[30] a model of progressive universalism should be applied in extending the package of covered palliative care services. Middle-income countries, in particular, should strive not only to have the Essential Package in place by 2030, but to work towards augmenting the package to include palliative radiation, surgery, and chemotherapy, as well as slow-release, off-patent morphine formulations or other long-acting opioids. The larger and costlier package should also be publicly

financed exclusively for poor people to avoid generating catastrophic or impoverishing health expenditures.

The Commission presents only one Essential Package, without differentiating explicitly between children and adults, to minimise the complexity of implementing palliative care in the most resource-constrained countries. However, children are particularly at risk for inadequate or ineffective access to palliative care.[114] We have therefore included the medicines, equipment, basic needs support, and human resources that we deem essential for paediatric palliative care in our Essential Package.

We worked closely with leading research groups that specialise in developing packages of cost-effective interventions and aligned our Essential Package using their established methodology.[69,167,174,175] In line with the nomenclature commonly used in leading research on priority-setting tools, our package is called essential because it contains the most basic elements to satisfy the palliative care needs of the population. Following WHO principles, the Essential Package was also designed with due regard to public health relevance, evidence on efficacy and safety, and comparative cost-effectiveness. Many more comprehensive packages exist, such as those including access to palliative surgery, radiotherapy, and chemotherapy, which are essential for relieving SHS for many patients with cancer, but providing this larger array of services depends on a country's resources for health.

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In formulating the Essential Package, the Commission focused on the necessary medicines, equipment, and human resources but recognises the need for social and spiritual support to alleviate suffering. Palliative care provides the following interventions: (1) prevention, assessment, and treatment of physical symptoms; (2) prevention, assessment, and treatment of psychological symptoms, including supportive and culturally appropriate counselling for patients and their families about diagnosis, prognosis, and treatment options and bereavement support for family members; (3) intersectoral social supports to alleviate patients' and caregivers' suffering due to extreme poverty; and (4) support to respond to suffering that is spiritual in nature.[67,176]

Hence, palliative care encompasses two interventions that are strictly health-related, which correspond to medicines, equipment, and human resources in the Essential Package, and two interventions that are necessary complements but should not be funded or provided by the health sector. The Commission strongly recommends that basic social supports be implemented for families living in extreme poverty as a necessary complement to the Essential Package and financed over and above the health budget, in conjunction with and as part of antipoverty and social welfare programmes. Toward alleviation of spiritual suffering, the Commission calls for compassionate training of all palliative care providers to sensitise them to support the spiritual needs of patients and families.[177] Every effort should be made to facilitate access to spiritual counselling appropriate to the beliefs and needs of the patient and family. These services, however, should not be financed by the health budget or considered the responsibility of government. Traditionally, these services have been provided by not-for-profit and often faith-based actors, and the government should support policies to enable their participation in palliative care.

Medicines

The list of medicines in the Essential Package is based on WHO's Essential Medicines List[15] and is supported by other published reports.[178] Each item in the Essential Package is deemed by the Commission's panel of doctors, many of whom are experts in clinical palliative care in LMICs, to be essential for the relief of at least one symptom or type of physical or psychological suffering that contributes to the total burden of SHS worldwide. Some of these items might also alleviate spiritual suffering and ease the financial burden of the family and hence reduce social suffering.

Medicines included in the Essential Package for both adults and children meet the following three criteria: (1) they are necessary to prevent or effectively relieve the specific symptoms or types of suffering most commonly associated with any of the 20 health conditions described in section 1; (2) their safe prescription or administration requires a level of professional capacity that is typically available in a primary care setting if augmented by basic training in palliative care; and (3) in keeping with WHO guidelines, they must be the medicines in their class that best balance accessibility on the world market, clinical effectiveness, safety, ease of use, and minimal cost (panel 2). In countries where certain medicines are not available or are especially costly, we suggest acceptable substitutes. For each of the medicines in the Essential Package, we describe indications for use mapped to symptoms, possible substitutes, routes of administration, and specific dosing recommendations.

The Commission strongly endorses the 2017 WHO Essential Medicines List[15] and the 2017 WHO Essential Medicines List for Children.[179] The list of medicines in the Essential Package is largely derived from these lists and is almost entirely a cost-minimising subset of the Essential Medicines List, with minor deviations discussed below.

Morphine must be available both as an oral, immediate-release preparation and as an injectable preparation for any patient with moderate or severe pain or with terminal dyspnoea that cannot be adequately relieved by other means. These preparations tend to be the least expensive and are the most essential.

Although most medicines in the Essential Package are already commonly available in health systems, assuring safety and accessibility of morphine is more complex. Ensuring a balanced approach between appropriate access to controlled medicines and prevention of

Panel 12: Ensuring safe and adequate access to morphine

Morphine, in both injectable and oral immediate-release formulations, must be accessible by any referral, provincial, or district hospital, and oral immediate-release morphine should be safely accessible by prescription locally, so that obtaining medicine, at appropriate and necessary doses, is feasible for the patient, family, or caregiver without undue travel or financial burden. This means that clinical staff at community health centres must be trained in palliative care and opioid analgesia, safe storage facilities must be available, and links to referral hospitals and doctors trained in palliative care must be in place.

All doctors, including those working in primary care settings, should be legally and institutionally empowered and appropriately trained to prescribe an adequate supply of morphine for inpatients and outpatients in any dose necessary to provide adequate relief, as defined by the patient, in keeping with internationally accepted palliative care guidelines. Whenever clinically possible, oral morphine rather than the injectable form should be prescribed. All doctors should be trained to assess and treat opioid side-effects, to assess for and minimise risk of opioid dependence and opioid diversion for non-medical uses, and to avoid injudicious use of morphine for mild pain or chronic non-malignant pain.

To maximise safe access to morphine for legitimate use, some countries allow nurses with special training to prescribe morphine under the supervision of a doctor.[66] This strategy should be considered in countries where access to doctors is limited.

Model guidelines for opioid management are available and should be used to develop regulations relevant to local context.[180,181] All hospitals, health centres, clinics, and pharmacies must store morphine in a locked and well anchored box or cupboard at all times, keep records[182] of the remaining supply at all points in the supply chain, and record the amount dispensed for a patient and the amount wasted or returned. The national or provincial competent authorities for opioid supply should track opioid prescribing or dispensing patterns of hospitals, health centres, doctors, and pharmacies and investigate unexpectedly high or low levels of prescribing or dispensing. This requires investment in systems and infrastructure for monitoring. Mexico has implemented electronic prescribing and should evaluate and disseminate the results of this programme.[183]

In keeping with WHO's principle of balancing maximum accessibility of opioids for medical uses with minimum risk of opioid diversion,[6,12,42] additional precautions might be necessary in areas with high rates of crime or violence. For example, it might not be possible to make morphine safely accessible at the community level in areas with high crime rates. In these places, accessibility must be ensured at the district level or higher in ways that do not increase the financial burden for patients and their families. Where home or clinic supplies of morphine are frequently stolen, or patients and their families are put at risk by carrying or storing morphine, patients needing morphine might have to either travel to a hospital to receive morphine or be admitted to a hospital as an inpatient.

non-medical use, diversion, and trafficking of controlled substances[6,42] is required (panel 12).

Not all medicines in WHO's Essential Medicines List[15] section on palliative care and pain treatment are included in the Essential Package because the Commission's aim was to create a minimum, least-cost list. The following items are excluded from our Essential Package: slow-release oral morphine, transdermal fentanyl, docusate sodium, midazolam, aspirin, codeine, and cyclizine. Less expensive and more accessible medications with similar efficacy and safety data are part of our proposed Essential Package (a detailed explanation of each exclusion is provided in the additional online material).

Five medicines in our Essential Package are included in the Essential Medicines List[15] but not in the palliative care section: oral and injectable furosemide (a low-cost, strong diuretic, available in most health-care centres; useful in treating shortness of breath and painful oedema or ascites), oral omeprazole, oral fluconazole, metronidazole (for topical use), and injectable naloxone.[15] We advocate for the inclusion of these medicines in the palliative care section of WHO's Essential Medicines List.

Despite exclusion in WHO's Essential Medicines List, the Essential Package includes petroleum jelly because this low-cost, non-prescription compound is essential in many resource-poor settings for the management of wounds and wound dressing and because it can be useful for managing and preventing skin lesions of different types, including diaper rash.

Oral and injectable haloperidol and oral fluoxetine, or another selective serotonin-reuptake inhibitor (SSRI), are sometimes considered psychiatric or psychotropic medicines, yet they have multiple essential uses in palliative care.[184–187] For example, haloperidol is the first-line medicine in many cases, not only to treat agitation and delirium,[188,189] but also for relief of nausea, vomiting, and anxiety.[190] An SSRI such as fluoxetine is the first-line treatment for depressed mood or persistent anxiety (if empathetic care is unsuccessful or insufficient), both of which are common in patients with serious, complex, or life-limiting health problems. Doctors at all levels should be trained and permitted to prescribe these medicines. Patients with more severe psychiatric illnesses, such as psychotic or bipolar disorders, should be referred for specialist psychiatric care whenever possible.

Panel 13: Frugal, disruptive palliative care equipment innovation

The Commission identified several key pieces of equipment that are essential in low-income country settings, yet are too expensive to include in the Essential Package. In response, the Commission researched and posits innovative, alternative, low-technology options that could be locally sourced at reasonable cost. We call for incentives for frugal and disruptive innovation to produce low-cost solutions for palliative care patients.[191,192] This presents opportunities to promote markets, intervene through advocacy, and develop and implement research funding that includes students and small businesses.

The Commission reviewed air, water, and covered foam mattresses and concluded they are acceptable, low-cost options for avoiding and treating pressure ulcers. At least one type of mattress should be made accessible at low cost in resource-constrained settings.

Managing human waste at the end of life or from people with bladder or bowel dysfunction is a huge financial and health challenge for people in all parts of the world, especially for poor families, and reduces quality of life for the patient and caregiver. Diapers should be used for incontinence to avoid skin infections and ulceration,[193,194] whereas plastic bags and cotton can be used in very low-income settings to produce simple diapers for adult patients on site. Even in places like Rwanda and Kenya,[195] where plastic bags are prohibited from use as part of laudable environmental protection initiatives,[196] specialised medical use is approved or should be negotiated.

The global market for adult diapers is growing, and sales will likely surpass baby diapers within a decade.[197] Contrary to the comparable case of feminine hygiene products, few low-cost alternatives are available for adult diapers.[198–200] Developing and testing new and less expensive adult diaper technologies is crucial, yet without incentives, few innovations have been developed or tested in low-income settings.[201–205] Opportunities exist for design innovations that could reduce price, improve quality, and be environmentally friendly.

Some materials and equipment, including non-sterile gloves for infection control and hygiene and dressing materials for wounds, are usually available at all levels of health-care systems. Widely available reusable plastic or rubber gloves intended for household cleaning can be used by family caregivers for patient hygiene. When these simple materials are not accessible in the poorest settings, they need to be included in the equipment of the Essential Package or in the package of in-kind support.

If prices can be brought down or low-cost options identified, wheelchairs, canes, crutches, simple hearing aids, eyeglasses, and white canes for people with vision impairment should be in the Essential Package. Wheelchairs could not be included in the Essential Package because of cost, although they would improve mobility and reduce deprivation and the care burden for families. Innovative private–public partnership work is underway to design, produce, and market affordable wheelchairs for low-income settings, and this needs to be incentivised for palliative care.[206,207] In India, models in the US$75–125 range have been documented,[208–210] and mass production in China and Taiwan could reduce cost to $50.[211] Low-cost technology is being developed in India[212] and Mexico for electric-powered wheelchairs.[213]

Equipment

Equipment for the Essential Package meets the following criteria: (1) necessary for relief of at least one type of physical or psychological suffering; (2) locally available; (3) simple to use with basic training; and (4) small enough to be located in a clinic. The equipment should also be the most inexpensive, effective design, and our Commission researched and developed several innovative, low-cost alternatives (panel 13).

The Essential Package includes oxygen, nasogastric tubes (for vomiting refractory to medicines, administration of medicines or fluids), urinary catheters (to manage bladder dysfunction or outlet obstruction), foam, water, or air pressure-reducing mattresses (to relieve pressure ulcers and pain), a locked safebox for opioids (secured to a wall or immovable object), a flashlight with rechargeable battery (if there is no access to electricity for safe administration of medicines), and cotton and plastic bags or adult diapers (to reduce risk of skin ulceration and infection, and caregiver risk and burden).

Human resources and training

The Commission developed a minimum staffing model for achieving expanded coverage of the Essential Package, based on published recommendations[214] and on the opinions of our clinical experts. The effectiveness of these staffing models depends on the training and empowerment of health-care professionals who are often reluctant to use opioids because of fear or stigma.[215–220] Expanded coverage and maximising the capacity of local, non-specialised health personnel also necessitates training and innovation to allow for staffing based on competencies rather than professions (additional online material).

Palliative care multidisciplinary teams and competency profiles were designed for each level of care (district hospital, referral hospital, primary or community health centre, and home-based care), and consider the following categories of personnel to provide clinical, administrative, and logistics support, as appropriate and necessary and in ways that link each level of care to maximise access: doctors (specialised in palliative care or other disciplines, general practitioners), nurses (specialised in palliative care and general), social workers and counsellors,

psychiatrists, psychologists, counsellors, physical therapists, pharmacists, community health workers, clinical support staff (diagnostic imaging staff, laboratory technician, nutritionist), non-clinical support staff (administration, cleaning), and volunteer community and home care providers. Each level of care requires a specific mix of specialties using referral systems and technology (ie, telemedicine) to access and create linkages across levels.

The Essential Package includes the estimated essential number of full-time-equivalent staff members for a specific number of inpatient and outpatient cases, considering each level of care: specialised palliative care doctors, specialised doctors (eg, oncologists), general practitioners, specialised palliative care and general nurses, social workers, psychologists, community health workers, and other support staff to provide essential palliative care. Community health centres would be staffed mainly by nurses and sometimes also by a general practitioner who would supervise community health workers.

Staffing should be based on competencies rather than professions, and tasks often undertaken by the specialised health-care professionals who are present in high-income countries but severely lacking in LMICs can be taken up by other staff.[16,17] Our human resources model and estimates therefore consider an important and expanded role for general and community nurses who can be trained in providing palliative care services, and for community health workers who can visit patients at home. In Uganda, for example, nurses with special training are legally able to prescribe morphine.[66] General practitioners with basic palliative care training or training in managing and treating specific health conditions, such as HIV disease, can and should provide basic palliative care to their patients.

The training required for health-care providers to implement palliative care at each level of health care has been recommended by WHO and described in the scientific literature.[214,221–223] The European Association for Palliative Care[37,38] has developed a step-wise educational approach by levels of care to reflect the scope and focus of professionals involved in the delivery of palliative care. To achieve universal access, basic palliative care training should be made widely available and integrated into all undergraduate medical and nursing school curricula. Additionally, training in medicine and in nursing leading to specialist certification in both adult and paediatric palliative care will generate a corps of specialists that can become palliative care leaders, teachers, and implementers for every country.

Neither palliative care specialists nor general practitioners can be expected to respond effectively to cases that would be better suited to specialists such as psychiatrists, neonatologists, or surgeons. Yet we recognise that if specialists are not available in resource-constrained environments, it is the responsibility of the person providing palliative care to offer what is possible rather than leaving the patient and family without any type of care and exposed to SHS.

The Essential Package specifies that basic psychological support can be provided not only by psychologists but also by other professionals at any level of the health-care system. This requires basic training in psychological support and palliative care. However, the high prevalence of anxiety, depressive disorders, and complicated grief makes participation of trained psychotherapists in palliative care highly desirable.[224–228] Health-care professionals at all levels of care should routinely ask patients with serious, complex, or life-limiting health problems if they would like to receive spiritual counselling.[229] We also advocate for local, volunteer spiritual counsellors to visit patients whenever possible.

The important and often underused role of community health workers, and particularly their ability to work effectively outside of a health centre, is widely discussed in the scientific literature about health systems.[230–233] In palliative care, community health workers can have an essential role by paying frequent visits to patients at home, in both urban and rural settings, especially where community or public health nurses are not available to provide necessary home care.[81,214,234] With a few hours of additional training, community health workers can provide emotional support, recognise uncontrolled symptoms, and identify unfulfilled basic needs for food, shelter, or clothing or improper use of medications.[235] Community health workers can also report their findings to clinicians and can help organise an appropriate response such as a change in prescription, a home visit by a nurse or doctor, or transportation of the patient to a medical facility.

We assume that volunteers, and especially family members, will provide support to patients at all levels of care and that much of this care will be provided at home.[120] Worldwide, the responsibility for caregiving falls on women, which fuels gender inequities.[125] Although the Essential Package does not include funding for caregivers through the health system, we advocate for social supports, especially for those in extreme poverty (panel 14). We also highly recommend that public policies be implemented in all countries to train and protect family caregivers, to avoid illness and exhaustion and to ensure that they do not lose their employment or source of income.[248]

Next steps: refining and augmenting the Essential Package to provide a full spectrum of palliative care

Developing and presenting an Essential Package specifically for paediatric palliative care should be high priority. The complementary needs of children for play and education must be taken into account.[249] Nurses at all levels should have a good understanding of growth and development and of family-centred palliative care.

Panel 14: **Social support: an essential intersectoral[175] complement to the Essential Package of health services**

Social supports for patients and family caregivers are needed to promote dignity at the end of life and to ensure that families do not sacrifice basic needs and are not driven into poverty while caring for loved ones.[236,237] In line with the supporting literature on inter-sectoral interventions and essential packages of health interventions,[175,238] and using a diagonal approach,[239] the Commission recommends that the Essential Package be accompanied by minimum social supports (basic food packages, cash payments for housing, transportation vouchers for visits to clinics or hospitals for the patient and a caregiver, support for funeral costs, and in-kind support for patients and families to adapt the living space) and well developed, community-integrated programmes for patients and families living in extreme poverty to ensure that patients can access the Essential Package of health services. Social supports should be delivered and financed through antipoverty or social welfare or development programmes rather than by the health system.

Most existing programmes are small in scale. One of the few palliative care programmes to provide social support has been implemented and co-managed by the Malawi Ministry of Health and a local non-governmental organisation in an impoverished, rural district in Malawi and is integrated with treatment programmes for HIV/AIDS and non-communicable diseases. When enrolled in the palliative care programme, patients are screened and then provided with food packages, cash transfers, transportation vouchers, in-kind, and housing support, as needed.[81]

To scale up these efforts, we propose that social support for families in need of palliative care be integrated into means-tested, antipoverty, and social development programmes often operated and financed by ministries of education and social development, working with ministries of health.[240–242] These community-integrated programmes already protect basic needs of families living in extreme poverty, but additional budget and programme design elements are required to include patients in need of palliative care. Mexico introduced a bill in 2016 to provide a cash-based subsidy to poor, terminal patients to help them pay for non-health-related needs, since palliative care is covered by Seguro Popular.[243]

The social support components are costly, especially for low-income countries, but constitute poverty alleviation instruments and enable effective access to palliative care. We produced rough estimates of the cost of the social supports mentioned above, considering only patients living in extreme poverty (daily income less than US$1·90).[244] In Mexico, based on data on subsidies provided to families by existing anti-poverty programmes, and given the small proportion of families living below the poverty line (3%), social supports for palliative care represent a very small additional cost (about 1% of the health components of the Essential Package). For Rwanda, however, as for other low-income countries, the additional cost is considerable, largely because more than 60% of families live in extreme poverty. Social supports would represent an additional cost of about 30% of the health components of the Essential Package and would be, in practice, an antipoverty package for the most financially vulnerable families with palliative care needs. In addition to facilitating the delivery of palliative care health services, social supports reduce risk of impoverishment and offer potential cost savings from reduced hospital admissions, all of which should be considered in a cost-benefit analysis.

A related social support to consider in future implementation research is group life insurance that includes funeral support and can be group purchased through social welfare programmes.[245–247] Culturally and medically appropriate burial or disposal of corpses are a major financial burden for families, and evidence from Kerala suggests that families and patients highly value support for these items, although they believe that this should not be financed from the health budget or provided by the health ministry.[130]

We advocate for countries to move towards universal access to an ideal package of evidence-based palliative care health interventions carefully selected for cost-effectiveness and implemented alongside professional training and monitoring to ensure a balanced approach that minimises the risk of inappropriate drug use and diversion.[6] A next step in assuring effective access to palliative care would entail augmenting the Essential Package with basic, high-priority interventions that require both doctors and nurses with training or experience in additional disciplines and hospitals with capacity to provide these interventions. The Commission considers that universal access to palliative surgery, palliative radiotherapy, and palliative chemotherapy be of highest priority for inclusion in an augmented package.[250–255] These interventions can improve quality of life, could enable dose-reduction or even elimination of morphine therapy for pain relief, and would improve patients' functional status. Slow-release oral morphine or transdermal fentanyl, which balances safety, effectiveness, and low cost and is in line with WHO's Essential Medicines List,[15] should be considered for inclusion in the augmented Essential Package, but only after universal access to oral and injectable immediate-release morphine has been guaranteed and with appropriate controls on marketing by the pharmaceutical industry.

Cost of the Essential Package

The Commission collected primary data on each component of the Essential Package from Rwanda (low income), Vietnam (lower-middle income), and Mexico (upper-middle income). To collect these data, we relied on key informants in countries where the Commission had strong links to palliative care specialists and access to

	Rwanda*			Vietnam†			Mexico		
	Reported price (US$)	Lowest international price (US$)	Highest international price (US$)	Reported price (US$)	Lowest international price (US$)	Highest international price (US$)	Reported price (US$)	Lowest international price (US$)	Highest international price (US$)
Medicines	52	18	78	27	23	96	122	28	119
Morphine (oral or injectable)	20	8	50	14	12	76	90	14	84
Equipment	31	..	..	5	..	..	31	..	..
Palliative care team (human resources)	121	..	..	78	..	..	584	..	..
Operational costs (8% of total)	16	14	18	9	9	14	59	51	59
Total	219	182	248	119	115	194	796	694	793
Percentage of GDP‡	0·25%	0·21%	0·28%	0·04%	0·04%	0·06%	0·03%	0·03%	0·03%
Percentage of health expenditure§	3·35%	2·78%	3·79%	0·56%	0·54%	0·92%	0·50%	0·44%	0·50%
Percentage of public health expenditure¶	8·79%	7·31%	9·94%	1·04%	1·00%	1·69%	0·97%	0·84%	0·96%

Prices are per patient in US$. International prices are buyer prices as reported in the 2014 International Drug Price Indicator Guide, MSH (http://erc.msh.org/dmpguide/). GDP=gross domestic product. *For Rwanda, fluoxetine was substituted with selective serotonin-release inhibitors, and disposable diapers were substituted with reusable cloth diapers. †Estimates for Vietnam do not include parenteral fluconazole as pricing for this medicine was unavailable. ‡GDP, World Development Indicators, World Bank (http://data.worldbank.org/indicator/NY.GDP.MKTP.CD). §Health expenditure, total (percentage of GDP), World Development Indicators, World Bank (http://data.worldbank.org/indicator/SH.XPD.TOTL.ZS). ¶Health expenditure, public (percentage of total health expenditure), World Development Indicators, World Bank (http://data.worldbank.org/indicator/SH.XPD.PUBL). Source: WHO Global Health Estimates 2015.

***Table 5*: Per-patient cost of the Essential Package in Rwanda, Vietnam, and Mexico, by medicine prices**

databases. For medicines and equipment, we collected the lowest available, public sector, wholesale buyer price for each country and included the cost of situating the item at a provider site that is accessible to a patient. For Rwanda and Vietnam, the prices include the cost of delivering the item to a hospital. For Mexico, the buyer-negotiated price includes situating the item at a public sector health provider (clinic or hospital). We also considered medical substitutes for medicines that are not available in specific countries or only at very high prices (additional online material).

To cost the human resources component of the Essential Package, we collected data on public sector salaries specific to each type of provider at different levels of care. Our data are the monthly total pre-tax (including mandatory benefits), full-time equivalent reported salaries, and we scale the data to account for the recommended mix of human resources and the number of inpatients and outpatients in each country by health condition.

We also considered the most basic operational inputs to support the provision of the Essential Package at every level of care. These include a small proportion of the cost of infrastructure maintenance, administrative overhead, basic laboratory and imaging facilities, emergency room services, and facility costs. On the basis of findings from a literature review, we have added on average 8% to our overall costs of the Essential Package.[256–260]

We accessed prices for each of the Essential Package medicines from the International Drug Price Indicator Guide, which contains a range of prices from pharmaceutical suppliers, international development organisations, and government agencies. We present wholesale buyer prices of medicines (which are usually accessible to government agencies using international competitive bidding or tender) that are both cheapest and of the highest quality. We analysed lowest and highest prices reported in the database for 2014.[261] We harvested data for multiple years and compared highest and lowest prices of morphine in the dataset and in recent literature.[262] By harvesting the lowest wholesale buyer prices from this dataset, our costing represents the best prices that a country could potentially have accessed in a given year compared with highest possible prices that any country paid. These wholesale prices do not include the cost of transporting the item to a hospital or making it accessible to the patient.

Detailed information on datasets, costing, and methods is available in the additional online material.

International variation in the price of medicines

Variations in the price paid by health-care institutions, especially for morphine, both determine and fuel the global inequities in access to palliative care and in managing the burden of SHS.[262] The Commission identified substantial variation between countries in the prices paid for medicines and hence in the cost of the Essential Package. Certain medicines were purchased at particularly high prices. Countries could benefit from important savings if they had access to best-case international, wholesale prices, especially for oral and injectable morphine, and we recommend the creation of

global and regional price-stabilisation platforms to aggregate demand and provide more explicit and effective dissemination of pricing information. The possible savings from lower medicine prices would have a large effect on the total cost of the Essential Package, especially in low-income countries, where salaries tend to be low and the cost of morphine is a particularly high proportion of the Essential Package cost.

Comparing the lowest prices in the International Drug Price Indicator Guide with the purchasing prices that countries reported, Vietnam is purchasing medicines in the Essential Package at a relatively competitive price, Rwanda could do substantially better with access to international lowest prices, and Mexico is a particularly poor performer in purchasing injectable morphine, although the prices paid for most other medicines are competitive.

In Rwanda, a low-income country, the annual cost of universal access to the Essential Package, even at lowest international reported prices ($182 per patient with SHS, or $1·45 per capita), is about 7·3% of total public expenditure on health—a much higher share than in the other countries (table 5). By comparison, the cost per year of universal access to the Essential Package, as a proportion of total public expenditure on health, would cost 1·0% in Vietnam ($115 per patient with SHS, $0·81 per capita) and 0·8% in Mexico ($694 per patient with SHS, $2·50 per capita) using lowest international prices. Reported equipment prices, and especially the price of oxygen, are high in Rwanda. Mexico, in addition to paying high prices for injectable morphine, pays medical staff high salaries. As a proportion of gross domestic product (GDP), the cost is 0·21% in Rwanda, 0·04% in Vietnam, and 0·03% in Mexico.

The cost of the entire package of medicines in Rwanda using country reported prices is almost three times the cost using lowest international prices. The difference is much smaller for Vietnam, only about 20% higher than lowest international prices, whereas for Mexico there is a more than four-fold difference between country reported and lowest international prices. In Rwanda, the reported price of injectable morphine is almost six times the lowest reported price in the International Drug Price Indicator Guide. In Mexico, the documented price of injectable morphine purchased in the public sector in late 2014 was many times higher than the lowest reported international price and indeed exceeded the highest international price recorded in the International Drug Price Indicator Guide. Although in Mexico, prices include the cost of situating the medicine, the prices of other medicines, including oral morphine are much more competitive and in line with international prices.

We also analysed the dispersion by year in wholesale buyer prices reported in the International Drug Price Indicator Guide for 2011–14.[261] We found a huge discrepancy in prices—a more than ten-fold difference between the highest and lowest price in several cases, and up to a five-fold difference in median price—between countries and by year for both oral and injectable morphine. Only in 2011, and only for injectable morphine, was the variation in price low; by contrast, in 2013, the highest price was 37 times the lowest price reported in the dataset. The median price across years varies much less. We also noted a stable lowest price of $0·011 per mg for injectable morphine in 2012, 2013, and 2014, which we traced to purchasing by the health department of South Africa. These data are evidence of the need for global collective action to aggregate demand and to support LMICs with information and negotiating capacity to secure stable, lowest prices. The data also suggest that national strategies are needed to assist in local purchasing and facilitating a safe supply chain.

We projected the cost estimates of the Essential Package across LMICs by income group for low-income, lower-middle-income, and upper-middle-income countries using the reference country-reported medicine prices (from Rwanda, Vietnam, and Mexico for low-income, lower-middle-income, and upper-middle-income countries, respectively) and the lowest and highest international buyer prices. We used reference country-reported costs of equipment and human resources (additional online material). At lowest international medicine prices, the total cost of covering the Essential Package for all people with SHS is 2·4% of public health expenditure for lower-middle-income countries, and 2·2% of public health expenditure for upper-middle-income countries. The total cost is about 0·04% of GDP for lower-middle-income countries and 0·07% of GDP for upper-middle-income countries. For low-income countries, the proportions are much higher: 14·4% of public health expenditure and 0·35% of GDP.

Applying the highest global prices for all medicines, the Essential Package would represent about 2·5% of public expenditure on health in upper-middle-income countries (about a 15% increase) and 3·6% of public expenditure on health for lower-middle-income countries (an increase of about 50%). For low-income countries, the cost increases by 26%, to more than 18·2% of average public expenditure on health.

The cost of the Essential Package for children at lowest reported international prices is a small proportion of the overall cost for all people with SHS. At lowest medicine prices, the cost of the Essential Package for paediatric decedents with SHS is 1·5% of public sector health expenditure in low-income countries, 0·13% of public sector health expenditure in lower-middle-income countries, and 0·03% of public sector health expenditure in upper-middle-income countries. Using our limited data on the paediatric non-decedent burden of SHS, the total cost (decedent and non-decedent) is 2·7% of public sector health expenditure in low-income countries, 0·23% of public sector health expenditure in lower-middle-income countries, and 0·05% of public sector

health expenditure in upper-middle-income countries (additional online material).

A detailed analysis is called for to assess the supply and demand factors that characterise the market for pain relief medicines, especially morphine, and to explain the very large variation in prices. This information should help to develop the price-stabilisation platforms that we are recommending and enable countries to have access to better international pricing data as a tool for effective negotiation by countries and for civil society advocacy. Global institutions should develop or strengthen existing programmes and institutions to support countries in accessing and negotiating stable and lowest prices with quality guarantees.

Comparative costs

Although a rigorous cost-effectiveness analysis was beyond the scope of our report, we compared the costs of the Essential Package with cost estimates of UHC packages. Our Essential Package follows the most recent Disease Control Priorities[25] methods and is one of the least costly of the components that form the essential UHC package. For low-income countries, the Essential Package costs about $2·16 per capita per year at lowest reported international medicine prices, which is 2–3% of the essential UHC package. We also compared the cost of the Essential Package with previous calculations of the cost of a minimum package of universal primary health care services, including benchmark expenditures from the High Level Taskforce on Innovative International Financing for Health Systems, the Commission on Macroeconomics and Health, and Chatham House.[263,264] The Essential Package cost is about 3% of the cost of these UHC packages.

There is a range of potential benefits of extending access to palliative care and pain relief, and an extended cost-effectiveness analysis[33,265,266] is appropriate to evaluate the health and non-health, financial, and equity consequences of adopting and publicly financing the Essential Package. Although this research was beyond the scope of the Commission, for Vietnam we analysed the potential benefit of universal coverage through public finance of the Essential Package in terms of SHS days averted and financial risk protection.

The scientific literature about the introduction of palliative care reports a 25–35% reduction in end-of-life hospital admissions, which could mean important cost-saving in LMICs.[19–23] Most studies have been undertaken in high-income countries, but some data are available for low-income countries. We undertook a projection for Mexico, comparing the cost of universal coverage of the Essential Package to the potential for reduced admissions to hospital. We identified the hospitalisations for the health conditions associated with SHS from which patients died in public sector health facilities,[267] and we analysed data on the number of days in hospital and daily hospital costs. Applying a potential reduction of 25–35%, the savings would have been $66–92 million in 2015. This saving would fully offset the projected cost of extending the Essential Package at lowest international wholesale prices to all patients with SHS who need palliative care and who die each year in public hospitals, which we estimate would cost about $40 million. Alternatively, this saving could offset the projected cost of $62 million for offering the Essential Package to all of the 21% of Mexicans living in poverty and who are likely to experience SHS.[268]

A more expansive package would be more likely to reduce hospital admissions. As discussed above, this is also an important next research step for priority setting on palliative care that focuses on expanding and costing the package of covered health services. Using data from the Mexican Social Security Institute,[267] we estimated the costs for Mexico of including palliative surgery for all health conditions, as needed, and chemotherapy and radiotherapy for patients with cancer.[250,252,254] Assuming that all necessary complementary hospital services are in place, which would require a large additional public investment (not accounted for in our calculation), the provision of these additional health services augments the overall cost of the Essential Package, using lowest international medicine prices and including an expanded human resource base, by about 7%. We also did not consider the possible reductions in the cost if access to palliative surgery and radiation therapy reduces the need for morphine. The projected cost of offering this augmented palliative care package to the 21% of the Mexican population living in poverty,[268] assuming access to lowest international prices, is about $67 million per year.

Future research and in-depth analytic work on cost effectiveness and choices about public finance of the Essential Package and augmented packages will be important. To measure the cost effectiveness of the package, it is necessary to compare the wide range of benefits from incorporating palliative care into health care and of alleviating SHS, through channels such as: reduced risk of impoverishment, reduced symptoms and unnecessary treatment, and higher quality care-giving that is less taxing on the caregiver and promotes gender equity.

The cost of closing the global divide in access to opioids

The absence of morphine in LMICs is emblematic of the most extreme inequity in the world, and we demonstrate this in our analysis of unmet need. As with other studies,[11] we assume that the need for and access to morphine is a tracer of overall access to palliative care and pain relief.

Our conceptual framework and findings presented in section 1 indicate that pain is only one of the many symptoms associated with SHS, but estimating the unmet need for each type of suffering or for each Essential Package component was impossible because

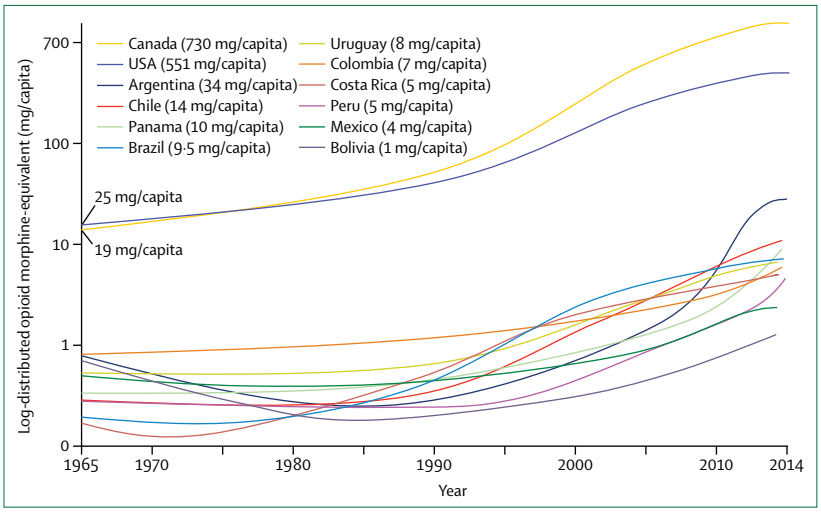

***Figure 8*: Distributed opioid morphine-equivalent in the Americas, 1965–2014**
Because of the very large differences between Canada and USA and Latin America, we use log distributed opioid morphine-equivalent. Numbers in parenthesis indicate the distributed opioid morphine-equivalent for each country in 2014. Source: International Narcotics Control Board (Stata-generated, 1-year lagged moving average trends).

Panel 15: Towards access to pain relief medicines in Africa: lessons from Uganda

Pioneering steps towards palliative care access in Africa came from developing a model hospice and obtaining oral morphine in Uganda.[271] The advocacy and dedicated work of founding the non-governmental organisation Hospice Africa Uganda[272] was largely responsible for the decision in 1993 by Uganda's Minister of Health to import morphine powder and make oral morphine liquid. The next step in national access came in 2004, when the Ugandan Government legalised opioid prescribing by nurses and clinical officers with 9 months of palliative care training.

Hospice Africa Uganda has now contracted with the Ugandan Government to supply reconstituted liquid morphine for the entire public health-care system. Because Uganda has only one production facility that meets international standards, supplies can be purchased in bulk, the quality of the production process and the product can be carefully monitored, and supply chain security is facilitated.

The national consolidation and regional effect of the Ugandan programmes was facilitated by cooperation with global advocacy institutions[273] and through research and academic publications to disseminate results and develop a learning-exchange platform.[274] These learning-exchange efforts contributed to the decision of the ministries of health of Rwanda, Nigeria, Kenya, Swaziland, and Malawi to adopt the Ugandan model for producing and distributing liquid morphine.

data do not exist. However, such estimations should be a priority for future research and would require a country-specific analysis of access and use of a full range of palliative care interventions.

We developed measures of the unmet need for opioids across countries, by income regions (additional online material). Need was measured using estimates of the number of patients who have moderate or severe pain or other symptoms, such as dyspnoea, that should be treated with opioids, and the number of milligrams of oral and injectable morphine-equivalent that would be needed to alleviate their expected days suffering with these symptoms. We focused on opioids for pain relief but noted that small amounts are also needed to treat dyspnoea for patients with cancer or advanced cardiac or pulmonary disease.

We measured accessibility using country-reported data on morphine-equivalent opioid consumption (excluding methadone) that are gathered and reported by the INCB,[1] and have been widely used as a proxy for access to morphine.[11] We present the average for the most recent 3 years for which data were available (to account for annual variation and stocks).

Although the INCB labels these data as consumption data, they describe the opioids (in morphine equivalence) that were available in the country in a given year and delivered to a health facility for prescription or dispensing. Without information on proportion consumed by patients (as opposed to how much remained in stock at hospitals or pharmacies) or what health conditions justified the prescription, we avoid the terms use and consumption and instead speak only of the quantity available for prescription to patients, which we refer to as the distributed opioid morphine-equivalent (DOME). The difference between DOME and total need for pain relief medicine is a minimum measure of unmet need because availability of morphine does not equate to the amount dispensed or consumed by patients. Better data are required to more precisely measure unmet need.

DOME is highly inequitable, and GDP and the Human Development Index explain most of the difference in DOME between countries and over time, according to recent studies.[11] Canada, the USA, western and central Europe, and Oceania account for almost 95% of DOME and only 9% of the global population. Despite increases in DOME, with daily doses of opioid analgesics per million people doubling between 2001 and 2013, inequity has increased between LMICs and high-income countries.[11]

We considered the case of the Americas using data from the INCB and from the University of Wisconsin Pain and Policy Study Group on per-capita DOME that span from 1965 to 2014 (figure 8).[1,269] Although per-capita availability has increased in several countries in Latin America, DOME levels are still extremely low, and gaps have increased. Some countries in Latin America are only now approaching the levels that Canada and the USA reported in 1965, about 20 mg per capita, whereas DOME has increased exponentially in these high-income countries.

We estimated the unmet need for morphine for treatment of SHS for the 20 health conditions and average duration of suffering of decedents and non-decedents. The data at least partially account for the average medical need for morphine per patient being lower in poor countries than in high-income countries because of the variety of health conditions and diseases embodied in the SHS calculations (additional online material).

There are several caveats in interpreting our data and estimates, both within and between countries. The

estimates of unmet need are averages and do not necessarily indicate that all patients receive necessary or recommended medical access, even in high-income countries with high DOME. Some patients might receive morphine for health conditions or pain that should be treated with another medicine or intervention, whereas other patients who need strong opioids for pain relief do not have access. Our data also do not prove that countries with high DOME maintain a stockpile. Our measure of need refers to the 20 health conditions and the SHS days associated with those health conditions, yet morphine is needed to manage other health conditions and situations that produce severe pain, especially perioperative care, meaning that overall unmet need for opioids is higher than our estimates of unmet need for opioids for palliative care.[270] All estimates are best-case scenarios under the assumption that all DOME actually reaches patients in the necessary and appropriate quantities, given their medical need.

We also developed an indicator of unmet need for morphine-equivalent opioids that draws on earlier work[270] but uses DOME values from high-income countries in western Europe as a benchmark. For that group of countries, DOME is more than 18 300 mg per patient in need of palliative care. This is substantially lower than in the USA, Canada, or Australia but high enough to reflect need that goes beyond palliative care and includes, for example, perioperative pain and acute trauma for which use of a morphine-equivalent opioid for a short period of time is often medically indicated. We assume that this better reflects real gaps in LMICs where need is also likely to extend to these other areas of pain relief. We also adjusted for the fact that burden of disease is more skewed to chronic diseases and non-communicable diseases in those high-income countries, so that the quantity of morphine-equivalent opioids needed per patient tends to be higher. The calculations are described in greater detail in the additional online material.

In maps of DOME, Australia, Canada, and the USA stand out in stark comparison to the shrivelled developing regions of Latin America, Asia, and Africa and in lower-income countries of Europe (figure 1). In Canada and the USA, DOME is more than 68 000 mg and 55 000 mg, respectively. In high-income countries of western Europe, DOME levels are much lower, but at more than 18 000 mg per patient, they are still more than eight times the estimated need (about 2170 mg) per patient with SHS.

Country-specific data illustrate the inequities and severe lack of access to morphine to meet palliative care needs, and these are largely, but not entirely, explained by country income (figure 1). For example, Russia, at 124 mg per patient, has only enough morphine-equivalent to satisfy 8% of need. Mexico, at 562 mg per patient, can cover 36% of the need for patients with SHS, compared with only 16% in China (314 mg per patient) and 9% in Vietnam (125 mg per patient). India distributes only enough morphine equivalent to meet 4% of need (43 mg per patient). In the world's poorest countries such as Afghanistan (2 mg per patient) and Haiti (5 mg per patient), DOME is virtually nil. In Uganda, a country where programmes have been put in place to improve medical access to opioids (panel 15),[113] a DOME of 53 mg per patient is enough to satisfy 11% of palliative care need, whereas availability is close to zero elsewhere in Africa. Nigeria, for example, has less than 1 mg of DOME per patient.

	Unmet need due to conditions most associated with SHS (metric tonnes)	Total need due to conditions most associated with SHS (metric tonnes)	Projected unmet need (metric tonnes)	Projected total need (metric tonnes)	DOME (metric tonnes)
High-income countries	0·4	22·7	64·0	86·4	287·7
Upper-middle-income countries	25·1	34·7	281·2	290·8	9·6
Lower-middle-income countries	18·7	19·8	165·7	166·8	1·1
Low-income countries	4·3	4·4	37·1	37·2	0·1
Total	48·5	81·6	548·0	581·2	298·5

Table 6: **Morphine-equivalent unmet and total need for palliative care due to health conditions most associated with serious health-related suffering (SHS) and projected unmet and total need using western European benchmark, by country income group and distributed opioid morphine-equivalent (DOME) reported by the International Narcotics Control Board**

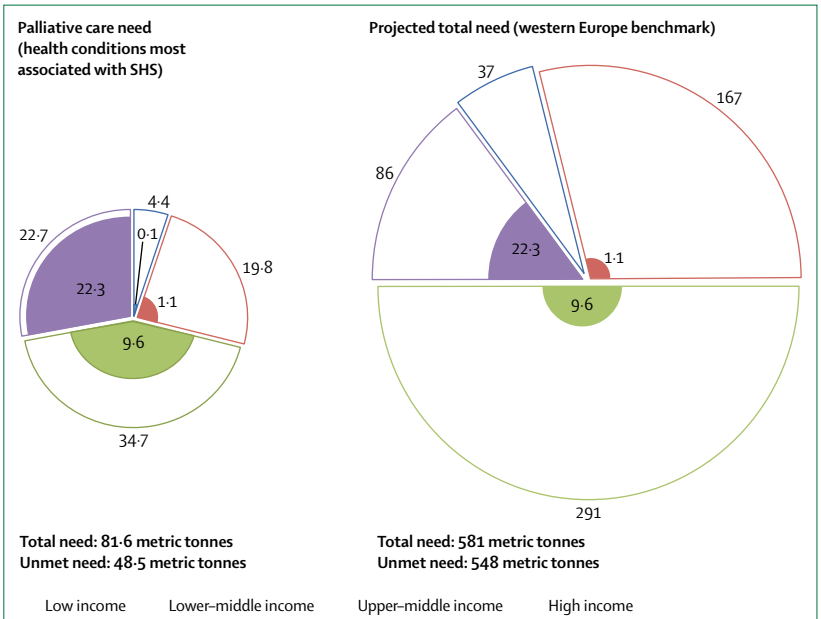

Figure 9: **Palliative care and projected total and unmet need for pain relief medication based on distributed opioid morphine-equivalent (DOME), by income group**
Numbers and coloured parts are DOME in metric tonnes, white parts are minimum estimates of unmet need, and the complete chart represents total need. Countries with DOME greater than need are not included.
Source: International Narcotics Control Board, average 2010–13.

	Region-specific price				Best price*			
	Price (US$, millions)	Percentage of global cost	Percentage of GDP	Percentage of PHE	Price (US$, millions)	Percentage of global cost	Percentage of GDP	Percentage of PHE
Low-income countries	69	11·5%	0·01753%	0·30489%	13	8·9%	0·00329%	0·05717%
Lower-middle-income countries	299	49·8%	0·00514%	0·11418%	56	38·6%	0·00096%	0·02143%
Upper-middle-income countries	231	38·5%	0·00117%	0·01900%	75	51·8%	0·00038%	0·00621%
High-income countries	1	0·2%	0·00000%	0·00002%	1	0·7%	0·00000%	0·00002%
Total	600	100%	0·00082%	0·0082%	145	100%	0·00020%	0·00200%

PHE=public health expenditure (World Bank Development Indicators, 2015). Median price assumptions: low-income and lower-middle income=US$0·16 per 10 mg morphine; upper-middle income=$0·10 per 10 mg morphine. *Best price is $0·03 per 10 mg morphine (median price for all high-income countries).

Table 7: **Estimated cost of addressing the unmet need for oral and injectable immediate-release morphine formulations for palliative care, by income group**

On average, the 10% poorest countries and people of the world have access to only 10 mg of DOME per patient, which is sufficient to meet less than 2% of estimated palliative care need. For the 10% wealthiest countries, the DOME is more than 47 000 mg per patient, which is more than 24 times the estimated palliative care need for the 20 health conditions in our analysis.

The differences between country income groups are also extreme (table 6, figure 9). Of the 298·5 metric tonnes of DOME in the world, only 10·8 metric tonnes were distributed to LMICs, and almost 90% of this (9·6 metric tonnes) is distributed to upper-middle-income countries. Only 1·1 metric tonne (0·4%) are distributed to lower-middle-income countries, and only 0·1 metric tonne to low-income countries, which is the equivalent of about 13 mg per patient with SHS.

We estimate that total need for morphine-equivalent opioids is 81·6 metric tonnes per year for palliative care for the 20 health conditions most associated with SHS, and countries fall short of meeting this need by 48·5 metric tonnes. The need for medical morphine for palliative care is largely unmet in low-income countries (98%), lower-middle-income countries (94%), and upper-middle-income countries (72%). Low-income countries account for 9% of the palliative care unmet need for morphine-equivalent opioids in the world, lower-middle for 39%, and upper-middle-income countries (including China and Russia) for 52%. DOME is slightly less than the palliative care need in a few high-income countries.

Using DOME of high-income, western European countries as a benchmark, gaps are much larger because they consider other medical needs in addition to palliative care. According to this projected measure, DOME in low-income countries meets less than 0·5% of total medical need. In lower-middle-income countries, DOME meets less than 1% of total need, and in upper-middle-income countries, about 3%. In several high-income countries in the Middle East, eastern Europe, Latin America, the Caribbean, and Asia, deficiencies in access are substantial, and for this reason almost 75% of total medical need for morphine equivalent opioids is unmet, considering high-income countries as a block. This contrasts with most western European countries, the USA, Canada, and Australia, where DOME is at or well above need. Still, high-income countries account for only 12% of unmet need, whereas upper middle-income countries accounted for 51%, lower-middle-income countries for 30%, and low-income countries for 7%. We estimate the total global need for morphine for medical use, under the western European benchmark, is about 581·2 metric tonnes, and the unmet need is almost 548 metric tonnes.

The dearth of pain relief medicine is a key component of the global palliative care access abyss. We estimated the cost of closing this gap and meeting the need for oral and injectable immediate-release morphine, measured as the difference between palliative care requirements and DOME. Although we recognise that closing the pain divide requires more than medicines (complementary training and more efficient and secure supply chains are also required), these additional investments can be catalysed by making medicines more affordable and available.

For this costing exercise, we used retail pharmacy seller prices reported for 10 mg of oral, solid morphine ($0·03 for high-income countries, $0·10 for upper-middle-income countries, and $0·16 for lower-middle-income and low-income countries).[262] These prices include some of the costs of importing, licensing, and distributing the medicines and making them available to patients outside a hospital. These prices could also reflect subsidies enacted by the government. Retail prices are therefore a better estimate of the real cost of closing the pain divide than the wholesale country price.

The cost of covering the unmet global need for oral and injectable immediate-release morphine—the difference between palliative care need and DOME—is small, especially if LMICs could obtain the same prices as high-income countries (table 7). The total annual cost to close this pain divide for palliative care (48·5 metric tonnes of morphine equivalent) for the 20 health conditions considered in our calculations of SHS is $600 million per year at current prices but would be much less ($145 million, equivalent to 0·0002% of global GDP) if

LMICs had access to the best global prices paid in high-income countries. For low-income countries, the cost of closing the gap, which is almost equivalent to total need, would be $69 million, which still corresponds to 0·3% of public sector health expenditure, but only $13 million at best price (0·06% of public sector annual health expenditure). For lower-middle-income countries, the annual cost is $299 million at current prices versus $56 million at best prices, and for upper-middle-income countries the price is $231 million at current prices versus $75 million at best prices.

We analysed the cost of closing the gap and meeting the unmet need for oral and injectable immediate-release morphine for all children younger than 15 years with SHS. In view of the small absolute number of cases each year, the cost at reported prices is $5·5 million for low-income countries, $8·3 million for lower-middle-income countries, and $700 000 for upper-middle-income countries per year. At best prices, the cost of closing the gap in need for pain medicine for children with SHS is $200 000 in upper-middle-income countries and $1·6 million in lower-middle-income countries. For low-income countries, the cost of meeting the need for morphine-equivalent for children with SHS is only $1 million—a cost that would cover all children with SHS because almost 100% of need is currently unmet.

The costs are very small by any global standard, and the Commission recommends that the World Bank, WHO, and UNICEF take the lead in establishing a special fund for children in need of opioids for the relief of pain and palliative care. The creation of a fund in collaboration with other entities, as has been done with the Global Fund to Fight AIDS, Tuberculosis and Malaria to improve women and children's health and with the Global Financing Facility in support of the Every Woman, Every Child global strategy, should be part of a broad programme focused on children, with provision of technical support to ensure safe delivery and management of medicines and paediatric formulations and efforts to expand access to all essential palliative care interventions, beginning with health. This fund should be accessible to low-income countries. For LMICs as a group, and for high-income countries with unmet need, the fund could stabilise prices, provide technical assistance, and act as an information exchange platform catalysing countries to prioritise pain relief and palliative care for children.[275] A fund for palliative care medicines for children should be part of a larger effort to create a financing facility for palliative care medicines, linked to broader efforts to facilitate treatment of chronic and non-communicable diseases and spearheaded by a global financing entity such as the World Bank.

The key conclusions and recommendations relating to the Essential Package for adults and children with SHS are listed in panel 16.

***Panel 16:* An Essential Package of resources and interventions to respond to the burden of serious health-related suffering: key recommendations**

- All countries should ensure universal access to an Essential Package by 2030
- The Essential Package should be publicly financed for all families that could face financial catastrophe or impoverishment
- Basic social supports should complement this package and be financed over and above the health budget, in coordination with social welfare programmes
- Policies and additional investment must be in place to ensure safe supply chains, to train and build up necessary human resources with an approach based on competencies in palliative care, and to avoid pressure to include costly formulations of pain medication
- Access to best international pricing for medicines, especially inexpensive, off-patent injectable and oral immediate-release morphine, is a priority for achieving universal coverage of the Essential Package
- All efforts to expand access to best prices and to reduce costs of pain medicines should be complemented with technical assistance to ensure safe supply chains and medical use
- Countries should develop a palliative care and pain relief package for children, taking special account of their specific social and spiritual needs.
- UNICEF can take the lead in establishing a special US$1 million annual fund for children living in low-income countries who are in need of opioids for the relief of pain and palliative care

***Panel 17:* Investment in health care and palliative care accessibility**

Previous efforts to quantify access to palliative care provide an important basis for analysing the relation between the degree of palliative care coverage and key health-system indicators. The Quality of Death Index (QDI), developed by *The Economist* Intelligence Unit, ranks the 80 countries on the palliative and health-care environment, human resources, affordability of care, quality of care, and community engagement.[278] The USA ranks sixth on the QDI and is the country with the highest level of health-care spending, the UK ranks first and spends only half as much on health care as the USA.[278]

The Global Atlas on Palliative Care at the End of Life[113] adopted a multi-method approach that groups countries into four levels: no known hospice-palliative care activity, capacity-building activity, isolated or generalised palliative care provision, and countries where hospice-palliative care services are at a stage of preliminary or advanced integration into mainstream service provision. Countries with higher levels of human development tend to have preliminary or advanced integration of service provision.[279]

Merging evidence from the QDI and the Global Atlas, the Commission analysed palliative care development and accessibility, out-of-pocket expenditure, total public sector health expenditure, and public health expenditure. We found that palliative care access, presented as a ratio of hospice-palliative care services to population for each country, decreases with higher out-of-pocket expenditure as a percent of total health expenditure and increases with higher public expenditure on health as a percentage of gross domestic product. Countries with high levels of human development rank higher in availability, affordability, and quality of palliative care.

Section 3. Strengthening health systems by integrating palliative care

> In Haiti, there are no nursing homes, long-term ventilation facilities, or home hospice services. Opioids such as morphine are not freely available…Often, patients who are nearing the end of their lives are taken home to die where they often experience air hunger as well as pain. In state hospitals where the human and medical resources

For the **Global Financing Facility** see https://www.globalfinancingfacility.org/introduction

For **Every Woman, Every Child** see https://www.everywomaneverychild.org

Panel 18: **Ten lessons for system-wide integration of palliative care in low-income and middle-income countries**

A review of country experiences from around the world rendered the following ten lessons, organised by health-system function:

Stewardship

1 **A legislative and normative framework is essential to guarantee the integration of palliative care and pain relief into health systems.**
Palliative care efforts are impossible to scale up without normative and legal frameworks. Yet these frameworks are insufficient and need to be complemented with financial and organisational measures to guarantee universal access to palliative care.[283] Experience in Mongolia, Uganda,[271] Mexico, and other countries shows that to be effective, any change in policy and legislation must be combined with affordable oral immediate-release morphine, palliative care training for clinicians and other providers, and implementation of model palliative care services for delivery to improve access.[284] In Costa Rica, although no law is in place, there is a decree, and palliative care services are fully integrated into the delivery system, including at the household level.

2 **Public awareness of and support for palliative care that can drive systemic policies and integration into universal health coverage usually derive from professional groups and non-governmental organisations (NGOs), often in association with international and regional civil society organisations. Government institutions tend to be late adopters of palliative care initiatives.**
Small, high-quality palliative care initiatives inside and outside of hospital settings have existed in several countries for decades.[285,286] Examples include the Pain and Palliative Care Society in Kerala, India, the Rwanda Hospice Palliative Care Centre, the Hospice Palliative Care Association of South Africa, and Hospice Africa Uganda. The pioneering work of these organisations can create the conditions for the eventual government-led implementation and scale-up of palliative care initiatives. Strong alliances between these palliative care providers and other national research and advocacy groups focused on universal health coverage, as well as with regional and international groups and societies, have been especially successful in achieving national policy change. An exception is Costa Rica's fully scaled up, public programme based at the National Centre for Palliative Care and Pain Control, which began with a pilot programme in the 1990s.

3 **Feedback between global and national policy making and evidence can drive policy change.**
Systemic policy change has often been driven by a combination of national and global civil society initiatives. This has been documented in India, Mexico, Nepal, and Uganda, often working with organisations such as WHO, international NGOs such as Human Rights Watch and the International Association for Hospice & Palliative Care, and universities, including schools of medicine and public health. Learning has been bi-directional, with country experience providing key inputs for global advocacy and global knowledge informing national policy making.[287,288]

4 **Monitoring and evaluation of palliative care interventions, programmes, or policies is uncommon yet essential for effective scale-up.**
Monitoring and evaluation strategies are needed to expand access to palliative care and pain relief and to scale-up palliative care programmes. However, very few countries have designed and implemented any strategies. In Colombia and Kerala, India, NGOs are pioneering policy monitoring frameworks. Asociación Cuidados Paliativos de Colombia and Asociación Colombiana de Cuidados Paliativos are collecting data on the progress of the implementation of Law 1733 on palliative care and monitoring changes in the status of palliative care in Colombia. In Kerala, Pallium India is monitoring implementation of the palliative care state policy.[289] The Mexican Ministry of Health has also begun gathering data on access to palliative care.

Financing

5 **System-wide integration of palliative care is facilitated by the existence of a national universal health coverage platform and integration into the package of covered services.**
Expansion of palliative care in South Africa was greatly facilitated by the country's commitment to universal health coverage. A major expansion of access to palliative care is anticipated in some of the countries in our sample due to its incorporation into the national health benefits package associated with a universal health coverage strategy. The approval in Colombia of Law 1733 in 2014 and the national guidelines on palliative care in 2016 guarantee universal access to palliative services. In Mexico, palliative care and pain relief services were added to the package of essential health services of Seguro Popular in 2016.[283,290]

Delivery

6 **The initial adoption of palliative care interventions by governments is usually associated with cancer or HIV disease. Expansion of access to palliative care and pain relief to other health conditions and for children has been slow and is associated with a leap from a disease-specific model to a systemic approach.**
Most palliative care initiatives in low-income and middle-income countries (LMICs) initially focus on cancer and, in Africa, on HIV disease. The first palliative care unit in Vietnam was established at the National Cancer Hospital in 2001. Palliative care in India began through the creation of pain clinics at cancer centres in Gujarat, Maharashtra, Kerala, and Karnataka in the 1980s.[291] In Colombia,

(Continues on next page)

(Panel 18 continued from previous page)

until 2014, most palliative care initiatives were limited to cancer. In Chile, the incorporation of palliative care into the Explicit Health Guarantees Programme continues to be limited to patients with advanced cancer. In South Africa and Rwanda, a large proportion of palliative care and pain relief services is offered only to HIV patients.[292]

7 **Community involvement in the provision of palliative care is crucial given the limited capacity of health systems in LMICs and the important role of home-based care.**
In the state of Kerala, India, success in providing palliative care is strongly dependent on its community-based nature. Organisations such as Neighborhood Networks in Palliative Care manage palliative care services, provide education to families, and build public awareness. In South Africa, which has a strong hospice tradition, a large proportion of outpatient and inpatient palliative care is provided by community-based organisations. These organisations can complement the efforts of governments to introduce palliative care in public clinics and hospitals.

8 **Strong small-scale or state-wide programmes can be a fulcrum for developing a national palliative care model and achieving systemic integration—especially in delivery.**
Local and state-wide palliative care experiences should be used as reference to integrate palliative care into national health systems. In Costa Rica, a successful pilot programme grew into a national network of 54 clinics linked to tertiary hospitals through referral. In Kerala, a single programme expanded into a network of 841 palliative care sites and prompted the design of palliative care policies in other states of India.[289]

Resource generation

9 **Training and capacity building for primary care providers, complemented by specialised medical education and certification, is essential in the expansion of access to palliative care.**
In Panama, effective access to palliative care services has depended on the expansion of undergraduate and graduate medical and nursing training in palliative care.[285] The same is true for South Africa, where the University of Cape Town now offers a master's degree in palliative care.[293] In Chile, health authorities have recognised that the expansion of effective palliative care depends on the incorporation of palliative care content in doctors' and nurses' training curricula and on post-graduate training in palliative care.[285] In Mexico, large-scale training of primary care doctors is underway to facilitate implementation of normative and legislative changes. Costa Rica has developed graduate-level, specialised training for doctors and nurses.

10 **Health systems research and lessons learned from country experiences need to be published and disseminated.**
Despite important country-based learning in the implementation of palliative care and the proliferation of reports on many aspects of universal health coverage, these two bodies of knowledge have not been combined to study the integration of palliative care into universal health coverage or health-system reform. Although advocacy documents exist, national researchers have been largely unable or uninterested in studying this topic. An implementation research agenda should be developed and pursued that reports on both successful and failed programmes and includes high-risk populations with special needs (eg, victims of humanitarian emergencies, migrant communities, and children).

are low, patients in pain from trauma or malignancy are treated with medications like ibuprofen and acetaminophen [...] Moreover, nurses are uncomfortable giving high doses of narcotics even if ordered to do so for fear of being "responsible" for the patient's death, even if the patient is terminal. Death in Haiti is cruel, raw, and devastatingly premature. There is often no explanation, no sympathy, and no peace, especially for the poor. Death's ubiquity, however, does not mean that it deserves any less attention or thought.[276]

Antonia P Eyssallenne, University of Miami School of Medicine and Hospital Bernard Mevs Project Medishare

In this section, we analyse national health systems and the global health system to identify potential strategies that could guarantee universal access to palliative care as an integral component of the global movement to achieve UHC. We anchor our health system analysis in universal access to the Essential Package, cognisant that it is the core of a more extensive and expensive package of palliative care interventions.

This section is divided into two parts. For countries, we review paths to strengthen health systems in ways that will allow palliative care to be effectively integrated into UHC strategies, and we highlight how guaranteeing universal access to effective, people-centred palliative care through a diagonal approach can improve health-systems performance.[17,24] We then consider how to increase the salience of global collective action and the global health system in the expansion of access to palliative care and pain relief, largely in support of the actions of countries.[277]

Introducing effective pain management for SHS through palliative care is a diagonal intervention because its implementation for a specific disease can drive systemic change that includes many diseases and strengthens surgical platforms with effective responses to perioperative pain relief, which is normally considered outside the realm of palliative care.[213]

The research in this section draws on several sources of data. We analysed international, cross-country indicator

***Panel 19:* Strengthening health-systems functions to expand access to palliative care and pain relief**

Stewardship

Priority setting

- Implement public education and awareness-building campaigns around palliative care and pain relief
- Incorporate palliative care and pain relief into the national health agenda

Planning

- Develop comprehensive palliative care and pain relief guidelines, programmes, and plans
- Integrate palliative care into disease-specific national guidelines, programmes, and plans
- Include palliative care and pain relief essential medicines in national essential lists

Regulation

- Establish effective legal and regulatory guidelines for the safe management of opioid analgesics and other controlled medicines that do not generate unduly restrictive barriers for patients
- Design integrated guidelines for provision of palliative care and pain relief that encompass all service providers

Monitoring and evaluation of performance

- Monitor and evaluate palliative care and pain relief interventions and programmes using an explicit outcomes scale, measuring coverage as well as effect
- Promote civil society involvement in performance assessment

Intersectoral advocacy

- Engage all relevant actors in the promotion and implementation of palliative care interventions and programmes through ministries of health

Financing

- Explicitly include palliative care interventions in national insurance and social security health-care packages
- Guarantee public or publicly mandated funding through sufficient and specific budgetary allocations starting with the Essential Package
- Develop pooled purchasing schemes to ensure affordable, competitive prices for palliative care inputs and interventions

Delivery

- Integrate palliative care and pain relief at all levels of care and in disease-specific programmes
- Design guidelines to provide effective and responsive palliative care and pain relief services
- Integrate pain relief into platforms of care, especially surgery
- Establish efficient referral mechanisms
- Implement quality-improvement measures in palliative-care initiatives
- Develop and implement secure opioid supply chain and ensure adequate prescription practices

Resource generation

Human resources

- Establish palliative care as a recognised medical and nursing specialty
- Make general palliative care and pain relief competencies a mandatory component of all medicine, nursing, psychology, social work, and pharmacy undergraduate curricula
- Require that all health and other professionals involved in caring for patients with serious, complex, or life-threatening health conditions receive basic training in palliative care and pain relief

Information and research

- Incorporate palliative care and pain relief access, quality, and financing indicators into health information systems
- Ensure that government-funded research programmes include palliative care

data from the Quality of Death Index[278] and the Global Atlas on Palliative Care at the End of Life[113] (panel 17). We also reviewed several country experiences to gather information on palliative care legislation and regulation, awareness, institutional actors and providers, financing, monitoring and evaluation, training, and research in addition to the data on frameworks, policies, legislation and barriers to accessing opioid analgesics.[280,281] The review of country experiences was based on a common framework that analysed integration of palliative care by health-system function in the context of efforts to achieve UHC (additional online material). We conducted in-depth health-systems reviews on Chile, Colombia, Costa Rica, India, Jamaica, Lebanon, Mexico, Panama,[282] Rwanda, South Africa, and Vietnam. We also incorporate information from our study of small-scale innovation cases from around the world.

The country-specific health-system experiences are reference points from which to develop policies and scale-up innovative programmes to speed up the development of palliative care in countries with limited experience (panel 18). Salient among the successful systemic experiences is Costa Rica, a country that has fully integrated palliative care in its health system, which has achieved more than 90% coverage.

We applied a national health-system model built around four essential functions: stewardship, financing, delivery, and resource generation (including human resources, facilities, technology, information, and research).[294] Expansion of access to palliative care should be integrated through each of these health-system functions, with an increasing role across the continuum of care from primary prevention to end of life.[70] Health-system subfunctions should be specifically strengthened

to expand access to palliative care and pain relief (panel 19).

Stewardship

Public education about palliative care and pain relief is key to expanding access. All relevant actors, including health professionals, policy makers, academic institutions, and NGOs, need to promote the messages of appropriate access in both the media and policy circles.

Strategic planning, which includes guidelines, programmes, and plans, is crucial to placing palliative care and pain relief on the national agenda. However, very few LMICs have national palliative care guidelines, plans, or specific programmes for managing pain relief.[278] With multiple health conditions, agencies, and disciplinary specialties involved in palliative care and pain relief, a cross-cutting programme or plan is essential to coordinate and define responsibilities.

Palliative care and pain relief need to be integrated into disease-specific interventions and programmes. A few LMICs have integrated palliative care into national plans for cancer or HIV. Vietnam, for example, issued guidelines on palliative care for patients with cancer and HIV/AIDS in 2006.[295] In Chile, the National Program for Palliative Care, launched in 1995, prompted the expansion of palliative care clinics, the availability and public funding of opioids for patients with advanced cancer, and the initial availability of palliative care for paediatric patients.[296] However, integration into disease-specific interventions is insufficient because it serves only a fraction of the population and often constrains the extension of palliative care to other population groups because it fuels the assumption that coverage is sufficient.

With respect to regulation, access to palliative care and pain relief should be guided by the principle of balance, which meets the dual obligation of governments to implement effective regulatory systems that guarantee access to controlled medicines for medical need and simultaneously prevent non-medical use, diversion, and trafficking.[6,42]

To achieve balance, countries should begin with an audit of existing legislative and regulatory frameworks to identify impediments to access to opioids for medical needs.[6] Several LMICs have introduced novel initiatives, often at the behest of advocacy and clinician groups dedicated to increasing access to palliative care and pain relief (panel 20).

Effective guidelines must go beyond legislation that permits medically necessary access for patients, to one that ensures such access by implementing a safe and enabling environment. Indeed, crucial control points exist throughout the opioid supply chain, and a broad range of potential regulatory schemes under international drug control conventions allow countries to tailor regulation closely to their local context.

Panel 20: **Improving access to morphine for moderate and severe pain: Jamaica, Nepal, Vietnam, and Mexico**

The limited access to morphine in low-income and middle-income countries is in large part the result of unduly restrictive barriers that interfere with rational medical use. Several countries have pioneered programmes to reduce these barriers.

In Jamaica, oral immediate-release morphine was available at only a few hospitals that produced it as a liquid from imported powder. Most hospitals found this process too cumbersome, and no central production facility existed. Local palliative care pioneers focused simultaneously on educating clinicians about pain relief at hospitals and advocating with the ministry of health for procurement of oral immediate-release morphine tablets at the ministry of health. Palliative care has now been included in the national, non-communicable disease strategy and the national cancer control plan, and oral immediate-release morphine tablets have been accessible in the private and public sectors since 2012.

In Nepal, where morphine was virtually unavailable, a local doctor convinced a Nepalese pharmaceutical company to produce oral morphine locally and to distribute it at cost to hospitals as a humanitarian gesture. Locally produced morphine liquid has been accessible since 2009, whereas 10 mg immediate-release morphine tablets have been available since 2011 and sustained-release morphine tablets since 2012.[297]

In Vietnam, a country with an epidemic of heroin dependence, the ministry of health convened a workshop with all stakeholders—including officials of the ministry of police and the country office of the United Nations Office of Drugs and Crime—to review, revise, and approve an action plan to make opioids accessible for pain relief. The result was the elimination of barriers in the prescription of opioids, in line with international standards, although persistent concerns about diversion and non-medical use continue to hamper implementation of the new regulations.

In Mexico, COFEPRIS, the national agency responsible for managing access to controlled substances, maintained out-dated policies that included the use of bar-coded, paper prescription pads available only in large cities and in small numbers. Physicians who were willing to prescribe controlled medicines were forced to travel regularly to obtain the pads and had to provide their home addresses. Sustained advocacy campaigns by a group of national non-governmental organisations, clinicians, and regional and global civil society organisations including Human Rights Watch, successfully informed leading policy makers, resulting in a major policy and regulatory shift to electronic prescribing in 2015.[298–300]

Governments must have policies in place to assure rational and balanced use of all formulations of opioid medications in the essential and augmented packages based on national estimates submitted to the INCB. This estimate should be done with consideration to the need, the system capacity to ensure the safety of the supply channel, and a cost-effectiveness analysis for priority setting in choosing which medicines and which formulations of such medicines are affordable and best suited to the country, always prioritising access to off-patent medicines.

By monitoring national supply of opioids, countries can assess whether their need for pain treatment medicines are being met and provide early warning of over-supply or unbalanced use, or both. We also recommend that countries monitor the supply and marketing of opioids and, on the basis of lessons learned in Canada and the USA (panel 4), create strong conflict-of-interest policies that restrict undue influence of all for-profit entities in the tendering, procurement, and

marketing of opioids, limit their involvement in setting indications and guidelines for use and prescription of opioid medications, and prevent any advertisement directly to health professionals or the public.

Strong, national regulatory agencies must be established and must maintain complete (ideally electronic) prescription records of controlled substances, monitor doctor-specific prescribing patterns and other points in the supply chain, and follow up with strong control and sanctions for any non-medical use and diversion by medical professionals. A safe environment is one that avoids over-use and reliance on opioids by incentivising and enabling medical professionals to safely apply palliative care and other interventions to their fullest potential. In environments where adequate control systems are not yet in place to ensure safe distribution, storage, and dispensing to community pharmacies, opioids should be managed centrally, patients might need to be temporarily admitted to hospital if they need morphine, and families will need travel support to obtain access.

Monitoring and evaluation of interventions and programmes should be developed, with measurements undertaken periodically and findings made publicly available. Frameworks should include an explicit outcomes scale, with benchmarks and impact indicators measuring not only coverage but also the reduction of pain and suffering. Guidelines have been developed,[70] and a set of indicators has been proposed for Latin America[301] that can be adapted for use elsewhere. Recent reports on palliative care for cancer include a proposed list of indicators for developing and monitoring national plans.[302,303]

Governments have the primary responsibility for monitoring and evaluation. However, civil society organisations, clinician groups, and academics can be engaged in monitoring and reporting progress and assessing performance, and governments should encourage and facilitate this engagement and provide open fora for discussion. The role of the NGO Pallium India in monitoring government implementation of Kerala's palliative care policy is a good example of successful stewardship through the participation of civil society.[289]

Good stewardship of palliative care and pain relief also relies on convening, coordinating, regulating, and monitoring all relevant actors and entities through the ultimate health authority—typically, the ministry of health. The health and non-health actors include the legislative and judicial entities, governmental actors at all levels, international entities, civil society and patient engagement groups, human rights advocates and organisations, and all types of for-profit and not-for-profit providers of medical care and products, including the pharmaceutical industry. Children have specific barriers to accessing adequate and appropriate palliative care and pain relief, so special efforts are needed to ensure their needs are met by including relevant actors who focus on children's rights.

Financing

The organisation of public financing to cover palliative care and pain relief is crucial, and the package of covered services and medicines must be integrated into all national insurance and social security programmes, spanning not only tertiary providers but also covering the cost of the Essential Package at district hospitals, primary care clinics, and some services at the household level. In Mexico's Seguro Popular, for example, this meant augmenting the package in the Fund for Personal Health Services, which covers care in general hospitals and clinics, although delivery and human resource capacity are lagging behind (panel 21). Chile, in its most recent reform, included palliative care in the package of Explicit Health Guarantees, the core component of the Acceso Universal con Garantías Explícitas Plan, which includes an explicit set of health benefits with a maximum copayment.[307] In Turkey, as of the 2014 legislative changes, palliative care is fully incorporated into the benefits package.[308]

Governments must also allocate sufficient public or publicly mandated resources to cover the package of explicitly defined palliative care interventions, including compensation for the dedicated time of health-care professionals at all levels of care, and to include surgery, radiotherapy, and chemotherapy in an expanded package of covered services.

Applying the novel concept of clinical overhead can assist in developing an appropriate financing model for palliative care, especially for pain relief. Clinical overhead finances three services that together are costly and should be offered to all patients irrespective of their specific health issue: stabilising severe symptoms, providing information and ideally a diagnosis, and giving a referral if appropriate.[309–311] The relief of severe pain should be included in clinical overhead because it is one of the most basic requests a patient makes of any health system and is central to guaranteeing quality, responsiveness, and security.

Well designed and appropriately financed palliative care relieves pressures on other parts of the health system and reduces overall costs. Palliative care networks that include hospice and home care not only can improve quality of life, but also enable patients to remain at home or in the community, thereby reducing unnecessary hospital admissions for symptom control and relief, particularly near the end of life. Hence, palliative care can reduce hospital overcrowding and costs for overburdened health systems and provide financial risk protection for patients and their families.[19,22,121,260,312–322]

> Mr J arrived at the not-for-profit foundation in Cali, Colombia, unable to communicate verbally, illiterate and living alone in extreme poverty.
>
> He had been diagnosed with laryngeal carcinoma seven years before and had a radical laryngectomy and a permanent tracheostomy. Six months before arriving at the hospice, he began to experience pain every time he

moved his head. Whenever the pain became unbearable, J went to the emergency room at the state university hospital, where he was given weak analgesics, sent home, and told that nothing else could be done for him.

When admitted to the hospice, he was in severe pain, had very poor hygiene, and the skin around the trach tube was red, swollen, and draining pus. He was assigned a bed in the ward, and given medications including a weak opioid for pain. Although he continued to have difficulty walking, sitting and swallowing, J refused to complain because he was afraid of being discharged from the hospice in the same way he was discharged from the hospital. We started liquid oral morphine in regular doses and lidocaine before each meal and reassured him that he would continue to be under the care of the palliative care team. Two days later, he was able to walk and feed himself and was discharged with weekly follow-up visits. J continued to deteriorate, and was eventually readmitted to the hospice. The pain and symptoms were kept under control until he died, 3 months later.

The government did not cover palliative care services, so the cost of his care was paid by a charity created for patients like J, who could not afford to pay.

Liliana De Lima, IAHPC Executive Director

Panel 21: Medical and nursing education in Mexico: need for capacity building

A Mexican law enacted in 2009 mandates that all terminally ill Mexicans have the right to publicly provided and financed palliative care. To make this possible, normative frameworks allow for general practitioners to provide palliative care and prescribe controlled medicines, including morphine.

Primary care providers must be empowered and trained to provide essential palliative care services and medicines at clinics throughout the country. Roll-out of training programmes, managed by the Mexican Ministry of Health, is underway across Mexico for primary care doctors. Future initiatives should also cover other primary care personnel, including nurses, social workers, and professional health promoters.

One of the most effective avenues is to integrate basic palliative care training into university curricula. Nevertheless, as of 2016, few of the many excellent universities in Mexico include even optional courses in palliative care. Results of a data review from all 111 government-certified doctor training programmes in the country revealed that only 17 programmes offered compulsory courses in palliative care as part of first-degree medical education, and only two programmes offered optional courses in palliative care. In our review of 99 of the 103 certified nursing schools, we found that only 12 schools offered a compulsory palliative care course, and only five schools offered an optional course on palliative care.

In many low-income and middle-income countries, students of medicine and nursing are required to do up to 1 year of social service, often in remote clinics. Students are forced to receive patients with severe serious health-related suffering and at end of life, yet they are not given the training or inputs to treat these patients. Testimony from Mexican students alludes to heroic efforts to respond by purchasing opioids at private pharmacies and reaching out to colleagues to guide them in administering these medicines.

In Mexico and in the rest of the world, ministries of health and education should seek to ensure that accredited medical and nursing training programmes include at least one compulsory course in palliative care. This would enable much more rapid advance towards universal coverage of palliative care services and ensure that care is provided in a more responsible and informed manner, particularly with respect to prescribing opioids.

Health service delivery

Health systems in LMICs should guarantee access to effective and responsive palliative care at all levels of care, from households to highly specialised hospitals. However, delivery of palliative care in both urban and rural settings requires appropriate equipment and medicines, health personnel trained in palliative care and pain management, and efficient referral mechanisms. Other than for opioids, the delivery of interventions included in the Essential Package do not rely on special managerial arrangements.

Effective and responsible delivery of opioids will rely on secure supply chains and up-to-date technology for strong monitoring and management systems. Research and exchanges of lessons learned across countries is key. The case study of Kerala, where 170 recognised medical institutions stock and dispense oral morphine,[305] and of Uganda, where an NGO hospice now supplies the national public health-care system, are worthy of study (panel 15).[271]

All health workers should have training both in technical procedures related to palliative care and pain relief and in interpersonal quality of care, a component of palliative care that is of paramount importance when dealing with patients with SHS who need close attention. Up-to-date clinical guidelines specifically designed for palliative care and pain relief interventions should be available at all levels of the health system.

Referral mechanisms are necessary, since continuity of care is essential. Community workers and primary care doctors and nurses should have regular communication with patients and should be able to efficiently refer them to other levels of care when necessary. Communication technologies, most notably mobile phones, enable primary care units and community health workers to link to specialty care relatively easily; for example, communication technology has been instrumental in expanding access to paediatric cancer care worldwide.[17,323] For palliative care, and in view of the difficulties patients have when travelling to high-level care facilities, communication technologies must be harnessed to expand effective access.[324]

The Commission reviewed palliative care delivery models and innovations around the world based on personal experience, unpublished materials, and site visits to Albania, India (panel 22), Jamaica, Malawi, Mongolia, Nepal, Uganda, the USA, and Vietnam. We identified several models and innovations in LMICs that have improved access or appear promising in terms of sustainability, scalability, and reproducibility in other settings. These innovative projects provide important lessons, but they must be rigorously assessed (panel 18). Rigorous quantitative or qualitative performance evaluation that would enable scale-up is lacking and should be a priority for research and international funding. Scaling up projects to the national level is challenging for even the most successful programmes.

Panel 22: Kerala: a community-based palliative care model

The development of palliative care in Kerala serves as a unique and noteworthy example of expanding access to palliative care within India. Of the 29 states, only Kerala, Maharashtra, and Karnataka have a palliative care policy.[304] Kerala was the first to adopt state-wide policy in 2008 and is the furthest along in integrating palliative care into health-care delivery. With 841 of India's 908 palliative care sites, Kerala has one of the largest networks of palliative care in the world.[305,306] As of 2014, 170 institutions stocked and dispensed oral morphine.

In 1993, only two clinics in Kerala, both attached to cancer hospitals, had oral morphine. The Pain and Palliative Care Society at Government Medical College in the government hospital at Kozhikode was established through the efforts of local champions alongside a clinical service and included community representation. However, the clinic operated without access to oral morphine, which is managed by stringent state-level rules that follow the 1985 Narcotic Drugs and Psychotropic Substances Act of India. Multiple barriers hindered access to oral morphine, including administrative processes across various government agencies to get necessary approvals and licenses, fear of non-medical use of opioids among policy makers, interrupted supply due to strict import regulations from the commercial manufacturer in Gujarat and there being no manufacturer in Kerala; and limited numbers of trained professionals to administer morphine.

Efforts to mainstream palliative care in Kerala began through sustained, targeted civil society advocacy, efforts by the community hospice organisations fostered by The Pain and Palliative Care Society, and support from international academic groups such as The Pain & Policy Studies Group at the University of Wisconsin. Public discourse and community pressure were important to prioritise palliative care within the Directorate of Health Services of the Government of Kerala. Familiarity with the laws and regulations governing opioid procurement and prescribing in Kerala made it possible to identify and sensitise government officials. This resulted in oral immediate-release morphine becoming widely accessible to treat pain in Kerala. 20 years later, locally produced oral immediate-release morphine is accessible in all 167 recognised medical institutions in Kerala State. No evidence of opioid diversion has been found.[96]

Pallium India was launched in 2003 and became responsible for submitting a proposal to the Government of Kerala to formulate a state policy on palliative care that was adopted in 2008. Pallium India has effectively functioned as an observatory to monitor implementation of the state policy and has worked on its mandate to expand palliative care nationally, helping establish palliative care centres in 11 states.

Several innovations explain the success of the Pallium India model. The community-based nature of palliative care in Kerala, with the creation of Neighbourhood Networks in Palliative Care, has been at the core of its success to date and of ongoing, statewide scale-up efforts. Trained volunteers are at the centre of the care networks. They organise and manage palliative care services, provide education to families, and build public awareness.[305] International collaborations with WHO, universities, and non-governmental organisations bolster the movement to improve access to palliative care in Kerala.

Panel 23: Training of clergy and faith-based personnel

Many patients and families turn to religion and faith in times of severe pain, distress, and suffering, especially at end of life and in moments of bereavement. Members of the clergy of their faith are asked to provide consolation and support as part of palliative care. Thus, faith and religious professionals need formal training in palliative care to protect and effectively care for the patients and families who seek their support and for themselves, given the risk of burnout.

We reviewed university and graduate training programmes for rabbis, Christian priests and ministers, and imams in the USA and the UK. Rabbis must have training in counselling and bereavement as part of their obligatory courses. For priests, some Master of Divinity programmes offer formal courses in counselling (including bereavement), but they are not always obligatory. Information on the formal training for imams is difficult to obtain, but it is included in programmes at several schools. All schools require training in settings such as hospitals or prisons.

Integration of religious professionals and practitioners into palliative care teams is common practice. Yet the interaction between mental care professionals and other health professionals and spiritual leaders can be complex and is poorly understood.[325] Integration of religious professionals and practitioners into palliative care teams is common practice. This aspect of palliative care teamwork deserves more formal review, and capacity-building programmes should be fully integrated and obligatory in certifying providers of spiritual care.

Even the Kerala palliative care programme, which has made tremendous progress in expanding within the state (panel 22, has yet to be integrated into nationwide health system planning and delivery.

Resource generation

National and local governments should undertake programmes with a focus on health education and awareness building to reduce barriers, guarantee appropriate use of opioids, and encourage acceptance of palliative care as a core component of disease management.

To provide palliative care services universally, countries need palliative care specialists in both multispecialty and single-specialty tertiary care units. Palliative care must be a recognised, licensed medical and nursing specialty or subspecialty in all countries so that doctors and nurses can be certified as specialists and practice as such. Each medical school and training institution should recognise palliative care as a specialty by establishing work units or job categories.

All medical professionals ought to have general competencies in palliative care and indeed, this is crucial

	WHO, UNICEF, and other UN agencies	World Bank and other development banks	Bilateral agencies	Trusts or foundations	Global and regional not-for-profit organisations	Academic institutions and think tanks	For-profit and corporate multinational and transnational entities
Stewardship							
Consensus building around the importance of palliative care	+++	++	+++	+	+++	+	
Strengthening the position on global and local agendas	+++	++	+++	+	+++	+	
Monitoring and evaluation of initiatives and accountability frameworks	+++		+	++	+++	+++	
Cross-sector advocacy	+++	+++	+	+	++	+	
Interinstitutional partnerships	++	++	++	++	++	++	+
Production of global public goods							
Basic, clinical, health-systems, and ethics research	++		++	+++	++	+++	
Information and databases	+++	+++	++	+	++	+++	
Development and update of guidelines and standards for national and international regulation	+++		+++		+++	+++	
Design of training materials for countries			++		++	+++	+++
Comparative evidence and analysis of initiatives and best practices	+++	++	++	++	++	+++	
Update the WHO Model List of Essential Medicines	+++				++	++	
Management of externalities							
Guidelines to avoid cross-border use of controlled medicines and ensure safe and effective prescribing	+++				++	++	
Global solidarity							
Expansion of global financial resources	+	+++	++	++			
Humanitarian assistance	+++	++	++	+++	+++		
Technical cooperation and training	+++	+	+++	++	+++	+++	+++

The symbols denote various levels of engagement by actor in the global health system, such that + denotes minimal engagement, ++ denotes moderate engagement, and +++ denotes strong engagement.

***Table 8*: Actors and services to expand access to palliative care, by global health system function**

for achieving universal access to the Essential Package. General, prespecialisation medical and nursing curricula and training must include at least one mandatory course in palliative care and pain management as a prerequisite for licensing (panel 21). All other professionals who provide aspects of palliative care, including social workers and clergy (panel 23), should also have some formal training.[326]

Countries without local palliative care expertise need external technical assistance. Global curricula should be made freely available so that all countries can use this resource for basic training in palliative care principles and build on it to adapt to local needs and circumstances. In Nepal, for example, palliative care training for doctors was provided in India with support from a foreign NGO. Since 2013, a visiting professor of palliative care has been in residence at one of Nepal's leading medical schools. With palliative care expertise available in the country, this medical school collaborated with the new Nepal Association of Palliative Care to create a 4 week course that has been approved by the Nepalese Government.[297] Professional training and access to oral, immediate-release morphine was facilitated with support from international groups such as the International Pain Policy Fellowship, organised by the Wisconsin Pain & Policy Studies Group.[327] Hospice Africa Uganda, a regional model (panel 15), now offers training and experiences for clinicians from sub-Saharan Africa and elsewhere in Africa.

Effective management of each of the health-systems functions relies on timely and reliable information about palliative care and pain relief. The results of the Commission's studies provide guidance on the development of strong data embedded in overall health-information systems, including cancer registries. There are three important considerations when developing national health-information systems with palliative care integration. The first consideration is the recognition of the need for palliative care and pain relief, based on the conceptual framework developed in section 1. The second

consideration is the development and provision of timely information on access to the Essential Package and other interventions, with strengthened data on opioid availability and consumption. Finally, the third consideration is research on palliative care and pain relief needs, effective interventions, access, and health-system responses. Since many of the necessary medications and devices in the Essential Package are low cost and hence have a low profit margin, little funding is available for innovations to improve access, despite the huge potential market. Limited information on successful projects, implementation, or delivery in resource-poor settings has been published.

Research should be incentivised by ensuring that governmental entities that fund research include explicit and specific budget lines for palliative care and pain relief, including implementation research. Governments should also fund and promote data collection and make these data publicly accessible to facilitate research and knowledge exchange. In Mexico, for example, national survey data collected from palliative care providers can benefit the research community once it is made public and only if it is open access.[328]

For the **International Agency for Research on Cancer** see https://www.iarc.fr/

Governments should work with researchers to establish research priorities. In Lebanon, the National Committee for Pain Relief and Palliative Care identified priority research areas as part of national planning. In response to the efforts of palliative care advocates, the Lebanese Ministry of Public Health established the National Committee for Pain Relief and Palliative Care in 2011, charged with developing a national plan that included research. The suggested research priorities included identification of gaps in palliative care services, education, and policy as well as ways to close the gaps. However, implementation of these national palliative care research priorities has been hampered by inadequate funding exacerbated by the economic strain of the war in neighbouring Syria and the resultant refugee crisis.

Research is a global public good and should be supported by global institutions and guided by regional priorities where possible. A research agenda on palliative care has been developed for Africa[329] with notable publications that have benefited palliative care development in the region, and this should be replicated for other areas. Not all countries have to fund the actual research, but they should all have the capabilities to adapt findings to specific national contexts and apply them (panel 18).[272]

Global, collective action to expand access to palliative care and pain relief in LMICs

Universal access to palliative care requires global collective action through the participation of actors whose primary purpose is to improve health—WHO and its regional offices, multilateral development banks, multinational corporations, and international civil society groups—guided by rules and norms governing their interactions.[330] The scope of action for the global health system should include recommendations, health products, and health-focused activities that can be provided most effectively by global institutions.[41,331]

The four core functions of the global health system are stewardship, production of global public goods, management of externalities, and mobilisation of global solidarity (table 8).[294,332] Stewardship, led by ministries of health, includes convening for negotiation and consensus building, setting priorities, evaluating actors and actions to ensure mutual accountability, and advocating for health across sectors. The production of global public goods includes knowledge and technology through research and development and the generation of standards and guidelines, information and databases, and comparative evidence and analysis (as, for example, by the International Agency for Research on Cancer). Management of externalities implies the prevention or mitigation of negative health effects, that is, situations or decisions originating in one country that might affect others, through tools such as surveillance and information sharing and preparedness and response coordination. Finally, the mobilisation of global solidarity is implemented mostly through the provision of overseas assistance in the form of development financing, technical cooperation, and humanitarian support.

Global stewardship

WHO has recently taken steps to include palliative care on the global policy agenda by adopting the 2014 WHA Resolution 67.19, which engages the global health system more actively in palliative care and recognises it as an essential component of comprehensive and universal health care.[42] The resolution was the result of concerted global collective action that involved not only multilateral agencies led by WHO, but also global NGOs devoted to human rights and palliative care issues (table 8).

Consistent with this resolution was the inclusion of palliative care in WHO's definition of UHC and, hence, in the core of the agenda for strengthening health systems.[27–29] Palliative care is now included in the services covered by UHC initiatives along with health promotion, disease prevention, curative treatment, and rehabilitation.[213] This important step forward in linking palliative care to the UHC agenda must be upheld in all international and national work on UHC.[333]

Despite the resolution and the definition of UHC, most countries have yet to make real progress in integrating palliative care into policies and national health systems. Global collection action around palliative care must be focused on facilitating and assisting countries to achieve this objective. A review of framework conventions and global strategies that have been implemented around other health priorities would provide important insight into how to move forward.

Advocacy by international and regional agencies has been essential to spur change (eg, the adoption of global resolutions). NGOs have also undertaken much of the global policy and health-systems analysis, sometimes working with clinicians and academics.[113,244,257,262,334]

An important measure driven by collective action of international agencies and NGOs was the adoption by the UN General Assembly Special Session on the World Drug Problem (UNGASS), in 2016, of a document that articulated a strong commitment to "improving access to controlled substances for medical and scientific purposes".[335] UNGASS called for steps to address barriers related to legislation, regulatory systems, health-care systems, affordability, training of health-care professionals, education, awareness raising, estimates, assessment and reporting, benchmarks for consumption of substances under international control, and increased international cooperation and coordination.

Much of SHS is associated with non-communicable diseases. With the relatively recent addition of non-communicable diseases to the global agenda and related advocacy work, lessons can be learned and transferred to advocating for palliative care and pain treatment. We recommend building bridges between the non-communicable diseases and palliative care advocacy, academic, and policy communities.

Cross-sector advocacy, which involves a range of international institutions, is especially important in relation to opioids and other controlled medicines for which strong and ongoing collaboration between WHO, the INCB, the UNODC, and regional drug-control agencies is necessary to implement a balanced approach.

Promoting and facilitating international and inter-institutional exchange that generates innovation and collaboration platforms, including private–public partnerships, is a stewardship function that has great potential for expanding access to palliative care. Innovation in product development and adapting existing formulations of medicines and equipment for low-resource settings is necessary to reduce the cost and increase the acceptability, especially of the Essential Package.

In the development of their stewardship responsibilities, global health actors should also promote and participate in the assessment of national palliative care interventions, programmes, and policies—a crucial input for shared learning and accountability that does not exist. The evidence and lessons learned through these procedures should guide future palliative care activities and models. Indeed, assessments of national strategies should be a priority for not only global institutions, but also for all WHO regional offices and the regional development banks funding health programmes.

Accountability is a major challenge for palliative care, as it is for the global health system because no institution has been defined that mandates corrective action. Even for treaty-based commitments, such as the Framework Convention on Tobacco Control, strong accountability mechanisms have been difficult to establish. Notwithstanding this difficulty, we propose a global mechanism with a clear accountability framework to ensure progress on universal coverage of palliative care, and especially access to pain relief. In view of the interinstitutional nature of stewardship in this area and the limitations WHO has in holding member states accountable, a multistakeholder, accountability-focused group is needed to measure and regularly report on the progress of both global and national institutions. The *Lancet* Commission on Essential Medicines put forward similar proposals, and our Commission strongly supports these recommendations and suggests working jointly, at least with respect to access to medicines for pain relief.[336]

Production of global public goods

Despite the increasing demand for palliative care and its documented health, social, and economic benefits, a very small proportion of resources for health-care research—just 0·2% of total resources for cancer research in the UK and 1% of the 2010 total appropriation of the US National Cancer Institute—is devoted to palliative care.[337]

Basic, clinical, and health-systems research could improve the effectiveness and selection of medicines and interventions involved in palliative care, disseminate generalisable findings, and identify practices and models that could be implemented and scaled up in LMICs.[185,338] Comparative evidence and analysis of the design, implementation, and effect of palliative care interventions, services, programmes, and policies is crucial for the identification and dissemination of best practices in clinical, organisational, and policy contexts, and we conclude this report with a research agenda.

Research in ethical dimensions of palliative care is essential to address sensitive issues, such as the practical meaning of a dignified death. Palliative care research does encompass important ethical issues, including the patient's decision-making capacity and willingness to participate.[339–341]

A system of measures and indicators could provide priority-setting tools for palliative care and for access to pain relief medicines. As this Commission established through its initial work on the global burden of SHS, a new metric that accounts for this burden, using a people-centred approach, is needed. This new measure of the burden of suffering that would complement burden of disease data is essential for monitoring and priority-setting purposes, and it should be used as a priority-setting tool to assess the need for palliative care and guide health-system reform with respect to achieving UHC.

No consensus exists on the indicators and standards to be used for routine data collection and reporting in global health in relation to palliative care. The WHO Global Plan of Action on the Prevention and Control of

Non-Communicable Diseases 2013–2020[342] includes one cancer-focused indicator related to palliative care but sets no specific targets, and palliative care is not explicitly included in UHC in the SDGs. Selective indicators should be developed, data collected and harmonised, and results published and disseminated globally. Cancer registries provide key input into these health-information systems, and ongoing efforts to develop registries, led by the International Agency for Research on Cancer, deserve support from the palliative care community.

Global public goods related to palliative care should continue to include the design of clinical guidelines for palliative care. WHO is updating the cancer pain guidelines it first published in 1996, but to date no comprehensive palliative care guidelines for LMICs have been planned, and the Commission recommends that WHO and its partners make that a priority.

Basic competencies in palliative care and pain relief for primary care doctors vary little between countries, so there is an ideal opportunity to implement standardised, global, online curricula that can be easily translated and used internationally to move rapidly forward in training personnel (eg, WHO's Planning and implementing palliative care services: a guide for program managers[214]). Universities and foundations can play an important part in developing curricula and managing online courses.

International policy on controlled substances has been dominated by efforts to limit and control the illicit production, trafficking, and misuse, with little or no attention to the requirement of the UN drug control conventions to ensure adequate access to legally produced and controlled substances for the relief of pain and suffering. In recent years, WHO, the INCB, the Commission on Narcotic Drugs, and the UN Office on Drugs and Crime have taken steps to correct this long-standing imbalance. Breakthroughs include the 2010 publication of national policies on controlled substances[6] by WHO, aimed at helping countries reduce regulatory and other barriers to availability of these medicines while preventing diversion and misuse. Also in 2010, the UN Commission on Narcotic Drugs initiated a process with the UN Office on Drugs and Crime to revise its Model Drug Laws and address the need to ensure adequate availability for medical use.[343] In 2011, the INCB began establishing cutoff points for inadequate supply of controlled substances.[344] Most countries submit estimates to the INCB that are so low that demand for opioid cannot be met, resulting in stockouts and undertreatment. The work of the Commission and recent reviews of INCB data provide key evidence to establish more appropriate cutoffs and processes for monitoring progress.[11]

In 2013, the WHO Expert Committee on the Selection and Use of Essential Medicines approved an application by the International Association for Hospice and Palliative Care to include an evidence-based list of medicines for pain relief and palliative care in WHO's Essential Medicines List.[15] Based on the approval of this application, the WHO Committee added a section on pain and palliative care.[179] Global public goods should continue to include a review of WHO's Essential Medicines List and regional efforts to make these medicines available and accessible to countries.

Several knowledge inputs can be most readily developed by researchers in educational institutions, and these can be combined with shadow monitoring frameworks effectively designed and disseminated by international NGOs. Some important examples include: the Quality of Death Index[278] commissioned by the Lien Foundation (a Singaporean philanthropic organisation) and developed by *The Economist* Intelligence Unit; the series of policy briefs, situational analyses, and recommendation documents by Human Rights Watch, used as policy levers in many countries; the Atlas of Palliative Care in Latin America, developed by the Latin American Association for Palliative Care; the Atlas of Palliative Care in Europe, developed by the European Association for Palliative Care; the Atlas of Palliative Care in Africa, developed by the African Association for Palliative Care; and the collaboration of the Worldwide Hospice and Palliative Care Alliance on the WHO Global Atlas.[113,285,326]

Management of externalities

There are many reasons to assume that the diversion and non-medical use of drugs is not a function of increasing medical access to morphine in LMICs, but rather a consequence of inadequate safeguards to minimise such diversion in certain high-income countries.[94,96] First, the drugs most frequently associated with non-medical use are synthetic opioids such as hydrocodone, oxycodone, and fentanyl, not the oral or liquid immediate-release morphine needed in LMICs for the relief of severe pain and palliative care. Second, by contrast with the increasing epidemic of non-medical use of opioids in the USA, other high-income countries such as Austria, Germany, Switzerland, and the UK report high opioid consumption rates for the treatment of severe pain, palliative care, and dependence syndrome and little or no non-medical use.[101] Although data are scarce, diversion of morphine and other basic opioid used in palliative care in LMICs appears to be minimal.[96]

The diversion and misuse of opioids in the USA and in other countries should be addressed by the global health system in coordination with other global entities and the respective national governments. To manage this, the INCB has recommended: (1) undertaking studies at the national, regional, and international level to better understand the dynamics underlying the uncontrolled prescription and distribution of these products; (2) the development of guidelines on best practices to deal with these externalities; and (3) the provision of technical assistance to build capacity for the design and enforcement of laws to cope with the problems related to the uncontrolled use of opioids and other similar medicines.[345]

Global entities and countries must develop balanced strategies to maximise access to morphine for medical uses and minimise the risk of diversion and non-medical use. Lessons learned and best practice should be shared, and countries that report high consumption of opioids and little or no non-medical use can share their experiences with countries where there is over-consumption or underconsumption.

Mobilisation of global solidarity

The convening power of UN agencies and their ability through such interactions to socialise countries and actors into a common position are powerful mechanisms for mobilising global solidarity around palliative care.

Financial barriers to accessing palliative care could be overcome in view of the low cost of an Essential Package. Sustainable financing and expanded financial capacity will stimulate and facilitate universal access to palliative care, especially in low-income countries.

In view of the wide variation in prices for medicines, especially for morphine, countries could save on their cost by establishing global or regional purchasing and procurement funds and platforms that include the medicines in the Essential Package. Financing platforms, established and managed by a global entity such as the World Bank, should be designed to aggregate and expand demand and thereby reduce and stabilise prices. Countries should be offered the opportunity to participate in pooled purchasing by regional organisations, working with a select few mission-driven, not-for-profit medicine suppliers and supply-chain managers. These funds could make the markets for palliative care medicines, especially opioids, more functional so companies that produce the medicines are more likely to offer negotiated prices even if profit margins are slim, as is the case for many palliative care medicines that are required in LMICs. The Pan American Health Organization (PAHO) Strategic Fund is an example of such a financing platform.

A knowledge sharing platform on the prices of medicines would complement these funds. Disseminating data and advocating around access and reduced prices could spur both governments to act and providers to behave more responsibly. Although financing platforms for medicines are important, it is not enough to generate expanded access to the Essential Package. Funding for medicines must be complemented by technical assistance for safe supply chains, monitoring, and building clinical human resources to leverage these medicines, and especially opioids.

Palliative care for children presents special challenges and opportunities. In view of the relatively small number of patients, the cost of the Essential Package and the cost of closing the divide in provision of pain relief is very small. We recommend that the World Bank, as a leading global development financing facility with expertise in innovative financing, spearhead an effort that should include The Global Fund, WHO and its regional offices (especially PAHO), and UNICEF to finance palliative care for children. The fund should focus on low-income countries and begin with pain relief medicines in appropriate paediatric formulations. There is an important precedence in collaboration between UNICEF and the Global Fund to working in a coordinated way to allow governments and beneficiary communities to implement integrated community case management of childhood illness. However, UNICEF has been largely silent about children's need for palliative care to date (only one major report[346] focuses explicitly on the topic), and this is a breach of the spirit and objectives of the SDGs and the global movement to fulfil the rights of children. The palliative care movement is an opportunity to use palliative care for children as the basis to spawn access for other populations, using lessons learned from HIV/AIDS.[39]

Funding for global advocacy and research for palliative care in LMICs has been, and continues to be, scarce.[47] With a few notable exceptions, foundations and bilateral funders have not prioritised work on palliative care. To develop the necessary global public knowledge goods, research funding will have to be identified.

Countries are failing to provide or are unable to provide health care, and international actors must step in to meet population health needs, including the need for palliative care. In humanitarian disasters, even the most basic inputs such as morphine are often not available. Global health organisations should also regularly include interventions and experts for palliative care pain relief in humanitarian assistance programmes, whether for natural or man-made disasters.

Finally, the global health community has an important role in training and capacity building in palliative care by providing technical assistance and disseminating knowledge. Training in all aspects of palliative care management, monitoring, research, and implementation should be part of international technical assistance.

Conclusions and recommendations

Alleviation of the burden of SHS from life-threatening or life-limiting health conditions and with the end of life is a global health and equity imperative

Most high-income countries have responded to SHS with effective palliative care interventions, yet the needs of poor people have been neglected, and there is little or no access to pain relief or palliative care in LMICs.

More than 25·5 million people, 45% of the 56·2 million who died in 2015, experienced SHS, and these estimates exceed previous reports[113] by about 25%. Furthermore, our estimates suggest that in 2015, an additional 35·5 million people with life-threatening or life-limiting health conditions experienced SHS, although they did not die. Summing decedents and non-decedents, more than 61 million people experienced SHS in 2015, and 80% of these people lived in LMICs.

For the **PAHO Strategic Fund** see http://www.paho.org/hq/index.php?option=com_content&view=article&id=12163%3Apaho-strategic-fund&catid=8775%3Aabout&Itemid=42005&lang=en

Summing the duration of all symptoms worldwide provides an upper bound estimate of 21·2 billion days of SHS symptoms for all patients. Using our lower bound indicator, which allows for complete symptom overlap, the estimate of the duration of SHS is still considerable, at more than 6 billion days.

We estimate that more than half of decedent need for palliative care is associated with premature deaths that could have been prevented or for which treatment could have extended the length of healthy life substantially. Most cases are in LMICs, and patients in LMICs account for at least 95% of the need for palliative care associated with HIV disease, premature birth and birth trauma, tuberculosis, and malnutrition. With increasing country income, the proportion of patients with SHS associated with non-communicable diseases, such as malignant neoplasm and dementia, increases.

Children and their families have specific and intensive palliative care needs, yet they can easily be overlooked because the absolute number of paediatric patients is much lower than the number of adult patients.[113] Yet the global inequities are especially poignant for the more than 5·3 million children younger than 15 years who experience SHS. Children face additional barriers to access. Our data show that more than a third of children who die have SHS. More than 98% of the almost 2·5 million children who die with SHS live in LMICs. In high-income countries, children who experience SHS account for less than 1% of all deaths associated with SHS, compared with 12% in LMICs overall and more than 30% in low-income countries. The proportion of child deaths associated with SHS that are preventable is especially high. The Commission stresses that access to paediatric palliative care is imperative everywhere but especially in LMICs.

The extremely limited availability in LMICs of morphine—the most essential of medicines to relieve SHS—is emblematic of the most extreme inequities in the world. The poorest 10% of countries and people of the world have access to only 10 mg morphine-equivalent per patient in need of palliative care. This tiny amount is sufficient to meet less than 2% of estimated palliative care needs for the relief of severe pain and dyspnoea, and it meets an even smaller proportion of total medical need. Countries in the world's wealthiest decile, by contrast, have access to more than 47 600 mg per patient with palliative care need. According to INCB registries from 2014,[1] 298·5 metric tonnes of morphine are available for medical use worldwide, and less than 4% is distributed to LMICs. Inequities have increased with time and gaps in access are widening.

The inadequate access to morphine for people in LMICs with a medical need is the result of obstacles in demand and supply in countries that have falsely linked local, medical access with national and international non-medical use. Access has been hampered because of fear of secondary effects instead of relying on strong policy and evidence to even-handedly meet need while simultaneously working to counter diversion.

Universal access to an affordable Essential Package of palliative care can alleviate much of the inequitable and preventable burden of SHS

The Commission developed an Essential Package that is the minimum standard that any health system, no matter how resource-constrained, should make accessible to all patients and families in need. The Essential Package includes medicines and equipment as well as the human resources to manage this effectively and appropriately. The list of medicines in the Essential Package is almost entirely a subset of the 2015 WHO Essential Medicines List[15] and Essential Medicines List for Children.[179] Five medicines in the Essential Package are not included in the section on palliative care in WHO's Essential Medicines List, and we advocate for their inclusion.

The Essential Package must make both oral, immediate-release and injectable morphine preparations available for any patient with moderate or severe pain or terminal dyspnoea that cannot be adequately relieved by other means. Although we advocate for the inclusion of slow-release morphine or transdermal fentanyl in an augmented package, countries should avoid pressure to make these more expensive slow-release opioids available until, and unless, more essential immediate-release oral morphine is universally available for patients in need. Countries should carefully evaluate the cost effectiveness of costly formulations in view of overall health budget restrictions and priority setting.

The Essential Package is lowest cost by design. It includes only off-patent formulations, is based on frugal innovation (panel 13) for necessary equipment, and is anchored in a staffing model based on competencies rather than professions. Tasks often undertaken by specialised medical personnel in high-income countries can be done by general practitioners and nurses or by community health workers empowered with the necessary skills to deliver palliative care and pain treatment, from the hospital to the home.

Our Essential Package is one of the least costly of the components that form the DCP3 Essential Universal Health Coverage Package.[25] For low-income countries, the annual cost of the Essential Package is about $2·16 per capita per year (or 2–3% of the cost of the essential UHC package). The Essential Package cost is also about 3% of the cost of minimum packages of universal primary health care services that have been presented by other international groups.[263,264]

Although it is not the primary role or financial responsibility of the health-care system to remediate social or spiritual suffering, these essential palliative care interventions are complementary to the health

interventions included in the Essential Package. Social suffering might prevent the delivery of effective palliative care health services, and the Commission recommends delivering and financing these by other social sectors. The alleviation of spiritual suffering is often essential for patients and families; the Essential Package includes appropriate training to ensure that palliative care professionals can be responsive and open to meeting these needs together with other professionals.

Universal access to the Essential Package relies on additional investment, which in low-income countries would be a high proportion of health expenditure, especially with the additional cost of ensuring safe supply chains and training. In view of budget constraints, this means trade-offs against other health-system priorities. To support decision makers, we propose a framework for measuring the value to patients and families of alleviating SHS that would complement existing metrics and enable balanced decision making. We propose mechanisms to further reduce the cost of the Essential Package by reducing the medicine costs with collective action and efficient delivery models. Finally, we encourage countries to incorporate extended cost-effectiveness models that include the full benefits of increased access to palliative care through reduced end-of-life hospital admissions, reduced risk of medical impoverishment, and the diagonal approach.

Prices paid vary for medicines, especially for injectable morphine, varies enormously between countries. For example, the overall cost of the medicines within the Essential Package in Rwanda, using currently reported prices, is nearly three times the cost of using lowest reported international prices, whereas the difference is almost six fold for injectable morphine. Access to best international prices for medicines would reduce overall costs of the Essential Package for low-income countries by about 25%. The retail cost of the unmet palliative care need for oral immediate-release and injectable morphine would be much reduced if LMICs could obtain the same prices as high-income countries: $600 million at current prices, compared with $145 million at the prices paid in high-income countries. At best international retail prices, the estimated annual cost of unmet, medical need for opioid analgesics for children in low-income countries is just over $1 million dollars.

LMICs can improve the welfare of poor people at modest cost by publicly financing the Essential Package of palliative care through full integration into UHC

We call for all countries to ensure universal access to the Essential Package by 2030 with dedicated, public, or publicly mandated funding that spans all relevant health conditions and diseases, for all families at risk of financial catastrophe or impoverishment. For wealthy population groups, and depending on the financing structure of each country's health system, the Essential Package should be integrated into the social security budget, the national health insurance system, or private insurance to achieve universal coverage of palliative care and pain relief. Incorporating palliative care and pain relief into the public health agenda of countries is essential to achieving SDG Target 3.8 for UHC by 2030.

We emphasise that the Essential Package covers only the most basic of medicines, equipment, and human resources and should not be the ultimate goal of any health system seeking to go beyond essential UHC and to effectively meet palliative care need. The Commission advocates for middle-income countries to move toward universal access to a more comprehensive package of evidence-based palliative care and pain relief interventions, increasing the size of the package as the public sector health budget expands. The augmented package should include palliative surgery, radiotherapy, chemotherapy, and the necessary equipment, as indicated in the palliative care chapter of WHO's List of Priority Medical Devices for Cancer Management, and a slow-release, off-patent morphine formulation.

For the **WHO List of Priority Medical Devices for Cancer Management** see http://www.who.int/medical_devices/priority/ncds/en/

Detailed recommendations are provided on the key actions that countries should take to expand access to palliative care and pain relief, considering each health-system function. We also share lessons for scale-up and integration of palliative care into UHC from country experiences of programmes and national policies in developing regions. One example is our call to countries to develop systemic national palliative care and pain relief plans. These should not be limited or anchored in specific diseases such as cancer or HIV, but rather take a system-wide and intersectoral approach. To be effective, national plans must include accountability instruments and measure progress in achieving measurable outcomes. Furthermore, even with financial protection, delivery will not occur without the training and human resources at all levels of care.

Human resource training is essential to extending access to the Essential Package, especially because inclusion of morphine will necessitate a balanced approach that ensures safe and appropriate access for patients with medical needs for opioids and minimises diversion. Countries require palliative care specialists to anchor national programmes, and we advocate for all countries to participate in global training, exchange, and telepalliative care programmes, build local capacities, and fill human resources gaps in the short-term and long-term.

Countries must also strive for access to reduced prices for the components of the Essential Package, especially injectable morphine. Individual countries are not likely to access best prices, and producers are not likely to offer best prices, without aggregate, advance-guaranteed markets, and this presents an important opportunity for countries to request and participate in regional and global pooled purchasing platforms. On the basis of

previous experience from other parts of the world, these platforms might also be used to negotiate with a small number of accredited manufacturers who are willing to supply low-cost, off-patent formulations purchased to order. Civil society must be called upon to take governments to task for not purchasing or extending licences for medicines at high prices unless universal coverage of the most basic, off-patent formulations has been achieved. This requires access to information and regional and global platforms should include knowledge exchange of prices paid by countries.

The Commission recommends complementing the Essential Package with key social supports (panel 14) that should be financed over and above the health budget and built into and provided through antipoverty and social welfare programmes. Serious financial barriers prevent patients from accessing palliative care because end-of-life situations and life-threatening disease can debilitate or destroy a family's capacity to generate income. Social supports that go beyond health care can prevent families from sacrificing basic needs in a desperate attempt to care for loved ones.

Access to opioid analgesics in LMICs should be increased in a stepwise and balanced manner to maximise the benefits of opioids and minimise diversion. Universal coverage must begin with off-patent, inexpensive immediate-release oral and injectable morphine. No slow-release opioid should be licensed for sale unless immediate-release oral morphine is universally accessible by prescription. Second, every country should implement rational, balanced opioid prescribing regulations that account for the medical need for opioids and the risk of diversion, while avoiding impediments that prevent appropriate access to medical care. Third, each country should implement clinical guidelines on appropriate opioid therapy for palliative care and pain relief to help doctors and other approved opioid prescribers. Fourth, expanding medical access to opioids as part of palliative care must be accompanied by training of opioid prescribers and handlers (including community health workers) who can monitor home use of opioids. Pain treatment in palliative care with opioids includes not only careful prescription in medically required amounts, but also regular visits with patients and families. Fifth, safety of the opioids must be ensured by preventing diversion through the procurement and supply distribution channels. Much non-medical use of opioids could be averted by responsible prescription by doctors and pharmacy practice and by intensive, yet balanced monitoring of unlawful or dangerous practice and rapid, appropriate responses by well informed regulatory authorities who have been sensitised to medical need. Overly restrictive legal and regulatory barriers could have a negative effect on opioid accessibility for medical use. Sixth, strong policies against conflict of interest should be implemented to restrict undue influence of all for-profit entities in the tendering, procurement, and marketing of opioids, in the setting of indications and guidelines for use and prescription of opioids, and in advertisement to health professionals or members of the public. Finally, opioid-use disorders must be recognised as medical problems and not criminalised, and evidence-based treatment for these problems should be made available to all who need them.

We call on countries, through their respective ministries of health, to launch new interinstitutional advisory groups (or to strengthen existing ones) that include palliative care and pain clinicians, civil society, and academics (including health economists and legal experts) to provide official and expert advice on policy related to palliative care and pain relief on a regular basis. In countries where such committees are not in place, we call on civil society to establish and host these groups as an interim step.

International and balanced collective action is essential to achieving universal coverage of palliative care and pain relief by facilitating effective access to essential medicines, while implementing measures to prevent non-medical use

Accountability is a major challenge in palliative care, as it is for the global health system overall, because there is no clearly definable institution to mandate corrective action. We propose a global mechanism with a clear accountability framework to ensure progress on universal coverage of palliative care and pain relief. Given the interinstitutional nature of palliative care stewardship and the limitations of WHO in holding member states accountable, the Commission proposes a multistakeholder, accountability-focused group to measure and regularly report on the progress of both global and national institutions. As a key stakeholder, the private sector is called upon to promote an enabling environment for averting SHS. The *Lancet* Commission on Essential Medicines put forward similar proposals, and we propose working jointly, at least on medicines for pain relief.[44,336] Accountability through monitoring and evaluation are essential for success, and this requires either separate and independent global and national commissions or a group working alongside institutions dedicated to achieving the SDGs.

The 2014 WHA Resolution is a powerful document, but according to the reports from both WHO[43] and civil society,[347,348] few countries have made real progress, and the resolution does not include an accountability framework. The Commission calls on WHO to follow on the Resolution with an accountability mechanism that includes specific indicators, associated targets, and recommendations for corrective action. Lessons can be learned from examples such the AIDS response and framework conventions.[39] Donor countries should make funds available to fully implement the resolution and to develop the global public knowledge goods that are essential implementation and advocacy tools.

Intersectoral work should ideally be led by WHO, although global, non-for-profit organisations have often filled this vacuum in ways that are laudable but not sustainable or effective in the long term. Although these organisations were catalytic in bringing about the landmark 2014 WHA Resolution on palliative care, WHO and other UN agencies are the forum for implementing the recommendations in the Resolution and the monitoring work outlined in this document.

Potential synergistic linkages exist between the palliative care and non-communicable diseases movements,[275] and the integration of policy, planning, and advocacy could lead to progress in both movements. Ageing, long-term care, and palliative care will become increasingly linked as demographic transition proceeds in LMICs. Falsely dichotomising these issues would reduce the opportunities to identify and implement diagonal interventions and joint platforms for action and policy research that can be effective in identifying synergies.

The huge unmet medical need for effective medicines for pain treatment demands a more balanced global policy to ensure that patients have safe and secure access while still preventing non-medical use. The global health system must maximise its potential to add value by taking steps to dismantle unnecessary access barriers to pain treatment and to develop model procedures and legislation that can guide national actors in handling medicines that could be diverted to non-medical use. The Commission also calls on the INCB to include access to opioids for medical need in its annual reporting.

Countries could have large potential savings on the cost of order if they had access to best-case international prices. Global collective action has an important opportunity to aggregate demand and support LMICs with information and negotiating capacity to secure low and stable prices, especially for injectable morphine. The Commission recommends that regional or global pooled purchasing facilities be established and led by a global financing entity such as the World Bank and that these be integrated into existing global and regional funds, WHO offices, and development banks.

Innovative product development and adaptation of existing formulations of medicines and equipment for low-resource settings will reduce cost and facilitate delivery, which will be necessary to achieve universal access to palliative care and pain relief. The Commission recommends a focus on promoting and facilitating international and interinstitutional exchange, including public–private partnerships, that generates frugal innovation and collaboration platforms.

Palliative care is almost never prioritised in emergency situations. The Commission calls on all international agencies to ensure that palliative care becomes an essential component of any response to humanitarian emergencies, natural disasters, and refugee crises.

Children continue to be an at-risk and neglected group, despite regional and global advocacy efforts to include them in the palliative care agenda.[114] To remedy this, the Commission puts forward several child-focused recommendations. We call on the World Bank, working with UNICEF, to spearhead an interinstitutional initiative to establish a special fund for children in low-income countries who are in need of palliative care and pain relief. A fund should include for all countries, and especially for LMICs, technical support for safe delivery and management of medicines and support for efforts to expand access to essential palliative care interventions, beginning with health. The cost of closing the pain divide for children is a pittance, and continuing to ignore this need violates the spirit, content, and aspirations of the SDGs. Furthermore, such a fund can provide a financing platform to catalyse provision of other medicines for treatment of chronic and non-communicable diseases for adults and children.

Better evidence and priority setting tools must be generated to adequately measure the global need for palliative care, implement policies and programmes, and monitor progress towards alleviating the burden of pain and other types of SHS

The Commission's work suggests the imperative of implementing a rigorous, vigorous, and substantive research agenda that provides the key knowledge inputs for closing the access abyss in palliative care and pain relief and the tools to both set and monitor global and national priorities and progress.

First we recommend the development of a strong set of metrics for priority setting in palliative care and pain relief. SHS has not been adequately measured or included in datasets, making the need for palliative care and pain relief largely invisible to policy makers and preventing health leaders from identifying effective responses that would integrate palliative care into UHC. The framework proposed by the Commission is a first step, and we recommend that a major research endeavour be mounted to develop the metrics and data to more effectively estimate the burden of SHS, to identify the associated need for palliative care and pain relief, and to measure the effect and effectiveness of future policies and programmes. This data collection strategy should incorporate social, spiritual, and caregiver needs in the need for palliative care.

We propose a measure of suffering intensity-adjusted life-years (SALYs), against which the efficacy of interventions could be judged in terms of SHS averted. SALYs should first be explored as an adaptation of existing measures of burden of ill health (QALYs and DALYs) to develop a comprehensive measure for economic evaluations of resources allocated across prevention, treatment, and palliation. By summing the benefits of financial protection and the diagonal benefits that accrue to other parts of the health and social system, such a measure would account for the value of alleviating SHS to the patient, the family, the health system, and the

economy. Comparing these benefits with the cost of the Essential Package and augmented packages through extended cost-effectiveness analysis would provide key information for choices around public finance.

These powerful priority-setting tools must translate into effective policies and programmes for countries seeking efficient and equitable health care and UHC. Implementation research and rigorous evaluation of both small-scale and large-scale palliative care activities, and their integration into UHC, are key to identifying replicable and scalable models and to measuring potential for reducing SHS and for cost savings. Documenting and disseminating successful country experiences and programmes to monitor and prevent non-medical use of opioids and research that evaluates outcomes in areas where access has been increased can provide further proof of concept for applying a balanced approach.

The Commission recommends that high priority be given to developing augmented palliative care packages with tools for choosing cost-effective interventions. This work should examine and assess human resource models with training based on competencies and with the incorporation of community health workers, nurses, and other health personnel. The needs for social support should be met through antipoverty and social welfare programmes, whereas research is needed to develop and evaluate intersectoral models that integrate health and other key interventions. Finally, the many opportunities for frugal innovation and for the use of innovative technology to extend the Essential Package and coverage should be reviewed in future research (panel 13).

The stark differences between countries in the prices paid for medicines in the Essential Package, especially for morphine, merits future research. First, complete price data should be gathered and the cost of improving supply chains analysed. Second, the role of the supply side and market organisation in generating these price differences should be analysed. Finally, consideration of the various models for price negotiation and aggregating demand, such as those used by the Clinton Health Access Initiative, PAHO, and the Global Fund, could provide relevant lessons for price stabilisation.

Detailed analysis of country-specific health systems as case examples can serve as a global public good for knowledge exchange and systems strengthening. Effective and efficient translation of policy to practise relies on explicit research on service planning at national and global level across the delivery chain. Country-specific analysis should be undertaken to map health services and points for palliative care integration and to identify potential systems levers for strengthening delivery. Integration of palliative care and UHC in LMICs could be accelerated by research on existing models.

Palliative care and pain relief interventions and policies are highly intersectoral. A complete and periodically updated political mapping exercise should be undertaken by WHO to strengthen global stewardship. Countries would benefit from a similar political mapping exercise.

Women carry a disproportionate burden of caregiving, so expanding palliative care will have collateral effects on the health, education, empowerment, and earnings capacity of women and girls. Future research should pinpoint these risks and identify effective gender proactive strategies and policies that value the contributions of women and caregiving. We recommend that national governments, based on this evidence, develop and implement gender-proactive and health-enhancing labour market policies that allow men and women to provide safe and supportive caregiving as a complement to palliative care.[125]

Palliative care has been marginalised within global health, but as the issue gains traction, it is becoming evident that there are specific population groups and diseases that are marginalised even within palliative care. Their needs must be identified through research. Little is known about gender inequity in access to palliative care, and this factor should be built into efforts to integrate palliative care into UHC. Malignant neoplasms and HIV disease have received the most attention in clinical, academic, and advocacy work on palliative care and pain relief. Certain cancers have been ignored because of the nature of the symptoms or the poverty of the affected groups. Similarly, certain groups of patients who live with HIV disease are at particular risk of stigma and exclusion.[39] Most other diseases that generate SHS, several of which are described in this Report, have been largely ignored in palliative care research and service provision, and this needs to be addressed through research and policy.

Vulnerable population groups such as children, elderly people, refugees, internally displaced persons and migrants, individuals affected by natural disasters and complex emergencies, and individuals in extreme poverty, have special needs and face additional barriers to accessing and using palliative care and pain relief. Innovative programmes are needed, and we call for future *Lancet* Commissions to focus on these groups, beginning with children and humanitarian emergencies.

We call on academia to promote and incorporate this agenda in its own research agenda and in research training and fundraising across all disciplines, including medicine, nursing, and the social sciences. International organisations, national governments, and civil society have an important role in monitoring scientific outputs, identifying gaps, and guiding resources for data collection and research on the neglected topic of palliative care and pain relief in LMICs. To support the research streams, non-governmental and governmental research funding agencies and foundations should incorporate palliative care and pain relief in their health and social development priorities.

Contributors

FMK was Chair of the Commission and PEF was co-Chair of the Commission. FMK, PEF, JF, ELK, LDL, and ABh developed the original idea for the Commission. PEF, RA, KMF, JF, DTJ, and MRR with FMK, EK, LDL, and ABh guided the structure and substantive focus of the report. FMK developed the scope and work plan of the Commission, participated in all working groups with the chairs, chaired the Commission meetings, led the Secretariat, led the data analysis, wrote all drafts of the report with editing and revision input from PEF, ELK, LDL, GAOA, SRC, DJH, DL, LR, and MdRSM, and secured and then managed the funding for the Secretariat and the Commission with support from KF, JS, RA, and ABh. LDL, ELK, and MRR co-chaired the Models and Innovations Working Group. DTJ and SV co-chaired the Economic Evaluation and Measurement Working Group. RA chaired the Universal Health Coverage, Health Systems, and Palliative Care Working Group. Chairs of the three working groups developed the substantive focus, guided and analysed inputs produced by their respective groups The working groups dedicated time and thought to capturing country-specific lessons and did the epidemiological, economic, and health-systems analysis. ELK led the Clinical Expert Group, which included LR, MRR, KMF, JFC, SA, CRN, PEP-C, MC, DS, and MG; developed the dataset on SHS, the Essential Package, and the costing analysis together with the Economic Evaluation and Measurement Group and Clinical Expert Group; collected the data on SHS, and compiled the dataset with XJK; provided text inputs for the report; and worked with the data analysis team to interpret all findings. LDL managed and developed the plan of the follow-up to the Commission and engagement of civil society and regional networks, with input from MRR, FMK, JD, SC, CG, EL, DS, EK, KF, and LR; provided text inputs for the report; developed conclusions and recommendations; managed and wrote testimonials; and wrote a case on Colombia. FMK and ABh led the core writing team, which included XJK, HA-O, OG-D, and NMR. FMK led the data analysis team, which included XJK, HA-O, ABh, NMR, and OMC, with contributions from CRN, QTK, PEP-C, and MdRSM. JF served as health systems and global health lead, working with OG-D. All Commissioners provided input into the formative discussions that generated the scope and work plan of the Commission and contributed ideas and substantive comments throughout the Commission process that shaped the content, findings, key messages, and conclusions of the Report. All Scientific Advisory Committee members contributed to sections related to their topic, country, and region expertise and provided core inputs in the form of quantitative, qualitative or health-systems data, and data analysis. DC wrote the panel on the history of palliative care. ME wrote the panel on training of clergy. NB wrote the panel on complex emergencies and provided guidance on the analysis of infectious diseases and emerging pathogens. The core country cases were led by JJ with PEP-C (Chile), LDL with NMR (Colombia), RS (Costa Rica), ABh and MRR (India), DS (Jamaica), HA-SH (Lebanon), EK with EW (Malawi), FMK (Mexico), BP (Nepal), ABi (Rwanda), LG (South Africa), EBKL (Uganda), SRC (USA), and ELK (Vietnam). JDD provided core input into the work on children's palliative care, and CZ provided core input to the work on early initiation of palliative care and both provided extensive comments and text inputs, initially as reviewers. All by-line authors and members of the study group contributed to the ideas and recommendations and to the structure of the report. All authors approved the final submitted version of the report. The report was prepared under the general direction of FMK. The authors alone are responsible for the views expressed in this Report, and they do not necessarily represent the views, decisions, or policies of the institutions with which they are affiliated.

Lancet Commission on Palliative Care and Pain Relief Study Group

Commission Chairpersons: Felicia Marie Knaul (Chair; University of Miami), Paul E Farmer (co-Chair; Harvard Medical School)
Commissioners: Huda Abu-Saad Huijer (American University of Beirut), George A O Alleyne (Director Emeritus, Pan American Health Organization), Rifat Atun (Harvard T.H. Chan School of Public Health), Agnes Binagwaho (Former Minister of Health, Rwanda and Vice Chancellor, University of Global Health Equity), Snežana M Bošnjak (Institute for Oncology and Radiology of Serbia), David Clark (University of Glasgow), James F Cleary (Carbone Cancer Center, University of Wisconsin School of Medicine and Public Health), José Ramón Cossío Díaz (Justice of The Supreme Court of Justice of the Nation, Mexico), Liliana De Lima (International Association for Hospice and Palliative Care), Kathleen M Foley (Weill Cornell Medical College), Julio Frenk (Former Minister of Health, Mexico, and President of the University of Miami), Cynthia Goh (Division of Palliative Medicine, National Cancer Centre Singapore), Pascal J Goldschmidt-Clermont (Leonard M. Miller School of Medicine, University of Miami), Mary Gospodarowicz (Princess Margaret Cancer Centre), Liz Gwyther (Hospice Palliative Association of South Africa), Irene J Higginson (King's College London), Thomas Hughes-Hallett (The Marshall Institute for Philanthropy and Social Entrepreneurship, London School of Economics and Political Science), David J Hunter (Nuffield Department of Population Health, University of Oxford), Dean T Jamison (University of California, San Francisco), Eric L Krakauer (Harvard Medical School), Diederik Lohman (Human Rights Watch), Emmanuel B K Luyirika (African Palliative Care Association), Maria Elena Medina Mora (National Institute of Psychiatry Ramon de la Fuente Muñiz), Faith N Mwangi-Powell (Options Consultancy Services), Sania Nishtar (Heartfile), Megan E O'Brien (American Cancer Society), Lukas Radbruch (University Hospital Bonn, International Association for Hospice and Palliative Care), M R Rajagopal (Pallium India), K Srinath Reddy (Public Health Foundation of India), María del Rocío Sáenz Madrigal (Former Minister of Health, Costa Rica, and Former Executive President of the Costa Rican Social Security Fund), Judith A Salerno (New York Academy of Medicine).
Scientific Advisory Committee Chairpersons: Afsan Bhadelia (co-Chair; Harvard T.H. Chan School of Public Health), Liliana De Lima (co-Chair; International Association for Hospice and Palliative Care).
Scientific Advisory Committee: Silvia Allende (Instituto Nacional de Cancerología), Hector Arreola-Ornelas (Fundación Mexicana para la Salud), Nahid Bhadelia (Section of Infectious Diseases, Boston University School of Medicine); Mariana Calderon (Médica Sur Hospital), Stephen R Connor (Worldwide Hospice Palliative Care Alliance), Victoria Y Fan (University of Hawaii at Manoa), Octavio Gómez-Dantés (National Institute of Public Health, Mexico), Jorge Jiménez (Pontificia Universidad Católica de Chile), Christian R Ntizimira (Rwanda Palliative Care and Hospice Organisation), Pedro E Perez-Cruz (Department of Internal Medicine, Faculty of Medicine, Pontificia Universidad Católica de Chile), Isaias G Salas-Herrera (Costa Rican Social Security), Dingle Spence (Hope Institute Hospital), Mark R Steedman (Deloitte LLP), Stéphane Verguet (Department of Global Health and Population, Harvard T.H. Chan School of Public Health).
Collaborators: Julia D Downing (International Children's Palliative Care Network); Bishnu D Paudel (National Academy of Medical Sciences, Bir Hospital); Maia Elsner (Harvard University); James A Gillespie (University of Sydney), Karen J Hofman (PRICELESS SA, Faculty of Health Sciences, School of Public Health, University of Witwatersrand); Xiaoxiao Jiang Kwete (Harvard T.H. Chan School of Public Health); Quach T Khanh (Ho Chi Minh City Oncology Hospital); Karl A Lorenz (Stanford University School of Medicine); Oscar Méndez-Carniado (Fundación Mexicana para la Salud, A.C.); Rachel Nugent (RTI International); Natalia M Rodriguez (University of Miami); Emily B Wroe (Partners in Health); Camilla Zimmermann (University of Toronto).

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References

1 International Narcotics Control Board. Narcotic drugs. Technical reports. Estimated world requirements for 2017—statistics for 2015. 2015. https://www.incb.org/incb/en/narcotic-drugs/Technical_Reports/narcotic_drugs_reports.html (accessed March 23, 2017).

2 UN. Sustainable Development Goal 3: ensure healthy lives and promote well-being for all at all ages. Progress of Goal 3 in 2017. https://sustainabledevelopment.un.org/sdg3 (accessed July 2, 2017).

3 Collahan D. Ends and means: the goals of health care. In: M Danis, ed. Ethical dimensions of health policy. New York: Oxford University Press, 2002: 395.

4 MD Magazine. Why are we still talking about opiophobia? Aug 22, 2011. http://www.mdmag.com/journals/pain-management/2011/may-2011/why-are-we-still-talking-about-opiophobia (accessed July 2, 2017).

5 International Narcotics Control Board. Availability of internationally controlled drugs: ensuring adequate access for medical and scientific purposes. New York, NY: United Nations, 2016.

6 Radbruch L, Scholten W, Payne S, et al. Ensuring balance in national policies on controlled substances. Geneva: World Health Organization, 2011.

7 Gawande A. Being mortal. Medicine and what matters in the end. New York, NY: Metropolitan Books, Henry Holt and Company, 2014.

8 Krakauer EL. To be freed from the infirmity of (the) age: subjectivity, life-sustaining treatment, and palliative medicine. In: Biehl JGB, Kleinman A, eds. Subjectivity: ethnographic investigations. Berkeley, CA: University of California Press, 2007: 381–96.

9 Global Commission on Drug Policy. The negative impact of drug control on public health: the global crisis of avoidable pain. Geneva: Global Commission on Drug Policy, 2015.

10 Csete J, Kamarulzaman A, Kazatchkine M, et al. Public health and international drug policy. *Lancet* 2016; **387:** 1427–80.

11 Berterame S, Erthal J, Thomas J, et al. Use of and barriers to access to opioid analgesics: a worldwide, regional, and national study. *Lancet* 2016; **387:** 1644–56.

12 Anderson ED, Davis CS. Breaking the cycle of preventable suffering: fulfilling the principle of balance. Philadelphia, PA: Temple Int'l & Comp, 2010.

13 Horton R. Offline: NCDs—why are we failing? *Lancet* 2017; **390:** 346.

14 Frost L, Reich M. Access: how do good health technologies get to poor people in poor countries? Cambridge, MA: Harvard Center for Population and Development Studies, 2008.

15 WHO. WHO model lists of essential medicines. 2017. http://www.who.int/medicines/publications/essentialmedicines/en/ (accessed July 2, 2017).

16 Knaul FM, Adami H-P, Adebamowo C, et al. The global cancer divide: an equity imperative. In: Knaul FM, Gralow JR, Atun R, Bhadelia A, eds. Close the cancer divide: an equity imperative. Cambridge, MA: Harvard University Press, 2012.

17 Knaul FM, Alleyne G, Piot P, et al. Health system strengthening and cancer: a diagonal response to the challenge of chronicity. In: Knaul FM, Gralow JR, Atun R, Bhadelia A, eds. Close the cancer divide: an equity imperative. Cambridge, MA: Harvard University Press, 2012.

18 Gudex C, Kind P. The QALY toolkit. York: Centre for Health Economics, University of York, 1988.

19 DesRosiers T, Cupido C, Pitout E, et al. A hospital-based palliative care service for patients with advanced organ failure in sub-Saharan Africa reduces admissions and increases home death rates. *J Pain Symptom Manage* 2014; **47:** 786–92.

20 Morrison RS, Dietrich J, Ladwig S, et al. Palliative care consultation teams cut hospital costs for Medicaid beneficiaries. *Health Aff (Millwood)* 2011; **30:** 454–63.

21 Kelley AS, Deb P, Du Q, Aldridge Carlson MD, Morrison RS. Hospice enrollment saves money for Medicare and improves care quality across a number of different lengths-of-stay. *Health Aff (Millwood)* 2013; **32:** 552–61.

22 Smith S, Brick A, O'Hara S, Normand C. Evidence on the cost and cost-effectiveness of palliative care: a literature review. *Palliat Med* 2014; **28:** 130–50.

23 UICC. The economics of cancer prevention and control: data digest. 2014. http://www.iccp-portal.org/economics-cancer-prevention-control-data-digest (accessed Sept 25, 2017).

24 Frenk J, Gomez-Dantés O, Knaul FM. The health systems agenda: prospects for the diagonal approach. The handbook of global health policy. West Sussex, UK: John Wiley & Sons, 2014: 425–39.

25 Watkins D, Qi J, Horton S. Costs and affordability of essential universal health coverage in low- and middle-income countries. DCP3 Working Paper Series Working Paper #20. Seattle, WA: University of Washington, 2017.

26 Rolles S, Murkin G, Powell M, Kushlick D, Saunter N, Slater J. The alternative world drug report. Bristol: Transform Drug Policy Foundation, 2016.

27 WHO. What is universal coverage? http://www.who.int/health_financing/universal_coverage_definition/en/ (accessed Feb 22, 2017).

28 WHO. Tracking universal health coverage: first global monitoring report. Geneva: World Health Organization, 2015.

29 WHO. World health statistics 2017: monitoring health for the SDGs. Geneva: World Health Organization, 2017.

30 Jamison DT, Summers LH, Alleyne G, et al. Global health 2035: a world converging within a generation. *Lancet* 2013; **382:** 1898–955.

31 Frenk J. Bridging the divide: global lessons from evidence-based health policy in Mexico. *Lancet* 2006; **368:** 954–61.

32 Sepulveda J, Bustreo F, Tapia R, et al. Improvement of child survival in Mexico: the diagonal approach. *Lancet* 2006; **368:** 2017–27.

33 Verguet S, Kim JJ, Jamison DT. Extended cost-effectiveness analysis for health policy assessment: a tutorial. *Pharmacoeconomics* 2016; **34:** 913–23.

34 Kawabata K, Xu K, Carrin G. Preventing impoverishment through protection against catastrophic health expenditure. *Bull World Health Organ* 2002; **80:** 612.

35 Consejo Nacional de Evaluación de la Política de Desarrollo Social. Medicion de la pobreza, Estados Unidos Medicanos. 2014. http://www.coneval.org.mx/Medicion/MP/PublishingImages/Pobreza_2014.jpg (accessed March 27, 2017).

36 WHO. The world health report 2000. Health systems: improving performance. Geneva: World Health Organization, 2000.

37 Gamondi C, Larkin P, Payne S. Core competencies in palliative care: an EAPC White Paper on palliative care education. Part 1. *Eur J Palliat Care* 2013; **20:** 86–91.

38 Gamondi C, Larkin P, Payne S. Core competencies in palliative care: an EAPC White Paper on palliative care education: part 2. *Eur J Palliat Care* 2013; **20:** 140–45.

39 Piot P, Abdool Karim SS, Hecht R, et al. Defeating AIDS—advancing global health. *Lancet* 2015; **386:** 171–218.

40 Bhutta ZA, Chen L, Cohen J, et al. Education of health professionals for the 21st century: a global independent Commission. *Lancet* 2010; **375:** 1137–38.

41 Blanchet N, Thomas M, Atun RA, Jamison DT, Knaul FM, Hecht R. Global collective action in health: the WDR+20 landscape of core and supportive functions. Helsinki: UNU-WIDER, 2014.

42 WHO. WHA67.19. Strengthening of palliative care as a component of comprehensive care throughout the life course. Geneva: World Health Organization, 2014.

43 WHO. Progress reports: report by the Secretariat. Geneva: World Health Organization, 2016.

44 Das P, Horton R. Essential medicines for universal health coverage. *Lancet* 2017; **389:** 337–39.

45 Marschall U, L'hoest H, Radbruch L, Häuser W. Long-term opioid therapy for chronic non-cancer pain in Germany. *Eur J Pain* 2016; **20:** 767–76.

46 Radbruch L, Sabatowski R, Petzke F, Brunsch-Radbruch A, Grond S, Lehmann KA. Transdermal fentanyl for the management of cancer pain: a survey of 1005 patients. *Palliat Med* 2001; **15:** 309–21.

47 Callaway M, Foley KM, De Lima L, et al. Funding for palliative care programs in developing countries. *J Pain Symptom Manage* 2007; **33:** 509–13.

48 De Lima L, Pastrana T. Evaluation of the effectiveness of workshops on the availability and rational use of opioids in Latin America. *J Palliat Med* 2016; **19:** 964–71.

49 Knaul FM, Farmer PE, Bhadelia A, Berman P, Horton R. Closing the divide: the Harvard Global Equity Initiative–*Lancet* Commission on global access to pain control and palliative care. *Lancet* 2015; **386:** 722–24.

50 The Economist. The new old. A blessing not a burden: the joys of living to 100. *The Economist*, July 6, 2017.

51 Beaglehole R, Bonita R, Horton R, et al. Priority actions for the non-communicable disease crisis. *Lancet* 2011; **377:** 1438–47.

52 Department of Economic and Social Affairs Population Division. World population ageing 2015. New York, NY: United Nations, 2015.

53 Institute for Health Metrics and Evaluation (IHME). GBD Compare Data Visualization. Seattle, WA: IHME, University of Washington, 2016.

54 UN. Sustainable Development Goals. 17 goals to transform our world. New York, NY: United Nations, 2015.

55 WHO. Universal health coverage (UHC). Fact sheet. December, 2016. http://www.who.int/mediacentre/factsheets/fs395/en/ (accessed March 29, 2017).

56 Porter ME. What is value in health care? *N Engl J Med* 2010; **363:** 2477–81.

57 Hui D, Bruera E. Integrating palliative care into the trajectory of cancer care. *Nat Rev Clin Oncol* 2016; **13:** 159–71.

58 Clark D. To comfort always: a history of palliative medicine since the nineteenth century. Oxford: Oxford University Press, 2016.

59 Saunders C. The symptomatic treatment of incurable malignant disease. *Prescr J* 1964; **4:** 68–73.

60 Bonica JJ VV. International symposium on pain of advanced cancer. New York, NY: Raven Press; 1979.

61 Mount B. The Royal Victoria Hospital palliative care service: a Canadian experience. In: Saunders CKR, ed. Hospice care on the international scene. New York, NY: Springer, 1997.

62 Clark D. International progress in creating palliative medicine as a specialized discipline. In: Hanks G, ed. Oxford textbook of palliative medicine, 4th edn. Oxford: Oxford University Press, 2010: 9–16.

63 WHO. Cancer pain relief. Geneva: World Health Organization, 1986.

64 WHO. Cancer pain relief and palliative care. Geneva: World Health Organization, 1990.

65 Sepulveda C, Marlin A, Yoshida T, Ullrich A. Palliative care: the World Health Organization's global perspective. *J Pain Symptom Manage* 2002; **24:** 91–96.

66 Jagwe J, Merriman A. Uganda: delivering analgesia in rural Africa: opioid availability and nurse prescribing. *J Pain Symptom Manage* 2007; **33:** 547–51.

67 WHO. WHO definition of palliative care. http://www.who.int/cancer/palliative/definition/en/ (accessed Feb 22, 2017).

68 Sixty-ninth World Health Assembly. Strengthening integrated, people-centred health services. Geneva: World Health Organization, 2016.

69 Krakauer E, Ali Z, Arreola H, et al. Chapter 12: palliative care in response to the global burden of remediable suffering. In: Jamison D, Horton S, Jha P, Laxminarayan R, Nugent R, Mock C, Danforth K, eds. Disease control priorities. Washington, DC: World Bank, 2017.

70 Amblàs J, Bauer R, Beas E, et al. Building integrated palliative care programs and services. May, 2017. http://kehpca.org/wp-content/uploads/Go%CC%81mez-Batiste-X-Connor-S-Eds.-Building-Integrated-Palliative-Care-Programs-and-Services.-2017-b.pdf (accessed Aug 29, 2017).

71 Krakauer EL. Just palliative care: responding responsibly to the suffering of the poor. *J Pain Symptom Manage* 2008; **36:** 505–12.

72 Zimmermann C, Swami N, Krzyzanowska M, et al. Early palliative care for patients with advanced cancer: a cluster-randomised controlled trial. *Lancet* 2014; **383:** 1721–30.

73 WHO. Cancer pain relief and palliative care. Report of a WHO expert committee. 1990. http://apps.who.int/iris/bitstream/10665/39524/1/WHO_TRS_804.pdf (accessed Sept 19, 2017).

74 Lynn J, Adamson DM. Living well at the end of life. Adapting health care to serious chronic illness in old age. Santa Monica, CA: RAND Corporation, 2003.

75 Murray SA, Kendall M, Boyd K, Sheikh A. Illness trajectories and palliative care. *Int Perspect Public Health Palliat Care* 2012; **30:** 2017–19.

76 Lunney JR, Lynn J, Foley DJ, Lipson S, Guralnik JM. Patterns of functional decline at the end of life. *JAMA* 2003; **289:** 2387–92.

77 Roeland EJ. Tailoring palliative care to the changing needs of people facing cancer. *J Clin Oncol* 2017; **35:** 813–15.

78 Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non–small-cell lung cancer. *N Engl J Med* 2010; **363:** 733–42.

79 Delgado-Guay MO, Hui D, Parsons HA, et al. Spirituality, religiosity, and spiritual pain in advanced cancer patients. *J Pain Symptom Manage* 2011; **41:** 986–94.

80 Zollfrank AA, Trevino KM, Cadge W, et al. Teaching health care providers to provide spiritual care: a pilot study. *J Palliat Med* 2015; **18:** 408–14.

81 Herce ME, Elmore SN, Kalanga N, et al. Assessing and responding to palliative care needs in rural sub-Saharan Africa: results from a model intervention and situation analysis in Malawi. *PLoS One* 2014; **9:** e110457.

82 Gwyther L, Brennan F, Harding R. Advancing palliative care as a human right. *J Pain Symptom Manage* 2009; **38:** 767–74.

83 Lohman D, Schleifer R, Amon JJ. Access to pain treatment as a human right. *BMC Med* 2010; **8:** 1.

84 Human Rights Watch. "Please, do not make us suffer any more…"; access to pain treatment as a human right. New York, NY: Human Rights Watch, 2009.

85 Lohman D, Wilson D, Marston J. Chapter 10: Advocacy and human rights issues. In: Gómez-Batiste X, Connor S, Eds. Building integrated palliative care programs and services. London: Worldwide Hospice Palliative Care Alliance, 2017.

86 National Academies of Sciences, Engineering and Medicine. Pain management and the opioid epidemic: balancing societal and individual benefits and risks of prescription opioid use. Washington, DC: National Academies Press, 2017.

87 Volkow ND, McLellan AT. Opioid abuse in chronic pain—misconceptions and mitigation strategies. *N Engl J Med* 2016; **374:** 1253–63.

88 Dunn KM, Saunders KW, Rutter CM, et al. Opioid prescriptions for chronic pain and overdose: a cohort study. *Ann Intern Med* 2010; **152:** 85–92.

89 Carroll I, Barelka P, Wang CK, et al. A pilot cohort study of the determinants of longitudinal opioid use after surgery. *Anesth Analg* 2012; **115:** 694–702.

90 Canadian Medical Association. Harms associated with opioids and other psychoactive prescription drugs. Ottawa: Canadian Medical Association, 2015.

91 CDC. Vital signs: overdoses of prescription opioid pain relievers—United States, 1999–2008. *MMWR Morb Mortal Wkly Rep* 2011; **60:** 1487.

92 Daubresse M, Chang H-Y, Yu Y, et al. Ambulatory diagnosis and treatment of non-malignant pain in the United States, 2000–2010. *Med Care* 2013; **51:** 870-78.

93 Paulozzi LJ, Mack KA, Hockenberry JM. Vital signs: variation among States in prescribing of opioid pain relievers and benzodiazepines—United States, 2012. *MMWR Morb Mortal Wkly Rep* 2014; **63:** 563–68.

94 Quinones S. Dreamland: the true tale of America's opiate epidemic. London: Bloomsbury Publishing, 2015.

95 CDC. Provisional counts of drug overdose deaths, as of 8/6/2017. Atlanta, GA: Centers for Disease Control and Protection, 2017.

96 Rajagopal MR, Joranson DE, Gilson AM. Medical use, misuse, and diversion of opioids in India. *Lancet* 2001; **358:** 139–43.

97 Logie DE, Harding R. An evaluation of a morphine public health programme for cancer and AIDS pain relief in sub-Saharan Africa. *BMC Public Health* 2005; **5:** 82.

98 Voon P, Karamouzian M, Kerr T. Chronic pain and opioid misuse: a review of reviews. *Subst Abuse Treat Prev Policy* 2017; **12:** 36.

99 Gawande AA. It's time to adopt electronic prescriptions for opioids. *Ann Surg* 2017; **265:** 693–94.

100 Humphreys K. Avoiding globalisation of the prescription opioid epidemic. *Lancet* 2017; **390:** 437–39.

101 Hauser W, Petzke F, Radbruch L, Tolle TR. The opioid epidemic and the long-term opioid therapy for chronic noncancer pain revisited: a transatlantic perspective. *Pain Manag* 2016; **6:** 249–63.

102 Radcliffe Institute For Advanced Study, Harvard University. Closing the pain divide. 2014. https://www.radcliffe.harvard.edu/exploratory-seminars/closing-pain-divide (accessed July 26, 2017).

103 Abajobir AA, Abate KH, Abbafati C, et al. Global, regional, and national under-5 mortality, adult mortality, age-specific mortality, and life expectancy, 1970–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2017; **390:** 1084–150.

104 Murray CJ, Ezzati M, Flaxman AD, et al. GBD 2010: design, definitions, and metrics. *Lancet* 2012; **380:** 2063–66.

105 Mehrez A, Gafni A. Quality-adjusted life years, utility theory, and healthy-years equivalents. *Med Decis Making* 1989; **9:** 142–49.

106 Abajobir AA, Abate KH, Abbafati C, et al. Global, regional, and national disability-adjusted life-years (DALYs) for 333 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2017; **390:** 1260–344.

107 Lampl C, Steiner TJ, Mueller T, et al. Will (or can) people pay for headache care in a poor country? *J Headache Pain* 2012; **13:** 67–74.

108 Ughasoro MD, Udem ND, Chukwudi NK, Korie FC, Uzochukwu BS, Onwujekwe EO. Caregivers' willingness-to-pay for a topical anesthetic cream for minor medical procedures in children. *Niger J Clin Pract* 2014; **17:** 506–10.

109 Malhotra C, Farooqui MA, Kanesvaran R, Bilger M, Finkelstein E. Comparison of preferences for end-of-life care among patients with advanced cancer and their caregivers: a discrete choice experiment. *Palliat Med* 2015; **29:** 842–50.

110 Singer AE, Goebel JR, Kim YS, et al. Populations and interventions for palliative and end-of-life care: a systematic review. *J Palliat Med* 2016; **19:** 995–1008.

111 Higginson IJ, Bausewein C, Reilly CC, et al. An integrated palliative and respiratory care service for patients with advanced disease and refractory breathlessness: a randomised controlled trial. *Lancet Respir Med* 2014; **2:** 979–87.

112 Morgan S, Yoder LH. A concept analysis of person-centered care. *J Holist Nurs* 2012; **30:** 6–15.

113 Connor SR, Bermedo MCS. Global atlas of palliative care at the end of life. Geneva: World Health Organization, Worldwide Palliative Care Alliance, 2014.

114 Connor SR, Downing J, Marston J. Estimating the global need for palliative care for children: a cross-sectional analysis. *J Pain Symptom Manage* 2017; **53:** 171–77.

115 Foley KM, Wagner JL, Joranson DE, Gelband H. Pain control for people with cancer and AIDS. In: Jamison DT, Breman JG, Measham AR, et al, eds. Disease Control Priorities in Developing Countries, 2nd edn. Washington, DC: The International Bank for Reconstruction and Development, The World Bank; New York, NY: Oxford University Press, 2006.

116 Cleary J, Gelband H, Wagner J. Cancer pain relief. In: Gelband H, Jha P, Sankaranarayanan R, Horton S, eds. Disease Control Priorities in Developing Countries, 3rd edn. Washington, DC: The International Bank for Reconstruction and Development, The World Bank; New York, NY: Oxford University Press, 2006.

117 Gómez-Batiste X, Martínez-Muñoz M, Blay C, et al. Utility of the NECPAL CCOMS-ICO tool and the surprise question as screening tools for early palliative care and to predict mortality in patients with advanced chronic conditions: a cohort study. *Palliat Med* 2016; **31:** 754–63.

118 WHO. Palliative care. Fact sheet number 402. Geneva: World Health Organization, 2015.

119 Schulz R, Sherwood PR. Physical and mental health effects of family caregiving. *Am J Nurs* 2008; **108** (suppl 9)**:** 23–27.

120 Emanuel N, Simon MA, Burt M, et al. Economic impact of terminal illness and the willingness to change it. *J Palliat Med* 2010; **13:** 941–44.

121 Emanuel RH, Emanuel GA, Reitschuler EB, et al. Challenges faced by informal caregivers of hospice patients in Uganda. *J Palliat Med* 2008; **11:** 746–53.

122 Pinquart M, Sörensen S. Differences between caregivers and noncaregivers in psychological health and physical health: a meta-analysis. *Psychol Aging* 2003; **18:** 250.

123 Gardiner C, Brereton L, Frey R, Wilkinson-Meyers L, Gott M. Exploring the financial impact of caring for family members receiving palliative and end-of-life care: a systematic review of the literature. *Palliat Med* 2014; **28:** 375–90.

124 Brinda EM, Rajkumar AP, Enemark U, Attermann J, Jacob K. Cost and burden of informal caregiving of dependent older people in a rural Indian community. *BMC Health Serv Res* 2014; **14:** 207.

125 Langer A, Meleis A, Knaul FM, et al. Women and health: the key for sustainable development. *Lancet* 2015; **386:** 1165–210.

126 Radbruch L, Kern M. Until the very end: is there equity in palliative care? *J Palliat Med* 2014; **17:** 262–63.

127 Shear MK, Reynolds CF 3rd, Simon NM, et al. Optimizing treatment of complicated grief: a randomized clinical trial. *JAMA Psychiatry* 2016; **73:** 685–94.

128 Kersting A, Brähler E, Glaesmer H, Wagner B. Prevalence of complicated grief in a representative population-based sample. *J Affect Disord* 2011; **131:** 339–43.

129 World Bank. Population, total. 2015. http://data.worldbank.org/indicator/SP.POP.TOTL (accessed June 6, 2017).

130 Bhadelia A. Development of a multidimensional measure of health justice for priority-setting in health systems strengthening. PhD thesis, Johns Hopkins University, 2017.

131 Nolte E, McKee M. Does health care save lives? Avoidable mortality revisited. London: The Nuffield Trust, 2004.

132 Knaul FM, Gralow JR, Atun R, Bhadelia A. Closing the cancer divide: an equity imperative. Cambridge, MA: Harvard University Press, 2012.

133 Pahuja M, Merlin JS, Selwyn PA. HIV/AIDS. In: Cherny NFM, Kaasa S, Portenoy RK, Currow DC, eds. Oxford textbook of palliative medicine. Oxford: Oxford University Press, 2015.

134 UN Programme on HIV/AIDS (UNAIDS). Ending AIDS. Progress towards the 90–90–90 targets. New York, NY: United Nations, 2017.

135 Vreeman RC, Gramelspacher AM, Gisore PO, Scanlon ML, Nyandiko WM. Disclosure of HIV status to children in resource-limited settings: a systematic review. *J Int AIDS Soc* 2013; **16:** 18466.

136 UN Programme on HIV/AIDS (UNAIDS). AIDSinfo. New York, NY: United Nations, 2017.

137 Gandhi NR, Shah NS, Andrews JR, et al. HIV coinfection in multidrug- and extensively drug-resistant tuberculosis results in high early mortality. *Am J Respir Crit Care Med* 2010; **181:** 80–86.

138 Yang J, Su S, Zhao H, et al. Prevalence and mortality of cancer among HIV-infected inpatients in Beijing, China. *BMC Infect Dis* 2016; **16:** 82.

139 Barnes E, Saxon C, Ahmad S. Cancer prevalence in a metropolitan HIV clinic. *J Int AIDS Soc* 2014; **17**(suppl 3)**:** 19651.

140 Gotti D, Raffetti E, Albini L, et al. Survival in HIV-infected patients after a cancer diagnosis in the cART Era: results of an Italian multicenter study. *PLoS One* 2014; **9:** e94768.

141 Riedel DJ, Mwangi EI, Fantry LE, et al. High cancer-related mortality in an urban, predominantly African-American, HIV-infected population. *AIDS (London, England)* 2013; **27:** 1109–17.

142 Ntizimira C, Ngizwenayo S, Krakauer E, Dunne M, Esmaili E. Addressing end-of-life care in cancer patients through "Ubuntu": lessons learned from Rwanda in global health perspective of humanity. *Curr Obstet Gynecol Rep* 2016; **5:** 273–78.

143 Slama S, Kim H-J, Roglic G, et al. Care of non-communicable diseases in emergencies. *Lancet* 2016; **389:** 326–30.

144 WHO. Ebola situation report. Geneva: World Health Organization, 2016.

145 Brett-Major DM, Jacob ST, Jacquerioz FA, et al. Being ready to treat Ebola virus disease patients. *Am J Trop Med Hyg* 2015; **92:** 233–37.

146 Rosoff PM. Caring for the suffering: meeting the Ebola crisis responsibly. *Am J Bioeth* 2015; **15:** 26–32.

147 Bah EI, Lamah M-C, Fletcher T, et al. Clinical presentation of patients with Ebola virus disease in Conakry, Guinea. *N Engl J Med* 2015; **372:** 40–47.

148 Danis M. Weighing the importance of palliation of symptoms for Ebola patients during the epidemic in west Africa. *Am J Bioeth* 2015; **15:** 70–72.

149 Lamontagne F, Clément C, Fletcher T, Jacob ST, Fischer WA, Fowler RA. Doing today's work superbly well—treating Ebola with current tools. *N Engl J Med* 2014; **371:** 1565–66.

150 Dhillon P, McCarthy S, Gibbs M, Sue K. Palliative care conundrums in an Ebola treatment centre. *BMJ Case Reports* 2015; published online Sept 10. DOI:10.1136/bcr-2015-211384.

151 Fowler RA, Fletcher T, Fischer WA, et al. Caring for critically ill patients with Ebola virus disease. Perspectives from west Africa. *Am J Respir Crit Care Med* 2014; **190:** 733–37.

152 Sagui E, Janvier F, Baize S, et al. Severe Ebola virus infection with encephalopathy: evidence for direct virus involvement. *Clin Infect Dis* 2015; **61:** 1627–28.

153 Pellecchia U, Crestani R, Decroo T, Van den Bergh R, Al-Kourdi Y. Social consequences of Ebola containment measures in Liberia. *PLoS One* 2015; **10:** e0143036.

154 Human Rights Watch. West Africa. Respect rights in Ebola response. Sept 15, 2014. http://www.hrw.org/news/2014/09/15/west-africa-respect-rights-ebola-response (accessed Aug 29, 2017).

155 McMahon SA, Ho LS, Brown H, Miller L, Ansumana R, Kennedy CE. Healthcare providers on the frontlines: a qualitative investigation of the social and emotional impact of delivering health services during Sierra Leone's Ebola epidemic. *Health Policy Plan* 2016: **31:** 1232–39.

156 Farmer P. The caregivers' disease. *London Review of Books* 2015; **37:** 25–28.

157 International Federation of Red Cross And Red Crescent Societies. Psychosocial support during an outbreak of Ebola virus disease. Aug 18, 2014. http://reliefweb.int/sites/reliefweb.int/files/resources/20140814Ebola-briefing-paper-on-psychosocial-support.pdf (accessed Aug 29, 2017).

158 Van Bortel T, Basnayake A, Wurie F, et al. Psychosocial effects of an Ebola outbreak at individual, community and international levels. *Bull World Health Organ* 2016; **94:** 210–14.

159 McIntyre T, Hughes CD, Pauyo T, et al. Emergency surgical care delivery in post-earthquake Haiti: Partners in Health and Zanmi Lasante experience. *World J Surg* 2011; **35:** 745–50.

160 Pan American Health Organization, WHO. List of products by therapeutic classification. Feb 10, 2013. http://www.paho.org/hai/index.php?option=com_content&view=article&id=7011&Itemid=240&lang=en (accessed Feb 6, 2017).

161 Shultz JM, Marcelin LH, Madanes SB, Espinel Z, Neria Y. The "trauma signature:" understanding the psychological consequences of the 2010 Haiti earthquake. *Prehosp Disaster Med* 2011; **26:** 353–66.

162 Matzo M, Wilkinson A, Lynn J, Gatto M, Phillips S. Palliative care considerations in mass casualty events with scarce resources. *Biosecur Bioterror* 2009; **7:** 199–210.

163 Institute of Medicine. Dying in America: improving quality and honoring individual preferences near the end of life. Washington, DC: National Academy of Sciences, 2015.

164 Dy SM, Aslakson R, Wilson RF, et al. Closing the quality gap: revisiting the state of the science. Volume 8: improving health care and palliative care for advanced and serious illness). *Evid Rep Technol Assess (Full Rep)* 2012; 1–249.

165 Powell RA, Schwartz L, Nouvet E, et al. Palliative care in humanitarian crises: always something to offer. *Lancet* 2017; **389:** 1498–99.

166 World Bank. World development report 1993: investing in health. *Commun Dis Rep CDR Wkly* 1993; **3:** 137.

167 Gelband H, Sankaranarayanan R, Gauvreau CL, et al. Costs, affordability, and feasibility of an essential package of cancer control interventions in low-income and middle-income countries: key messages from Disease Control Priorities, 3rd ed. *Lancet* 2016; **387:** 2133–44.

168 Bobadilla JL, Cowley P, Musgrove PA, Saxenian H. The essential package of health services in developing countries. World development report. Washington, DC: World Bank, 1994.

169 Knaul FM, Gonzalez-Pier E, Gomez-Dantes O, et al. The quest for universal health coverage: achieving social protection for all in Mexico. *Lancet* 2012; **380:** 1259–79.

170 Frenk J. Leading the way towards universal health coverage: a call to action. *Lancet* 2015; **385:** 1352–58.

171 Atun R, de Andrade LO, Almeida G, et al. Health-system reform and universal health coverage in Latin America. *Lancet* 2015; **385:** 1230–47.

172 Yip WC, Hsiao WC, Chen W, Hu S, Ma J, Maynard A. Early appraisal of China's huge and complex health-care reforms. *Lancet* 2012; **379:** 833–42.

173 Hughes D, Leethongdee S. Universal coverage in the land of smiles: lessons from Thailand's 30 Baht health reforms. *Health Aff (Millwood)* 2007; **26:** 999–1008.

174 Jamison DT. Disease Control Priorities, 3rd edition: improving health and reducing poverty. *Lancet* 2015; published online Feb 5. http://dx.doi.org/10.1016/S0140-6736(15)60097-6.

175 Watkins D, Nugent R, Yamey G, et al. Intersectoral policy priorities for health. In: Jamison D, Horton S, Jha P, Laxminarayan R, Nugent R, Mock C, Danforth K, eds. Disease Control Priorities. New York, NY: The World Bank, 2017.

176 De Lima L, Bennett MI, Murray SA, et al. International Association for Hospice and Palliative Care (IAHPC) list of essential practices in palliative care. *J Pain Palliat Care Pharmacother* 2012; **26:** 118–22.

177 Santos CSD, Paiva BSR, Lucchetti ALG, Paiva CE, Fenwick P, Lucchetti G. End-of-life experiences and deathbed phenomena as reported by Brazilian healthcare professionals in different healthcare settings. *Palliat Support Care* 2017; **15:** 425–33.

178 De Lima L, Krakauer EL, Lorenz K, Praill D, MacDonald N, Doyle D. Ensuring palliative medicine availability: the development of the IAHPC list of essential medicines for palliative care. *J Pain Symptom Manage* 2007; **33:** 521–26.

179 WHO. WHO model list of essential medicines for children. 2017. http://www.who.int/entity/medicines/publications/essentialmedicines/6th_EMLc2017.pdf?ua=1 (accessed Aug 29, 2017).

180 African Palliative Care Association. Guidelines for ensuring patient access to, and safe management of, controlled medicines. Kampala: African Palliative Care Association, 2013.

181 Radbruch L, Payne S. White paper on standards and norms for hospice and palliative care in Europe: part 1. *Eur J Palliat Care* 2009; **16:** 278–89.

182 United Nations Office on Drugs and Crime. Single convention on narcotic drugs, 1961. New York, NY: United Nations, 1961.

183 Comisión Federal para la Protección contra Riesgos Sanitarios. Estupefacientes, psicotrópicos y sustancias químicas. 2015. http://www.cofepris.gob.mx/AS/Paginas/EstupefacientesPsicotropicosYSustancias-Quimicas.aspx (accessed July 2, 2017).

184 Perkins P, Dorman S. Haloperidol for the treatment of nausea and vomiting in palliative care patients. *Cochrane Database Syst Rev* 2009; **2:** CD006271.

185 Lorenz KA, Lynn J, Dy SM, et al. Evidence for improving palliative care at the end of life: a systematic review. *Ann Intern Med* 2008; **148:** 147–59.

186 Ly KL, Chidgey J, Addington-Hall J, Hotopf M. Depression in palliative care: a systematic review. Part 2. Treatment. *Palliat Med* 2002; **16:** 279–84.

187 Jackson KC, Lipman AG. Drug therapy for delirium in terminally ill patients. *Cochrane Database Syst Rev* 2004; **2:** CD004770.

188 Grassi L, Caraceni A, Mitchell AJ, et al. Management of delirium in palliative care: a review. *Curr Psychiatry Rep* 2015; **17:** 550.

189 Prommer E. Role of haloperidol in palliative medicine: an update. *Am J Hosp Palliat Care* 2012; **29:** 295–301.

190 Walsh D, Davis M, Ripamonti C, Bruera E, Davies A, Molassiotis A. 2016 Updated MASCC/ESMO consensus recommendations: management of nausea and vomiting in advanced cancer. *Support Care Cancer* 2017; **25:** 333–40.

191 Basu RR Basu Banerjee PM, Sweeny EG. Frugal innovation: core competencies to address global sustainability. *J Manag Glob Sustain* 2013; **2:** 63–82.

192 Zeschky M, Widenmayer B, Gassmann O. Frugal Innovation in emerging markets. *Res-Tech Manag* 2011; **54:** 38–45.

193 Farage MA, Miller KW, Berardesca E, Maibach HI. Incontinence in the aged: contact dermatitis and other cutaneous consequences. *Contact Dermatitis* 2007; **57:** 211–17.

194 Sørbye LW, Finne-Soveri H, Ljunggren G, et al. Urinary incontinence and use of pads—clinical features and need for help in home care at 11 sites in Europe. *Scand J Caring Sci* 2009; **23:** 33–44.

195 de Freytas-Tamura K. In Kenya, selling or importing plastic bags will cost you $19,000—or jail. *The New York Times*, Aug 28, 2017.

196 The Delicious Day. First country to ban plastic bag: Rwanda! April 2, 2012. http://www.thedeliciousday.com/environment/rwanda-plastic-bag-ban/ (accessed Jan 19, 2017).

197 Coleman-Lochner L, Hymowitz C. The adult diaper market is about to take off. Feb 11, 2016. http://www.bloomberg.com/news/articles/2016-02-11/the-adult-diaper-market-is-about-to-take-off (accessed Aug 29, 2017).

198 UNDP. Japan's Unicharm Corp to bring affordable hygiene products to 36 million low-income women. Oct 11, 2012. http://www.undp.org/content/undp/en/home/presscenter/pressreleases/2012/10/11/japan-s-unicharm-corp-to-bring-affordable-hygiene-products-to-36-million-low-income-women-.html2016 (accessed Aug 29, 2017).

199 Menstrual Cup Reviews. Menstrual cups and pads in Africa. July 5, 2016. http://menstrualcupreviews.net/menstrual-cups-and-pads-in-africa/ (accessed March 27, 2017).

200 Ruhe N. New design of women's underwear could disrupt feminine hygiene market. *MedCity News*, June 2, 2015.

201 Caló E, Khutoryanskiy VV. Biomedical applications of hydrogels: a review of patents and commercial products. *Eur Polym J* 2015; **65:** 252–67.

202 Al-Samarrai NR, Uman GC, Al-Samarrai T, Alessi CA. Introducing a new incontinence management system for nursing home residents. *J Am Med Dir Assoc* 2007; **8:** 253–61.

203 Trowbridge MM, Wang B, Gutshall D, Rodenberg CA, Farage MA. A randomized, controlled trial comparing skin health effects and comfort of two adult incontinence protective underwear. *Skin Res Technology* 2016; published online Aug 8. DOI:10.1111/srt.12320.

204 Fader M, Cottenden A, Getliffe K, et al. Absorbent products for urinary/faecal incontinence: a comparative evaluation of key product designs. *Health Technol Assess* 2008; **12:** iii–iv, ix–185.

205 Pogorelc D. A diaper sensor and data is one startup's solution to helping manage incontinence in seniors. Aug 30, 2012. http://medcitynews.com/2012/08/a-diaper-sensor-and-data-is-one-startups-solution-to-helping-manage-incontinence-in-seniors/?rf=1 (accessed Aug 29, 2017).

206 Shore SL. Use of an economical wheelchair in India and Peru: Impact on health and function. *Med Sci Monit* 2008; **14:** PH71–79.

207 Jefferds AN, Beyene NM, Upadhyay N, et al. Current state of mobility technology provision in less-resourced countries. *Phys Med Rehabil Clin N Am* 2010; **21:** 221–42.

208 Kaundal V, Singh R. Low cost robotic wheel chair for disabled people in developing countries. Conference on advances in communication and control systems. Amsterdam: Atlantis Press, 2013: 277–583.

209 Authier EL, Pearlman J, Allegretti AL, Rice I, Cooper RA. A sports wheelchair for low-income countries. *Disabil Rehabil* 2007; **29:** 963–67.

210 Zipfel E, Cooper RA, Pearlman J, Cooper R, McCartney M. New design and development of a manual wheelchair for India. *Disabil Rehabil* 2007; **29:** 949–62.

211 Pearlman J, Cooper RA, Krizack M, et al. Lower-limb prostheses and wheelchairs in low-income countries. *IEEE Eng Med Biol Mag* 2008; **27:** 12–22.

212 Pearlman J, Cooper R, Chhabra H, Jefferds A. Design, development and testing of a low-cost electric powered wheelchair for India. *Disabil Rehabil Assist Technol* 2009; **4:** 42–57.

213 Romero B, Camacho A, Varona J, Delgado C, Velazquez R. A low-cost electric power wheelchair with manual and vision-based control systems. *AFRICON* 2009: 1–6.

214 Krug E, Kelley E, Loring B, Bouësseau M-C, Varghese C. Planning and implementing palliative care services: a guide for programme managers. Geneva: World Health Organization, 2016.

215 Jamison RN, Sheehan KA, Scanlan E, Matthews M, Ross EL. Beliefs and attitudes about opioid prescribing and chronic pain management: survey of primary care providers. *J Opioid Manag* 2014; **10:** 375–82.

216 Jamison RN, Scanlan E, Matthews ML, Jurcik DC, Ross EL. Attitudes of primary care practitioners in managing chronic pain patients prescribed opioids for pain: a prospective longitudinal controlled trial. *Pain Med* 2016; **17:** 99–113.

217 Kwon JH. Overcoming barriers in cancer pain management. *J Clin Oncol* 2014; **32:** 1727–33.

218 Esquibel AY, Borkan J. Doctors and patients in pain: conflict and collaboration in opioid prescription in primary care. *Pain* 2014; **155:** 2575–82.

219 Amoatey Odonkor C, Addison W, Smith S, Osei-Bonsu E, Tang T, Erdek M. Connecting the dots: a comparative global multi-institutional study of prohibitive factors affecting cancer pain management. *Pain Med* 2016; **18:** 363–73.

220 Laursen L. Palliative care: the other opioid issue. *Nature* 2016; **535:** S16–17.

221 Krakauer EL, Cham NTP, Khue LN. Vietnam's palliative care initiative: successes and challenges in the first five years. *J Pain Symptom Manage* 2010; **40:** 27–30.

222 Aldridge MD, Hasselaar J, Garralda E. Education, implementation, and policy barriers to greater integration of palliative care: a literature review. *Palliat Med* 2016; **30:** 224–39.

223 Centeno C, Ballesteros M, Carrasco JM, Arantzamendi M. Does palliative care education matter to medical students? The experience of attending an undergraduate course in palliative care. *BMJ Support Palliat Care* 2016; **6:** 128–34.

224 Harrington CB, Hansen JA, Moskowitz M, Todd BL, Feuerstein M. It's not over when it's over: long-term symptoms in cancer survivors—a systematic review. *Int J Psychiatry Med* 2010; **40:** 163–81.

225 Nardelli S, Pentassuglio I, Pasquale C, et al. Depression, anxiety and alexithymia symptoms are major determinants of health related quality of life (HRQoL) in cirrhotic patients. *Metab Brain Dis* 2013; **28:** 239–43.

226 de Cerqueira AC, Semionato de Andrade P, Godoy Barreiros JM, Teixeira AL, Nardi AE. Psychiatric disorders in patients with multiple sclerosis. *Compr Psychiatry* 2015; **63:** 10–14.

227 Vincent HK, Horodyski M, Vincent KR, Brisbane ST, Sadasivan KK. Psychological distress after orthopedic trauma: prevalence in patients and implications for rehabilitation. *PM R* 2015; **7:** 978–89.

228 Riedel O, Klotsche J, Spottke A, et al. Frequency of dementia, depression, and other neuropsychiatric symptoms in 1,449 outpatients with Parkinson's disease. *J Neurol* 2010; **257:** 1073–82.

229 Elsner F, Schmidt J, Rajagopal MR, Radbruch L, Pestinger M. Psychosocial and spiritual problems of terminally ill patients in Kerala, India. *Future Oncol* 2012; **8:** 1183–91.

230 Frenk J, Chen L, Bhutta ZA, et al. Health professionals for a new century: transforming education to strengthen health systems in an interdependent world. *Lancet* 2010; **376:** 1923–58.

231 Maru D, Farmer P. Human rights and health systems development: confronting the politics of exclusion and the economics of inequality. *Health Hum Rights* 2012; **14:** 1–8.

232 Franke MF, Kaigamba F, Socci AR, et al. Improved retention associated with community-based accompaniment for antiretroviral therapy delivery in rural Rwanda. *Clin Infect Dis* 2013; **56:** 1319–26.

233 Lewin SA, Dick J, Pond P, et al. Lay health workers in primary and community health care. *Cochrane Database Syst Rev* 2005; **1:** CD004015.

234 Sallnow L, Kumar S, Numpeli M. Home-based palliative care in Kerala, India: the neighbourhood network in palliative care. *Progress Palliat Care* 2013; **18:** 14–17.

235 Jack BA, Kirton JA, Birakurataki J, Merriman A. The personal value of being a palliative care Community Volunteer Worker in Uganda: a qualitative study. *Palliat Med* 2012; **26:** 753–59.

236 Syed ST, Gerber BS, Sharp LK. Traveling towards disease: transportation barriers to health care access. *J Community Health* 2013; **38:** 976–93.

237 Carrillo JE, Carrillo VA, Perez HR, Salas-Lopez D, Natale-Pereira A, Byron AT. Defining and targeting health care access barriers. *J Health Care Poor Underserved* 2011; **22:** 562–75.

238 Watkins D, Jamison D, Mills A, et al. Universal health coverage and essential packages of care. In: Jamison D, Horton S, Jha P, Laxminarayan R, Nugent R, Mock C, Danforth K, eds. Disease Control Priorities. New York, NY: The World Bank, 2017.

239 Knaul FM, Bhadelia A, Atun R, Frenk J. Achieving effective universal health coverage and diagonal approaches to care for chronic illnesses. *Health Aff (Millwood)* 2015; **34:** 1514–22.

240 World Bank. A model from Mexico for the world. Nov 19, 2014. http://www.worldbank.org/en/news/feature/2014/11/19/un-modelo-de-mexico-para-el-mundo (accessed Feb 8, 2017).

241 Bhalla K, Bump J, Frost L, et al. Influencing multisectoral action for health, phase one, volume 2. Case studies on multisectoral action. New York, NY: Food and Agricultural Organization of the United Nations, 2016.

242 Glassman A, Todd J, Gaarder M. Latin America: cash transfers to support better household decisions. London: Center for Global Development, 2015.

243 Gaceta Parlamentaria. Número 4506-VI. Initiative issued by General Law that establishes the right to receive financial support for the terminally ill (in Spanish). 2016. http://gaceta.diputados.gob.mx (accessed Aug 31, 2017).

244 World Bank. Poverty headcount ratio at $1·90 a day (2011 PPP) (% of population). 2014. http://data.worldbank.org/indicator/SI.POV.DDAY (accessed July 2, 2017).

245 Dussel V, Bona K, Heath JA, Hilden JM, Weeks JC, Wolfe J. Unmeasured costs of a child's death: perceived financial burden, work disruptions, and economic coping strategies used by American and Australian families who lost children to cancer. *J Clin Oncol* 2011; **29:** 1007–13.

246 McManus R, Schafer C. Final arrangements: examining debt and distress. *Mortality* 2014; **19:** 379–97.

247 Foster L, Woodthorpe K. What cost the price of a good send off? The challenges for British state funeral policy. *J Poverty Soc Justice* 2013; **21:** 77–89.

248 The Lancet. Who cares for the carer? *Lancet* 2017; **389:** 763.

249 International Children's Palliative Care Network. Here are some frequently asked questions and answers about children's palliative care. http://www.icpcn.org/faq/ (accessed July 2, 2017).

250 Shulman LN, Wagner CM, Barr R, et al. Proposing essential medicines to treat cancer: methodologies, processes, and outcomes. *J Clin Oncol* 2016; **34:** 69–75.

251 Lutz ST, Jones J, Chow E. Role of radiation therapy in palliative care of the patient with cancer. *J Clin Oncol* 2014; **32:** 2913–19.

252 Miner TJ. Palliative surgery for advanced cancer: lessons learned in patient selection and outcome assessment. *Am J Clin Oncol* 2005; **28:** 411–14.

253 Meara JG, Leather AJ, Hagander L, et al. Global surgery 2030: evidence and solutions for achieving health, welfare, and economic development. *Lancet* 2015; **386:** 569–624.

254 Atun R, Jaffray DA, Barton MB, et al. Expanding global access to radiotherapy. *Lancet Oncol* 2015; **16:** 1153–86.

255 WHO. WHO list of priority medical devices for cancer management. WHO medical device technical series. Geneva: World Health Organization, 2017.

256 Naik G. Unlikely way to cut hospital costs: comfort the dying. Palliative-care unit offers painkillers and support; fewer tests, treatments. *Wall St J (East Ed)* 2004: A1, A12.

257 Rabow MW, Dibble SL, Pantilat SZ, McPhee SJ. The comprehensive care team: a controlled trial of outpatient palliative medicine consultation. *Arch Intern Med* 2004; **164:** 83–91.

258 Tamir O, Singer Y, Shvartzman P. Taking care of terminally-ill patients at home—the economic perspective revisited. *Palliat Med* 2007; **21:** 537–41.

259 Morrison RS, Penrod JD, Cassel JB, et al. Cost savings associated with US hospital palliative care consultation programs. *Arch Intern Med* 2008; **168:** 1783–90.

260 Hongoro C, Dinat N. A cost analysis of a hospital-based palliative care outreach program: implications for expanding public sector palliative care in South Africa. *J Pain Symptom Manage* 2011; **41:** 1015–24.

261 International Drug Price Indicator Guide. 2014. http://erc.msh.org/dmpguide/ (accessed Feb 8, 2017).

262 De Lima L, Pastrana T, Radbruch L, Wenk R. Cross-sectional pilot study to monitor the availability, dispensed prices, and affordability of opioids around the globe. *J Pain Symptom Manage* 2014; **48:** 649–59.

263 Shaw PS, Wang H, Kress D, Hovig D. Donor and domestic financing of primary health care in low income countries. *Health Systems Reform* 2015; **1:** 72–88.

264 McIntyre D, Meheus F. Fiscal space for domestic funding of health and other social services. London: Chatham House (The Royal Institute of International Affairs), 2014.

265 Verguet S, Murphy S, Anderson B, Johansson KA, Glass R, Rheingans R. Public finance of rotavirus vaccination in India and Ethiopia: an extended cost-effectiveness analysis. *Vaccine* 2013; **31:** 4902–10.

266 Verguet S, Laxminarayan R, Jamison DT. Universal public finance of tuberculosis treatment in India: an extended cost-effectiveness analysis. *Health Econ* 2015; **24:** 318–32.

267 Official Journal of the Federation. Agreement ACDO.AS3.HCT.280115 / 7.P.DF and its Annexes, issued by the H. Technical Council, held on January 28 of this year, relative to the approval of the Unit Costs by Level of Medical Care for the exercise 2015. Feb 11, 2015. http://www.dof.gob.mx/nota_detalle.php?codigo=5381602&fecha=11/02/2015 (accessed Sept 18, 2017).

268 Coneval. Medicion de la pobreza, Estados Unidos Mexicanos. 2014. http://www.coneval.org.mx/Medicion/MP/PublishingImages/Pobreza_2014.jpg (accessed March 27, 2017).

269 Maurer MA. New online tool for exploring global opioid consumption data. *J Pain Palliat Care Pharmacother* 2017; **31:** 45–51.

270 Duthey B, Scholten W. Adequacy of opioid analgesic consumption at country, global, and regional levels in 2010, its relationship with development level, and changes compared with 2006. *J Pain Symptom Manage* 2014; **47:** 283–97.

271 Merriman A, Harding R. Pain control in the African context: the Ugandan introduction of affordable morphine to relieve suffering at the end of life. *Philos Ethics Humanit Med* 2010; **5:** 10.

272 Rhee JY, Garralda E, Torrado C, et al. Palliative care in Africa: a scoping review from 2005–16. *Lancet Oncol* 2017; **18:** e522–31.

273 Treat the Pain, American Cancer Society. Federal Ministry of Health and American Cancer Society launch pain free hospital initiative. http://pressroom.cancer.org/painfreehospitalinitiativeprogram (accessed Feb 13, 2017).

274 O'Brien M, Mwangi-Powell F, Adewole IF, et al. Improving access to analgesic drugs for patients with cancer in sub-Saharan Africa. *Lancet Oncol* 2013; **14:** e176–82.

275 Nishtar S. The NCDs Cooperative: a call to action. *Lancet* 2017; published online Sept 18. http://doi.org/10.1016/S0140-6736(17)32481-9.

276 Eyssallenne AP. How far do you go? Intensive care in a resource-poor setting. *N Engl J Med* 2012; **367:** 8–9.

277 Donabedian A. An introduction to quality assurance in health care. Oxford: Oxford University Press, 2002.

278 Economist Intelligence Unit. The 2015 quality of death index. Ranking palliative care across the world. 2015. London: The Economist Group, 2015.

279 Lynch T, Connor S, Clark D. Mapping levels of palliative care development: a global update. *J Pain Symptom Manage* 2013; **45:** 1094–106.

280 Sharkey L, Loring B, Cowan M, Riley L, Krakauer EL. National palliative care capacities around the world: results from the World Health Organization Noncommunicable Disease Country Capacity Survey. *Palliat Med* 2017; published online June 1. DOI:10.1177/0269216317716060.

281 Shakarishvili G, Atun R, Berman P, Hsiao W, Burgess C, Lansang JA. Converging health systems frameworks: towards a concepts-to-actions roadmap for health systems strengthening in low and middle income countries. http://www.ghgj.org/Shakarishvili_Converging%20Health%20Systems%20Frameworks.pdf (accessed Sept 26, 2017).

282 Aramis Da Costa Foster G. Advances in the national palliative care program in Panama (in Spanish). Meeting of Work Group on Effective Models of Palliative Care Services in Latin America and the Caribbean. Dec 8–9, 2016. http://www.paho.org/hq/index.php?option=com_content&view=article&id=12824%3Awork-group-on-effective-models-of-palliative-care-services-in-latin-america-and-the-caribbean&catid=1872%3Acancer&Itemid=40602&lang=en (accessed Sept 26, 2017).

283 Diario Official. Ley 1733 de 2014. Sept 8, 2014. http://jacevedo.imprenta.gov.co/tempDownloads/49D2681506357782644.pdf. Colombia. Sept 8, 2014. http://jacevedo.imprenta.gov.co/tempDownloads/49D2681506357782644.pdf (accessed Sept 18, 2017).

284 Stjernsward J, Foley KM, Ferris FD. The public health strategy for palliative care. *J Pain Symptom Manage* 2007; **33:** 486–93.

285 Pastrana T, Torres-Vigil I, De Lima L. Palliative care development in Latin America: an analysis using macro indicators. *Palliat Med* 2014; **28:** 1231–38.

286 Covarrubias-Gómez A. Las clínicas del dolor en México. *Revista Mexicana de Anestesiología* 2008; **31:** 66–70.

287 Dantés OG, Sesma S, Becerril VM, Knaul FM, Arreola H, Frenk J. Sistema de salud de México. *Salud Pública de México* 2011; **53:** s220–32.

288 Frenk J, Knaul FM, Dantés OG. Closing the relevance-excellence gap in health research: the use of evidence in the Mexican health reform. Global policy making and health research leadership. London: Pro-Brook Publishing, 2004: 48–53.

289 Rajagopal MR. The current status of palliative care in India. 2015. http://www.cancercontrol.info/cc2015/the-current-status-of-palliative-care-in-india/ (accessed Aug 29, 2017).

290 Miranda P. Seguro Popular amplió cobertura para sus afiliados. *El Universal*, Dec 22, 2016.

291 Khosla D, Patel FD, Sharma SC. Palliative care in India: current progress and future needs. *Indian J Palliat Care* 2012; **18:** 149.

292 Harding R, Higginson IJ, Gwyther L. HIV-related pain in low- and middle-income countries with reference to sub-Saharan Africa. In: Merlin JS, Selwyn PA, Treisman GJ, Giovanniello AG, eds. Chronic pain and HIV: a practical approach. Edison, NJ: John Wiley & Sons, 2016: 150–56.

293 Gwyther L. Palliative medicine education at the University of Cape Town. *eHospice*, June 27, 2013. http://www.ehospice.com/southafrica/Default/tabid/10689/ArticleId/5478 (accessed Aug 29, 2017).

294 Murray CJ, Frenk J. A framework for assessing the performance of health systems. *Bull World Health Organ* 2000; **78:** 717–31.

295 Krakauer EL, Ngoc NT, Green K, Van Kham L, Khue LN. Vietnam: integrating palliative care into HIV/AIDS and cancer care. *J Pain Symptom Manage* 2007; **33:** 578–83.

296 Ministerio de Salud de Chile. Norma general técnica no. 32. Programa nacional de alivio del dolor y cuidados paliativos. Santiago: Ministerio de Salud de Chile, 2009.

297 Paudel BD, Ryan KM, Brown MS, et al. Opioid availability and palliative care in Nepal: influence of an international pain policy fellowship. *J Pain Symptom Manage* 2015; **49:** 110–16.

298 COFEPRIS. Sistema de Recetarios Electrónicos para Medicamentos de Fracción I. Secretaría de Salud, Mexico, 2015. http://www.cofepris.gob.mx/Paginas/Recetarios%20y%20libros%20electrónicos.aspx (accesed Sept 9, 2017).

299 COFEPRIS. Solicitud de Permiso para Utilizar Recetarios Especiales con Códigos de Barras para Prescribir Estupefacientes. Sistema Electrónico de Trámites Sanitario. Secretaría de Salud, Mexico, 2015. http://www.cofepris.gob.mx/Documents/RecetariosLibros/ManualRecetarios.pdf (accesed Sept 9, 2017).

300 Consejo General de Salubridad. Lanzamiento de Recetarios y Libros Electrónicos. Gobierno de Mexico. México, 2015. http://www.csg.gob.mx/descargas/pdfs/galeria/nota_recetario_libros_electronicos.pdf (accesed Sept 9, 2017).

301 Pastrana T, Torres-Vigil I, De Lima L. Palliative care development in Latin America: an analysis using macro indicators. *Palliat Med* 2014; **28:** 1231–38.

302 WHO Unit Name MND. Evaluation of six WHO palliative care demonstration sites. Geneva: World Health Organization, 2017.

303 WHO. Cancer control: knowledge into action. WHO guide for effective programmes; module 5. Geneva: World Health Organization, 2007.

304 Rajagopal MR, Joranson DE. India: opioid availability. An update. *J Pain Symptom Manage* 2007; **33:** 615–22.

305 Kumar SK. Kerala, India: a regional community-based palliative care model. *J Pain Symptom Manage* 2007; **33:** 623–27.

306 Directorate General of Health Services Ministry of Health & Family Welfare. Proposal of strategies for palliative care in India. November, 2012. http://palliumindia.org/cms/wp-content/uploads/2014/01/National-Palliative-Care-Strategy-Nov_2012.pdf (accessed Aug 29, 2017).

307 Aguilera X, Castillo-Laborde C, Ferrari MN, Delgado I, Ibanez C. Monitoring and evaluating progress towards universal health coverage in Chile. *PLoS Med* 2014; **11:** e1001676.

308 Atun R. Directive for the change to the Social Security Institute health implementation directive (in Turkish). Dec 24, 2014. http://www.resmigazete.gov.tr/eskiler/2014/12/20141224-17.htm (accessed March 29, 2017).

309 Jha P, Ranson K, Bobadilla JL. Measuring the burden of disease and the cost-effectiveness of health interventions: a case study in Guinea. New York, NY: World Bank Publications, 1996.

310 Bobadilla JL, Cowley P. Designing and implementing packages of essential health services. *J Int Dev* 1995; **7:** 543–54.

311 Bobadilla JL, Cowley P, Musgrove P, Saxenian H. Design, content and financing of an essential national package of health services. *Bull World Health Organ* 1994; **72:** 653–62.

312 Ramsey SD, Bansal A, Fedorenko CR, et al. Financial Insolvency as a Risk Factor for Early Mortality Among Patients With Cancer. *J Clin Oncol* 2016; **34:** 980–86.

313 Postier A, Chrastek J, Nugent S, Osenga K, Friedrichsdorf SJ. Exposure to home-based pediatric palliative and hospice care and its impact on hospital and emergency care charges at a single institution. *J Palliat Med* 2014; **17:** 183–88.

314 Jung H-m, Kim J, Heo DS, Baek SK. Health economics of a palliative care unit for terminal cancer patients: a retrospective cohort study. *Support Care Cancer* 2012; **20:** 29–37.

315 May P, Normand C, Morrison RS. Economic impact of hospital inpatient palliative care consultation: review of current evidence and directions for future research. *J Palliat Med* 2014; **17:** 1054–63.

316 Smith TJ, Cassel JB. Cost and non-clinical outcomes of palliative care. *J Pain Symptom Manage* 2009; **38:** 32–44.

317 Rabow MW. What are the arguments that show outpatient palliative care is beneficial to medical systems? In: Goldstein NE, Morrison RS, eds. Evidenced-based practice of palliative care. Amsterdam: Elsevier, 2012.

318 Hanson LC, Usher B, Spragens L, Bernard S. Clinical and economic impact of palliative care consultation. *J Pain Symptom Manage* 2008; **35:** 340–46.

319 Albanese TH, Radwany SM, Mason H, Gayomali C, Dieter K. Assessing the financial impact of an inpatient acute palliative care unit in a tertiary care teaching hospital. *J Palliat Med* 2013; **16:** 289–94.

320 Chalkidou K, Marquez P, Dhillon PK, et al. Evidence-informed frameworks for cost-effective cancer care and prevention in low, middle, and high-income countries. *Lancet Oncol* 2014; **15:** e119–31.

321 Davis MP, Temel JS, Balboni T, Glare P. A review of the trials which examine early integration of outpatient and home palliative care for patients with serious illnesses. *Ann Palliat Med* 2015; **4:** 99–121.

322 Mosoiu D, Dumitrescu M, Connor SR. Developing a costing framework for palliative care services. *J Pain Symptom Manage* 2014; **48:** 719–29.

323 Knaul FM, Bhadelia A, Bashshur R, et al. Innovative delivery of cancer care and control in low-resource scenarios. In: Knaul FM, Gralow JR, Atun R, Bhadelia A, eds. Close the cancer divide: an equity imperative. Cambridge, MA: Harvard University Press, 2012.

324 Howitt P, Darzi A, Yang GZ, et al. Technologies for global health. *Lancet* 2012; **380:** 507–35.

325 Elsner M. Literature review: bereavement counselling and the role of religion. 2016. http://www.as.miami.edu/media/college-of-arts-and-sciences/content-assets/mia/docs/General%20Literature%20Search.pdf (accessed Sept 26, 2017).

326 Bausewein C, Daveson BA, Currow DC, et al. EAPC White Paper on outcome measurement in palliative care: Improving practice, attaining outcomes and delivering quality services. Recommendations from the European Association for Palliative Care (EAPC) Task Force on Outcome Measurement. *Palliat Med* 2016; **30:** 6–22.

327 Bosnjak S, Maurer MA, Ryan KM, Leon MX, Madiye G. Improving the availability and accessibility of opioids for the treatment of pain: the International Pain Policy Fellowship. *Support Care Cancer* 2011; **19:** 1239–47.

328 Arreola-Ornelas H. Presentation of country case-studies. Meeting of the Work Group on Effective Models of Palliative Care Services in Latin America and the Caribbean. Dec 8–9, 2016. http://www.paho.org/hq/index.php?option=com_content&view=article&id=12824%3Awork-group-on-effective-models-of-palliative-care-services-in-latin-america-and-the-caribbean&catid=1872%3Acancer&Itemid=40602&lang=en (accessed Sept 26, 2017).

329 Powell RA, Harding R, Namisango E, et al. Palliative care research in Africa: consensus building for a prioritized agenda. *J Pain Symptom Manage* 2014; **47:** 315–24.

330 Szlezak NA, Bloom BR, Jamison DT, et al. The global health system: actors, norms, and expectations in transition. *PLoS Med* 2010; **7:** e1000183.

331 Jamison DT, Frenk J, Knaul F. International collective action in health: objectives, functions, and rationale. *Lancet* 1998; **351:** 514–17.

332 Frenk J, Moon S. Governance challenges in global health. *N Engl J Med* 2013; **368:** 936–42.

333 The Organization of American States. Inter-American convention on protecting the human rights of older persons (A-70). http://www.oas.org/en/sla/dil/inter_american_treaties_a-70_human_rights_older_persons.asp (accessed Sept 11, 2017).

334 Human Rights Watch. Pain tears me apart. Feb 3, 2016. https://www.hrw.org/report/2016/02/04/pain-tears-me-apart/challenges-and-progress-ensuring-right-palliative-care-morocco (accessed Feb 13, 2017).

335 UNGASS. Special sessions of the United Nations General Assembly on the world drug problem. 2016. http://www.unodc.org/ungass2016/ (accessed March 29, 2017).

336 Wirtz VJ, Hogerzeil HV, Gray AL, et al. Essential medicines for universal health coverage. *Lancet* 2017; **389:** 403–76.

337 Sleeman KE, Gomes B, Higginson IJ. Research into end-of-life cancer care—investment is needed. *Lancet* 2012; **379:** 519.

338 Field D, Clark D, Corner J, Davis C. Researching palliative care. New York, NY: Open University Press, 2001.

339 Jubb AM. Palliative care research: trading ethics for an evidence base. *J Med Ethics* 2002; **28:** 342–46.

340 Casarett D. Ethical issues in palliative care research. In: Cherny N, Fallon M, Kaasa S, Portenoy RK, Cuirrow DC, eds. Oxford textbook of palliative medicine, 5th edn. Oxford: Oxford University Press, 2015.

341 Casarett DJ, Knebel A, Helmers K. Ethical challenges of palliative care research. *J Pain Symptom Manage* 2003; **25:** S3–5.

342 WHO. Global action plan for the prevention and control of NCDs 2013–2020. 2013. http://apps.who.int/iris/bitstream/10665/94384/1/9789241506236_eng.pdf?ua=1 (accessed Aug 29, 2017).

343 United Nations Office on Drugs and Crime. Promoting adequate availability of internationally controlled narcotic drugs and psychotropic substances for medical and scientific purposes while preventing their diversion and abuse. https://digitallibrary.un.org/record/734928?ln=en (accessed Oct 3, 2017).

344 International Narcotics Control Board. Report of the International Narcotics Control Board on the availability of internationally controlled drugs: ensuring adequate access for medical and scientific purposes. New York, NY: United Nations, 2010.

345 International Narcotics Control Board. The Report of the International Narcotics Control Board for 2006. New York, NY: United Nations, 2007.

346 Connor SR, Sisimayi C. Assessment of the need for palliative care for children. Three country report: South Africa, Kenya and Zimbabwe. New York, NY, and Assagay, South Africa: UNICEF and International Children's Palliative Care Network, 2013.

347 Jackson K. Update on implementation of the 2014 World Health Assembly resolution on palliative care—report released. eHospice, May 23, 2016. https://www.ehospice.com/ArticleView/tabid/10686/ArticleId/19399/language/en-GB/Default.aspx (accessed March 21, 2017).

348 The Worldwide Hospice Palliative Care Alliance. Civil society report: update on implementation of the 2014 WHA resolution on palliative care. London: The Worldwide Hospice Palliative Care Alliance, 2016.

Special Article

Mapping Levels of Palliative Care Development: A Global Update

Thomas Lynch, PhD, Stephen Connor, PhD, and David Clark, PhD
International Observatory on End of Life Care (T.L.), Lancaster University, Lancaster; Worldwide Palliative Care Alliance (S.C.), London; and School of Interdisciplinary Studies (D.C.), University of Glasgow, Glasgow, United Kingdom

Abstract

Our purpose is to categorize palliative care development, country by country, throughout the world, showing changes over time. We adopt a multi-method approach. Development is categorized using a six-part typology: Group 1 (no known hospice-palliative care activity) and Group 2 (capacity-building activity) are the same as developed during a previous study (2006), but Groups 3 and 4 have been subdivided to produce two additional levels of categorization: 3a) Isolated palliative care provision, 3b) Generalized palliative care provision, 4a) Countries where hospice-palliative care services are at a stage of preliminary integration into mainstream service provision, and 4b) Countries where hospice-palliative care services are at a stage of advanced integration into mainstream service provision. In 2011, 136 of the world's 234 countries (58%) had at least one palliative care service—an increase of 21 (+9%) from 2006, with the most significant gains having been made in Africa. Advanced integration of palliative care has been achieved in only 20 countries (8.5%). Total countries in each category are as follows: Group 1, 75 (32%); Group 2, 23 (10%); Group 3a, 74 (31.6%); Group 3b, 17 (7.3%); Group 4a, 25 (10.7%); and Group 4b, 20 (8.5%). Ratio of services to population among Group 4a/4b countries ranges from 1:34,000 (in Austria) to 1:8.5 million (in China); among Group 3a/3b countries, from 1:1000 (in Niue) to 1:90 million (in Pakistan). Although more than half of the world's countries have a palliative care service, many countries still have no provision, and major increases are needed before palliative care is generally accessible worldwide. J Pain Symptom Manage 2013;45:1094–1106.

Key Words

Palliative care, hospice, map, global development

Introduction

Interest in the comparative analysis of palliative care development has been evident, particularly in Europe, since the late 1990s.[1] The first study to review palliative care using comparative methods was reported in 2000, and it focused on seven countries in Western Europe.[2] In 2003, a study commissioned by the Open Society Foundation International Palliative Care Initiative (IPCI) successfully mapped the development of palliative care across 28 former communist countries in Eastern Europe and Central Asia.[3] As a direct

Address correspondence to: Thomas Lynch, PhD, International Observatory on End of Life Care, Institute for Health Research, Alexandra Square, Lancaster University, Lancaster LA1 4YT, United Kingdom. E-mail: t.lynch@lancaster.ac.uk

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result of the IPCI project, the International Observatory on End of Life Care (IOELC) was established by D. C. at Lancaster University in the U.K. The IOELC used comparative methods in its reviews of hospice-palliative care activity and devised a common template to present its research-based reports on countries; this resulted in major reviews of palliative care development in Africa (26 countries), the Middle East (six countries), and South East Asia (three countries) as well as a study covering the whole of India. The European Association for Palliative Care (EAPC) Task Force on the Development of Palliative Care in Europe began in 2003 under the leadership of Professor Carlos Centeno, and has substantially contributed to the agenda of documenting the progress of palliative care across countries and regions.[4] Jaspers and Schindler[5] reviewed hospice and palliative care provision in Germany compared with those in ten other European countries, and Gronemeyer et al.[6] undertook a comparative review of palliative care provision in 16 countries across Eastern and Western Europe.

Emerging from this series of studies was an ambitious attempt in 2006 to measure and classify the development of palliative care in every country in the world. The IOELC built on a basic description that had been produced earlier by the Hospice Information Service but attempted to build more depth into the analysis by developing a four-part typology depicting the levels of hospice-palliative care development across the globe: no known hospice-palliative care activity (Group 1 countries); capacity building activity (Group 2 countries); localized hospice-palliative care provision (Group 3 countries); and countries where hospice-palliative care services were reaching a measure of integration with the mainstream health care system (Group 4 countries). By presenting a "world map" of hospice-palliative care development, the study sought to contribute to the debate about the growth and recognition of palliative care services and, in particular, whether or not the four-part typology reflected sequential levels of palliative care development.[7] This mapping project was commissioned by the Worldwide Palliative Care Alliance, with funding from Help the Hospices in the U.K., and the National Hospice and Palliative Care Organization in the U.S.

Since 2006, there have been further comparative studies on palliative care development. For example, in 2008, the work of the EAPC Task Force on the Development of Palliative Care in Europe was extended in a collaborative study that specifically focused on the 27 member states of the European Union.[8] This study was important in moving beyond a descriptive comparison of the data to sketch out the beginnings of a more detailed method for ranking the 27 countries by the level of their palliative care development. A study commissioned by the Lien Foundation in Singapore and carried out by the Economist Intelligence Unit was published in 2010. This too attempted a ranking of palliative care development, this time in 40 countries of the world, and with a more complex set of indicators.[9] In 2011, a report from Human Rights Watch also documented the state of pain and palliative care services in 40 countries.[10]

Methods

Although the 2006 study has been heavily cited in the literature and adopted as a tool for international palliative care advocacy, it became clear that the rankings might benefit from refinement and the method of categorization also could be made more robust. To update the original findings and also address the definitional and methodological concerns, the 2006 mapping exercise was repeated in 2011, with some new criteria in the ranking. Within the typology, changes have been made in the criteria for the level of palliative care development in Groups 3 and 4, and these have been subdivided to produce two additional levels of categorization (Groups 3a, 3b, 4a, and 4b).

Location and Extraction of Relevant Data

Data on palliative care development were initially collected from the following sources: published articles in peer reviewed and professional journals, books and monographs, palliative care directories, palliative care and related websites, data provided by the EAPC Task Force for the Development of Palliative Care in Europe, IOELC reviews and databases, as well as gray literature and conference presentations (Fig. 1). We explored questions of palliative care coverage, public awareness, education

and training, opioid availability, and reimbursement. We also focused on service types and settings, the impact of palliative care on policy, links with academic institutions, and the relationship between palliative care services and other mainstream service providers. Critical points included whether there was evidence of government support, the implementation of strategic plans, published research, and palliative care elements in medical as well as nursing curricula and accredited courses.

In-country "key experts" in palliative care were particularly important sources of data for the study. Palliative care "champions" with extensive knowledge of both national and international development were identified in a variety of ways: within the sources cited above, from their participation in the previous study in 2006, from information provided by 66 national palliative care associations, and from international palliative care sources (International Association for Hospice and Palliative Care, Help the Hospices, and Worldwide Palliative Care Alliance). In countries where a champion was identified, they were requested to 1) provide information on the number and different types of palliative care services in their country, and 2) indicate which category within the new typology most accurately reflected the current status of palliative care in their country. Eighty-five palliative care champions were identified, and they provided information about the status of palliative care in their respective countries. Where no palliative care champion could be identified, regional palliative care associations (e.g., Asia Pacific Hospice Palliative Care Network and African Palliative Care Association) acted as "proxies" and provided valuable information on behalf of a further 77 countries.

In countries where a palliative care champion could not be identified and where the information from a regional palliative care association was not available, data collected from the initial sources identified above (particularly from the previous study in 2006) were revisited to determine to which category the country in question should be allocated; knowledge gained by the authors while working on other hospice and palliative care-related projects (e.g., work undertaken with the Open Society Foundation IPCI) also was used to achieve this objective. In total, the status of palliative care development in 72 countries was calculated in this manner. In cases where categorization of a particular country was unclear (approximately 14 in total), the authors undertook a consultative process with each other. The initial categorization was made by T. L. based on the available evidence; S. C. and D. C. then conferred on cases that were particularly difficult to categorize, using their extensive and detailed knowledge of many of the countries in the study, in some cases based on visits made to those countries in recent years. The country in question was then allocated to one of the following categories based on its *perceived* level of palliative care development:

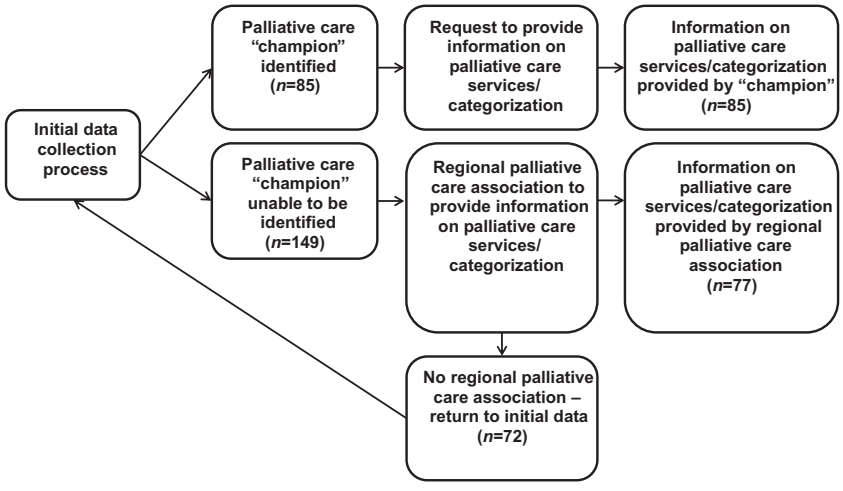

Fig. 1. Method of locating and extracting relevant data.

Group 1 Countries: No Known Hospice-Palliative Care Activity. Although we have been unable to identify any palliative care activity in this group of countries, we acknowledge there may be instances where, despite our best efforts, current work has been unrecognized.

Group 2 Countries: Capacity Building Activity. In this group of countries, there is evidence of wide-ranging initiatives designed to create the organizational, workforce, and policy capacity for the development of hospice-palliative care services although no service has yet been established. The developmental activities include attendance at, or organization of, key conferences; personnel undertaking external training in palliative care; lobbying of policy makers and Ministries of Health; and incipient service development.

Group 3 Countries

Group 3a: Isolated Palliative Care Provision. This group of countries is characterized by the development of palliative care activism that is patchy in scope and not well-supported; source of funding that is often heavily donor-dependent; limited availability of morphine; and a small number of hospice-palliative care services that are often home-based in nature and limited in relation to the size of the population.

Group 3b: Generalized Palliative Care Provision. This group of countries is characterized by the development of palliative care activism in several locations with the growth of local support in those areas; multiple sources of funding; the availability of morphine; several hospice-palliative care services from a community of providers who are independent of the health care system; and the provision of some training and education initiatives by the hospice organizations.

Group 4 Countries

Group 4a: Countries Where Hospice-Palliative Care Services Are at a Stage of Preliminary Integration into Mainstream Service Provision. This group of countries is characterized by the development of a critical mass of palliative care activism in a number of locations; a variety of palliative care providers and types of services; awareness of palliative care on the part of health professionals and local communities; the availability of morphine and some other strong pain-relieving drugs; limited impact of palliative care on policy; the provision of a substantial number of training and education initiatives by a range of organizations; and existence of (or at least an interest in the concept of) a national palliative care association.

Group 4b: Countries Where Hospice-Palliative Care Services Are at a Stage of Advanced Integration into Mainstream Service Provision. This group of countries is characterized by the development of a critical mass of palliative care activism in a wide range of locations; comprehensive provision of all types of palliative care by multiple service providers; broad awareness of palliative care on the part of health professionals, local communities, and society in general; unrestricted availability of morphine and most strong pain-relieving drugs; substantial impact of palliative care on policy, in particular on public health policy; the development of recognized education centers; academic links forged with universities; and the existence of a national palliative care association.

Finally, global hospice-palliative care development was categorized using the revised typology, country by country, throughout the world; this development is depicted in a series of world and regional maps. The maps presented here make use of the United Nations (U.N.) list of 234 "countries or areas," which are grouped into 21 regions (such as Central America) and then allocated to eight "major areas" designated as "continents" (Sub-Saharan Africa; Middle East, North Africa, and Greater Arabia; North America; Central America and the Caribbean; South America; Asia; Europe; and Australia and Oceania). Significantly, the U.N. list includes small territories such as the Aland Islands, Isle of Man, and the Holy See (the Vatican). The size of these countries ranges from 17 million square kilometers (Russia), to 0.44 square kilometers (the Vatican). The most populated country is China, with around 1.35 billion people whereas the least populated is Pitcairn Island, with about 50 people.

Other Development Indicators

To gain a broader view of the development of a country, data also were collected regarding

human development. The U.N. Human Development Index[11] (HDI) measures a country's achievements in the three aspects of longevity, knowledge, and standard of living, which highlight the development in human rather than economic terms (The HDI was created to re-emphasize that people and their lives should be the ultimate criteria for assessing the development of a country, not economic growth). Figures relating to population size were taken from the World Health Organization website[12] (192 countries at that time) and supplemented by estimated figures from the World Fact Book[13] (42 countries), which are supplied by the U.S. Census Bureau and are based on statistics from population censuses and vital statistics registration systems.

Results

In 2006, 115 of the world's 234 countries (49%) had established one or more hospice-palliative care services; in 2011, 136 of the world's 234 countries (58%) had one or more hospice-palliative care services established—an increase of 21 countries (+9%). In 2006, 156 countries (67%) were actively engaged in either delivering a hospice-palliative care service or developing the framework within which such a service could be delivered; in 2011, there had been a slight increase in this number to 159 countries (68%)—an increase of 1%. Table 1 lists the countries in each of the six categories showing changes from 2006, and Fig. 2 displays these countries in a map of the world.

Palliative Care and Human Development

In most regions of the world, a strong association exists between palliative care and human development. Thirty (67%) of the 45 countries in Groups 4a/4b (preliminary/advanced palliative care integration) have a *very high* level of development as measured by the U.N. HDI, and five countries (11%) have a *high* level of human development. Only six countries (13%) in Groups 4a/4b have a *low* level of human development, yet this is a significant increase from the figure for 2006, which suggested that only one (3%) country from Group 4 was in the *low* development group. All six countries from Groups 4a/4b with *low* levels of human development are from Africa, suggesting that, in contrast to other regions of the world, the level of palliative care development in this particular area may not be concomitant with the overall levels of human development. In Group 1 (no known palliative care activity), only two (3%) of the 75 countries have a *very high* level of human development and seven (9%) countries have a *high* level of human development. By contrast, 20 (27%) countries in Group 1 have a *low* level of human development, and 33 (44%) countries in this group have no HDI at all (Table 2).

Ratio of Services to Population

Countries in Groups 4a/4b have multiple services; within this group, the ratio of services to population does not exceed 1:8.5 million (China). Countries in Groups 3a/3b frequently have a single service provision and a ratio of services to population that extends to 1:90 million (Pakistan) (Table 3).

Regional Variations

A regional analysis of palliative care development produces striking variations in the levels achieved by neighboring countries and in each country's ratio of services to population. In North America, both Canada and the U.S. are in Group 4b, whereas no palliative care activity could be identified in Greenland. In Latin America, Chile, Costa Rica, Puerto Rico, and Uruguay are in Group 4a, whereas several other countries in the region provide either a single or a relatively small number of palliative care services (Table 4); several Caribbean Islands also offer a single palliative care service.

In Western Europe, only small countries, such as Andorra, Monaco, and the Holy See (Vatican), or U.K. regions such as the Falkland Islands are in Groups 1 or 2; other U.K. regions such as Guernsey and the Isle of Man are in Group 3a. Greece is also in Group 3a, with Cyprus, Malta, and Portugal in 3b; the remainder of Western European countries are in Groups 4a/4b (Table 5).

In Central and Eastern Europe/Commonwealth of Independent States (CEE/CIS), countries such as Turkmenistan and Uzbekistan have no known palliative care capacity; this is in stark contrast to countries such as

Table 1
Distribution of Countries and Global Population by Category (2011), $N = 234$

Group 1 No known activity $n = 75$ (32%)	Afghanistan, American Samoa, Andorra, Anguilla, Antigua and Barbuda, Aruba, Benin, Bhutan, Burkina Faso, Burundi, Cape Verdi, Central African Republic, Chad, Comoros, Cook Islands, Djibouti, Equatorial Guinea, Eritrea, Falkland Islands, Faroe Islands, French Guiana, French Polynesia, Gabon, Greenland, Grenada, Guam, Guinea, Guinea-Bissau, Kiribati, Korea (DPR), Laos, Liberia, Libya, Liechtenstein, Maldives, Marshall Islands, Martinique, Mauritania, Mayotte, Micronesia, Monaco, Montserrat, Nauru, The Netherlands Antilles, New Caledonia, Niger, Norfolk Island, Northern Mariana Islands, Palau, Pitcairn, Saint Helena, Saint Kits and Nevis, Saint Pierre and Miquelon, Saint Vincent and the Grenadines, Samoa, San Marino, Sao Tome and Principe, Senegal, Solomon Islands, Somalia, Svalbard, Syria, Timor-Leste, Togo, Tokelau, Tonga, Turkmenistan, Turks and Caicos Islands, Tuvalu, US Virgin Islands, Uzbekistan (− from category 2), Vanuatu, Wallis and Fortuna, Western Sahara, Yemen.
Group 2 Capacity building $n = 23$ (10%)	Aland Islands (− from category 3), Algeria, Azerbaijan (− from category 3), Bolivia, British Virgin Islands, Democratic Republic of Congo, Dominica, Fiji, Haiti, Holy See (Vatican), Honduras (− from category 3), Madagascar, Mauritius, Montenegro (+ from category 1), Nicaragua, Oman, Palestinian Authority, Papua New Guinea, Qatar, Reunion, Seychelles, Suriname, Tajikistan, The Bahamas.
Group 3a Isolated provision $n = 74$ (31.6%)	Angola (+ from category 1), Armenia, Bahrain (+ from category 2), Bangladesh, Barbados, Belize (+ from category 2), Bermuda, Botswana, Brazil, Brunei (+ from category 2), Bulgaria, Cambodia, Cameroon, Cayman Islands, Colombia, Congo, Cuba, Dominican Republic, Ecuador, Egypt, El Salvador, Estonia, Ethiopia (+ from category 2), Ghana (+ from category 2), Gibraltar, Greece, Guadeloupe, Guatemala, Guernsey, Guyana, Indonesia, Iran (+ from category 2), Iraq, Isle of Man, Jamaica, Jersey, Kazakhstan, Korea (South), Kuwait (+ from category 2), Kyrgyzstan, Latvia, Lebanon (+ from category 2), Lesotho (+ from category 2), Macedonia, Mali (+ from category 1), Mexico, Moldova, Morocco, Mozambique (+ from category 2), Myanmar, Namibia (+ from category 2), Nigeria, Niue (+ from category 1), Pakistan, Panama, Paraguay (+ from category 2), Peru, Philippines, Reunion, Russia, Rwanda (+ from category 2), Saint Lucia (+ from category 2), Saudi Arabia, Sierra Leone, Sri Lanka, Sudan (+ from category 2), Gambia, Thailand, Trinidad and Tobago, Tunisia, Ukraine, United Arab Emirates, Venezuela, Vietnam.
Group 3b Generalized provision $n = 17$ (7.3%)	Albania, Argentina (− from category 4), Belarus, Bosnia and Herzegovina, Cote D'ivoire (+ from category 2), Croatia, Cyprus, Czech Republic, Georgia, India, Jordan, Lithuania, Malta, Nepal, Portugal, Swaziland, Turkey (+ from category 2).
Group 4a Preliminary integration $n = 25$ (10.7%)	Chile, China (+ from category 3), Costa Rica, Denmark, Finland, Hungary, Israel, Kenya, Luxembourg (+ from category 3), Macau (+ from category 3), Malawi (+ from category 3), Malaysia, Mongolia, The Netherlands, New Zealand, Puerto Rico (+ from category 2), Serbia (+ from category 3), Slovakia (+ from category 3), Slovenia, South Africa, Spain, Tanzania (+ from category 3), Uruguay (+ from category 3), Zambia (+ from category 3), Zimbabwe (+ from category 3).
Group 4b Advanced integration $n = 20$ (8.5%)	Australia, Austria, Belgium, Canada, France, Germany, Hong Kong, Iceland, Ireland, Italy, Japan, Norway, Poland, Romania, Singapore, Sweden, Switzerland, Uganda, U.K., U.S.

Poland and Romania that are in Group 4b (Table 6).

In Western Asia, only Israel is in Group 4a (preliminary integration); a number of other countries in the region offer limited palliative care provision and are in Groups 3a/3b (Table 7).

In Africa, no palliative care service could be identified in 28 of the continent's countries; this contrasts with the categorization of Uganda in Group 4b and several other countries in the region that are categorized in Group 4a (Table 8). A good example of progress in Africa is provided by Cote' D'Ivoire, which moved from Group 2 in 2006 to Group 3b in 2011. There are now 26 hospice-palliative care services in Cote D'Ivoire (22 government hospitals/health facilities, three mission hospitals, and one private hospital). The African Palliative Care Association (APCA) and other partners have worked in Cote D'Ivoire to develop palliative care; a palliative care infrastructure has been developed and palliative care services provided. Despite remaining in the same group as 2006 (Group 3), Nigeria is reported as "making progress" in the development of palliative care. The seven palliative care services in Nigeria include two private hospices and five government-owned, tertiary health, hospital palliative care services. There are five formally qualified physicians and four formally qualified nurse specialists practicing palliative care in the country. "Much progress" is reported from Kenya, where 44 services

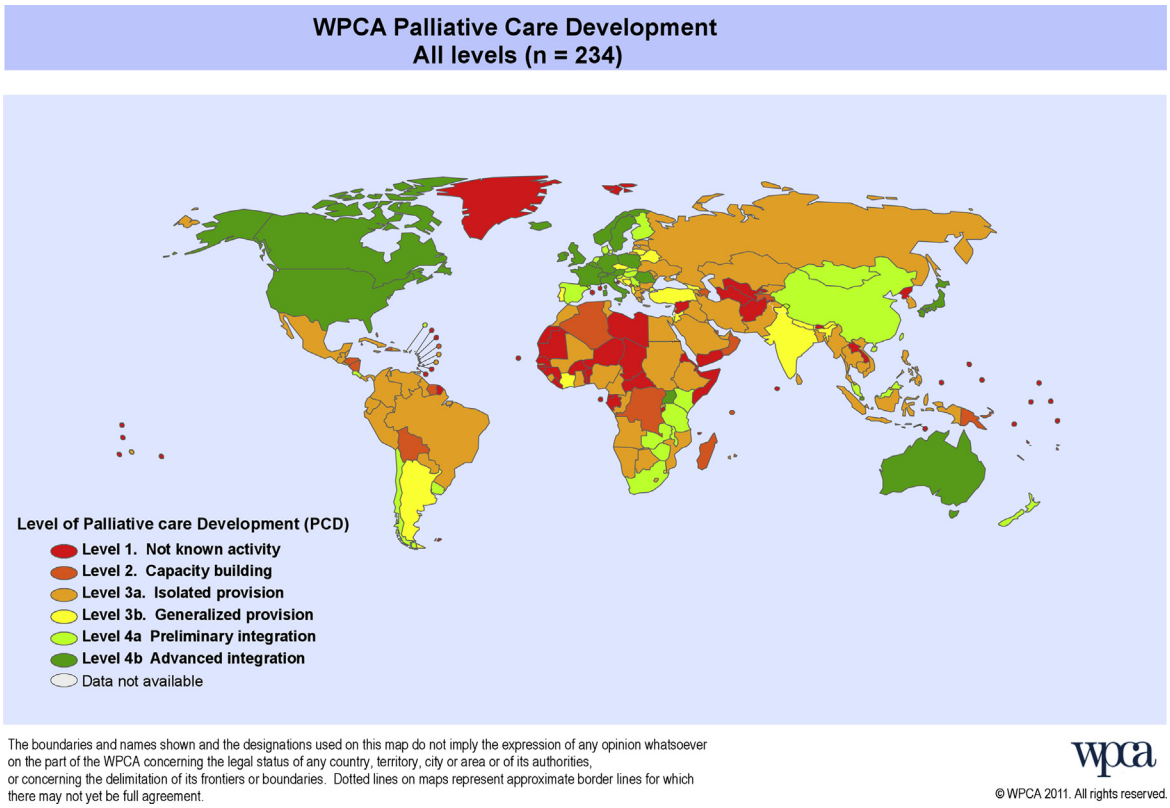

Fig. 2. WPCA Palliative Care Development All Levels ($n = 234$). The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the WPCA concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. WPCA = Worldwide Palliative Care Alliance.

currently exist, including the recent integration of palliative care into ten government hospitals. There are several medical institutions delivering educational courses on palliative care, and the discipline is gradually being integrated into the curricula of medical, nursing, pharmacy, and dental schools across the country (e.g., the Nursing Council of Kenya). In addition, the National Cancer Control Strategy contains explicit reference to palliative care. Some African countries with only a single palliative care service are beginning to develop education and training initiatives; for example, the organization "Pallia Familli," which provides home-based palliative care in Kinshasa, has organized several palliative care training and education initiatives in conjunction with the Congolese Federation for Palliative Care. Even countries such as Senegal that remain categorized as having "no known palliative care capacity," are reported as displaying "some aspects of capacity-building." The impact of

Table 2
Human Development and Levels of Palliative Care Development, by Group

Group	Total Countries (N)	Very High, n (%)	High, n (%)	Medium, n (%)	Low, n (%)	No HDI, n (%)
1	75	2 (3)	7 (9)	13 (17)	20 (27)	33 (44)
2	23	1 (4)	7 (30)	8 (35)	4 (17)	3 (13)
3a	74	8 (11)	23 (31)	20 (27)	14 (19)	9 (12)
3b	17	7 (41)	5 (29)	3 (18)	2 (12)	0 (0)
4a	25	12 (48)	4 (16)	3 (12)	5 (20)	1 (4)
4b	20	18 (90)	1 (5)	0 (0)	1 (5)	0 (0)
Total	234	48 (100)	47 (100)	47 (100)	46 (100)	46 (100)

HDI = Human Development Index.

Table 3
Ratio of Palliative Care Services to Population

Group	Lowest	Services (*n*)	Ratio 1:000s	Highest	Services (*n*)	Ratio 1:000s
3a	Niue	1	1	Pakistan	2	90,404
3b	Lithuania	65	51	Turkey	14	5344
4a	The Netherlands	295	56	China	159	8511
4b	Austria	247	34	Uganda	34	962

unpredictable and volatile political situations on the development of palliative care in the region is evident in countries such as Zimbabwe, which has moved erratically between different groups since the initial process of categorization commenced.

In the Asia Pacific and Oceania regions, Australia, Hong Kong, and Singapore have achieved advanced palliative care integration (Group 4b), although many other countries in the region offer either a limited number of palliative care services or no services at all (Table 9). It should also be noted that approximately one-fifth of the world's population is found in China, and one-sixth in India.

Table 4
Indicative Ratio of Hospice-Palliative Care Services to Populations Within the Americas and the Caribbean

Country	Services (*n*)	Population	Ratio 1:000s
Bermuda	2	68,679	34
United States	6568	314,659,000	48
Cayman Islands	1	51,384	51
Canada	500	33,573,000	67
Costa Rica	42	4,579,000	109
Puerto Rico	35	3,989,133	114
Uruguay	24	3,361,000	140
St. Lucia	1	172,000	172
Barbados	1	256,000	256
Belize	1	307,000	307
Argentina	90	40,276,000	448
Guadeloupe	1	452,772	453
Guyana	1	762,000	762
Chile	21	16,970,000	808
Trinidad and Tobago	1	1,339,000	1339
Jamaica	2	2,719,000	1359
Guatemala	5	14,027,000	2805
Panama	1	3,454,000	3454
Cuba	3	11,204,000	3734
Ecuador	3	13,625,000	4541
El Salvador	1	6,163,000	6163
Paraguay	1	6,349,000	6349
Colombia	7	45,660,000	6522
Mexico	14	109,610,000	7829
Brazil	22	193,734,000	8800
Peru	3	29,165,000	9722
Dominican Republic	1	10,090,000	10,090
Venezuela	1	28,583,000	28,583

In 2006, there was no known palliative care activity in 78 of the world's 234 countries (33%); by 2011, this figure had decreased by three countries (−1%) to 75. The number of countries that were demonstrating capacity-building potential in 2006 was 41 (18%); by 2011, this number had decreased by a total of 18 countries to 23 (−8%). Countries with localized hospice-palliative care provision in 2006 totaled 80 (34%); in 2011, the combined number of countries in Groups 3a and 3b totaled 91 (39%)—an increase of 11 countries (+5%). Finally, the division of Group 4 indicates that although 25 countries (10.7%) are now approaching integration with mainstream health service providers, only 20 countries (8.5%) have actually achieved this. In 2011, the total number of countries in Group 4 was 45 (19%), as opposed to 35 (15%) in 2006—an increase of 10 countries (+4%) (Tables 10–12).

Table 5
Indicative Ratio of Hospice-Palliative Care Services to Populations in Western Europe

Country	Services (*n*)	Population	Ratio 1:000s
Gibraltar	2	28,956	14
Isle of Man	4	84,655	21
Guernsey	2	65,068	33
Austria	247	8,364,000	34
Iceland	8	323,000	40
Jersey	2	94,161	47
UK	1295	61,565,000	48
Germany	1690	82,167,000	49
Belgium	210	10,647,000	51
Norway	88	4,812,000	55
The Netherlands	295	16,592,000	56
Sweden	140	9,249,000	66
Ireland	57	4,515,000	79
Spain	502	44,904,000	89
Switzerland	81	7,568,000	93
Luxembourg	5	486,000	97
Denmark	45	5,470,000	122
France	471	62,343,000	132
Italy	376	59,870,000	159
Cyprus	5	871,000	174
Malta	2	409,000	204
Finland	26	5,326,000	205
Greece	32	11,161,000	349
Portugal	20	10,707,000	535
Turkey	14	74,816,000	5,344

Table 6
Indicative Ratio of Hospice-Palliative Care Services to Populations in Central and Eastern Europe/Commonwealth of Independent States

Country	Services (*n*)	Population	Ratio 1:000s
Lithuania	65	3,287,000	51
Poland	432	38,074,000	88
Hungary	78	9,993,000	128
Latvia	16	2,249,000	141
Bulgaria	41	7,545,000	184
Slovenia	8	2,020,000	252
Republic of Macedonia	7	2,042,000	292
Mongolia	7	2,671,000	382
Romania	55	21,275,000	387
Belarus	21	9,634,000	459
Czech Rep	22	10,369,000	471
Slovakia	11	5,406,000	491
Albania	6	3,155,000	526
Georgia	7	4,260,000	608
Moldova	5	3,604,000	721
Russia	165	140,874,000	854
Croatia	5	4,416,000	883
BosniaHerzegovina	4	3,767,000	942
Ukraine	38	45,708,000	1202
Estonia	1	1,340,000	1340
Kyrgyzstan	3	5,482,000	1827
Serbia	5	9,850,000	1970
Kazakhstan	6	15,637,000	2606
Armenia	1	3,083,000	3083

Discussion

Since 2008, there has been an increase in the number of countries of the world that have established one or more hospice-palliative care services (+9%), although only a slight increase has occurred in the total number of countries actively engaged in either delivering a hospice-palliative care service or developing the framework within which such a service can be delivered (+1%). Since 2006, a total of 21 countries (9%) have moved from Groups 1/2 (no known activity/capacity building) into Groups 3/4 (some form of palliative care provision). It should be acknowledged, however, that, within the context of these results, there are many instances in

Table 7
Indicative Ratio of Hospice-Palliative Care Services to Populations in Western Asian Countries

Country	Services (*n*)	Population	Ratio 1:000s
Israel	17	7,170,000	422
Bahrain	1	791,000	791
Kuwait	2	2,985,000	1492
Jordan	4	6,316,000	1579
Lebanon	2	4,224,000	2112
UA Emirates	2	4,599,000	2299
Saudi Arabia	3	25,721,000	8573
Iraq	1	30,747,000	30,747
Iran	1	74,196,000	74,196

Table 8
Indicative Ratio of Hospice-Palliative Care Services to Populations in Africa

Country	Services (*n*)	Population	Ratio 1:000s
Swaziland	5	1,185,000	237
South Africa	210	50,110,000	239
Botswana	4	1,950,000	490
Namibia	3	2,171,000	724
Reunion Island	1	800,000	800
Cote d'Ivoire	26	21,075,000	811
Kenya	44	39,802,000	905
Uganda	34	32,710,000	962
Zimbabwe	13	12,523,000	963
Zambia	13	12,935,000	995
Malawi	9	15,263,000	1696
Gambia	1	1,705,000	1705
Lesotho	1	2,067,000	2067
Tanzania	20	43,739,000	2187
Congo	1	3,683,000	3683
Ghana	5	23,837,000	4767
Rwanda	2	9,998,000	4999
Tunisia	2	10,272,000	5136
Sierra Leone	1	5,696,000	5696
Cameroon	3	19,522,000	6507
Mali	1	13,010,000	13,010
Angola	1	18,498,000	18,498
Sudan	2	42,272,000	21,136
Nigeria	7	154,729,000	22,104
Mozambique	1	22,894,000	22,894
Egypt	3	82,999,000	27,666
Morocco	1	31,993,000	31,993
Ethiopia	2	82,825,000	41,412

Table 9
Indicative Ratio of Hospice-Palliative Care Services to Populations in the Asia Pacific and Oceania Regions

Country	Services (*n*)	Population	Ratio 1:000s
Niue	1	1000	1
Australia	320	21,293,000	67
New Zealand	48	4,266,000	89
Japan	686	127,156,000	185
Singapore	23	4,737,000	206
Korea (South)	97	23,906,000	246
Malaysia	110	27,468,000	250
Macau	2	573,003	286
Brunei	1	400,000	400
Hong Kong	15	7,122,508	475
Philippines	108	91,983,000	852
India	284	1,198,003,000	4218
Nepal	6	29,331,000	4889
Thailand	13	67,764,000	5212
Cambodia	2	14,805,000	7402
China	159	1,353,311,000	8511
Myanmar	3	50,020,000	16,673
Sri Lanka	1	20,238,000	20,238
Indonesia	10	229,965,000	22,996
Bangladesh	7	162,221,000	23,174
Vietnam	3	88,069,000	29,356
Pakistan	2	180,808,000	90,404

Table 10
Gross Changes in the Number of Countries in Each Category

Group	2006	2011	Change (*n*)	Change (%)
1	78 (33%)	75 (32%)	−3	−1
2	41 (18%)	23 (10%)	−18	−8
3	80 (34%)	91 (39%)	+11	+5
4	35 (15%)	45 (19%)	+10	+4

which palliative care remains inaccessible to the majority of a country's population.

A regional analysis of palliative care development between 2006 and 2011 indicates that the most notable regions involved in the change from Groups 1/2 (no known activity/capacity building) to Group 3a (isolated provision) are Africa (+9 countries), the Middle East (+5 countries), and the Americas/Caribbean (+3 countries). In the Middle East, a good example of progress is provided by Lebanon, which moved from Group 2 to Group 3a. In Africa, much progress has been initiated by the APCA, ably supported by funders such as the Open Society Foundation IPCI, among others. Angola moved from Group 1 to Group 3a because the APCA conducted an exploratory study there and initiated some palliative care contacts that resulted in a service being established. Ghana also moved from Group 1 to Group 3a because a national palliative care association was formed and several palliative care services have since been established. Ethiopia, Namibia, Rwanda, and Sudan all moved from Group 2 to Group 3a because a palliative care infrastructure had been developed and isolated palliative care services were provided, albeit at a low level. Cote d'Ivoire moved from Group 2 to Group 3b for the same reason, although the progress has been reported as "slightly greater" than in other countries of the region.

Progress from Group 3 to Group 4a again showed Africa as the most prominent region (+4 countries). Malawi, Tanzania, Zambia, and Zimbabwe changed category because of the work done by the APCA and other partners to develop and scale up palliative care in those countries; the APCA suggests that these countries have made "tremendous progress" in recent years and envisage them being recategorized to Group 4b (advanced integration) in the near future. Other African countries believed to be close to moving from Group 3 to Group 4 include Botswana, Cameroon, Morocco, and Nigeria. However, the impact of funding withdrawal by The Diana, Princess of Wales Memorial Fund from Africa in 2012 on the continued development of palliative care in the region is as yet unknown.

Progress is also reported in a number of CEE/CIS countries after prolonged support from international funders such as IPCI; for example, two countries moved from Group 3 to Group 4a. Slovakia was recategorized because several hospice beds are now available in hospitals and teaching hospitals, palliative care was being implemented in postgraduate education for physicians and undergraduate education for nurses, there was good availability of morphine, and a National Association of Palliative Care has been established. Serbia was recategorized as a result of the impact of its three-year National Strategy for Palliative Care Development, which would substantially increase the number of hospital/home-based palliative care teams and palliative care units

Table 11
Changes in Palliative Care Direction by Country 2006−2011

Group	Country (+/−)
1	Uzbekistan (− from category 2)
2	Montenegro (+ from category 1)/Aland Islands (− from category 3) Azerbaijan (− from category 3) Honduras (− from category 3)
3a	Angola (+ from category 1) Bahrain (+ from category 2) Belize (+ from category 2) Brunei (+ from category 2) Ethiopia (+ from category 2) Ghana (+ from category 2) Iran (+ from category 2) Kuwait (+ from category 2) Lebanon (+ from category 2) Lesotho (+ from category 2) Mali (+ from category 1) Mozambique (+ from category 2) Namibia (+ from category 2) Niue (+ from category 1) Paraguay (+ from category 2) Rwanda (+ from category 2) Saint Lucia (+ from category 2) Sudan (+ from category 2)
3b	Cote D'ivoire (+ from category 2), Turkey (+ from category 2), Argentina (− from category 4)
4a	China (+ from category 3) Luxembourg (+ from category 3) Macau (+ from category 3) Malawi (+ from category 3) Puerto Rico (+ from category 2) Serbia (+ from category 3) Slovakia (+ from category 3) Tanzania (+ from category 3) Uruguay (+ from category 3) Zambia (+ from category 3) Zimbabwe (+ from category 3)
4b	

Table 12
Changes in Palliative Care Direction by Region 2006–2011

Group	Region (+/−)
1	1 − CEE/CIS (− from group 2)
2	1 − CEE/CIS (+ from group 1)/1 − Europe (− from group 3) 1 − CEE/CIS (− from group 3) 1 − Americas/Caribbean (− from group 3)
3a	2 − Africa (+ from group 1) 7 − Africa (+ from group 2) 5 − Middle East (+ from group 2) 1 − Asia Pacific/Oceania (+ from group 1) 3 − Americas/Caribbean (+ from group 2)
3b	1 − Africa (+ from group 2) 1 − Europe (+ from group 2)/1 − Americas/Caribbean (− from group 4)
4a	2 − Asia Pacific/Oceania (+ from group 3) 1 − Europe (+ from group 3) 4 − Africa (+ from group 3) 1 − Americas/Caribbean (+ from group 2) 1 − Americas/Caribbean (+ from group 3) 2 − CEE/CIS (+ from group 3)
4b	

throughout the country, provide education and training initiatives for both health professionals and the families of patients, improve the availability of oral morphine and other forms of opioids, and ultimately result in the integration of palliative care into the Serbian health care system.

In Western Europe, the respondent from Luxembourg recategorized the country from Group 3 to Group 4a because of an increase in the number of hospice and palliative care units and the substantial development of palliative care education and training initiatives in the country; progress also has resulted from the introduction of a new law in 2009 regarding palliative care.

In the Americas/Caribbean, Uruguay was recategorized from Group 3 to Group 4a for several reasons: the number of hospice/palliative care services had increased, palliative care is now recognized in the National Health Program, a Diploma in Palliative Care had been introduced into the State University along with undergraduate palliative care programs in other universities, the national association was "developing rapidly," and the availability of opioids was described as "good." In contrast, although Argentina had made "major advances in palliative care over the last 20 years," there was still only localized hospice-palliative care provision; "great disparity" still existed in the palliative care that was provided, according to geography and differing levels of complexity; and areas still existed where palliative care was inaccessible. As a result, Argentina was recategorized from Group 4 to Group 3b.

Limitations

This study has certain limitations. As with the 2006 study, despite our best efforts in attempting to ascertain the status of palliative care development, there remained an absence of data for some countries. Also, the way in which services are counted proved problematic. Two systems operate in tandem. Services in five of the six continents tend to be counted by provider, irrespective of the number of services. In Europe, they are usually counted by type (e.g., home care, day care, inpatient units, or hospital teams). Although this allows a degree of comparability for services in the countries of Europe as well as within and across the other five continents, it also inhibits any comparable worldwide analysis. In addition, listing services by provider is by no means foolproof and could be a source of bias, as a country with few but large-scale provider organizations would show a lower ratio of services per capita compared with a country having several small providers. Differences in the way in which services are counted may be an artifact of the ways in which relevant studies have worked and the procedures of the "counting" organizations. We attempted to address these issues by listing the number of providers and services in the same category of data under the heading "services/providers," and attempting to glean clarification from key persons and local palliative care experts.

A major problem was that of standardization and definition in how services are characterized. Terms such as "hospice," "inpatient unit," or "mobile team" do not have a universal currency, and globally, there were difficulties in comparing "like with like." We also note the diversity of provision and the different "histories" of palliative care in specific jurisdictions and acknowledge the absence of agreed upon standards and quality measures globally. In addition, most data regarding palliative care development originate from

palliative care activists in each respective country, and this is acknowledged as a potential source of bias or inaccuracy.

Respondents were selected from data provided by a variety of sources, for example, the 2006 study, the EAPC Task Force for the Development of Palliative Care in Europe, IOELC reviews and databases, and information from work that we had undertaken on other related projects. Respondents in 2011 were asked to grade the level of palliative care development in their respective country. A limitation was that respondents often experienced difficulty in choosing between the divided Groups 3a or 3b and 4a or 4b. Some respondents suggested that their country "did not fit into any category," that their country was "somewhere on the border" between two categories, or that "strengths and limitations" existed within each subcategory. This situation was reflected in several countries in the CEE/CIS, where national palliative care associations had been formed but because of financial problems and political changes that resulted in inconsistent public health policy, the progress of palliative care remained "very slow." Respondents from the Americas/Caribbean also experienced some difficulty in determining between the newly divided categories, for example, the respondent from Panama stressed that her country was "not 3a at all, but cannot be categorized as 3b either." In the Asia Pacific and Oceania region, the respondent from Nepal experienced some difficulty in choosing between Groups 3a and 3b, whereas the respondent from Australia found differentiating between Groups 4a and 4b somewhat problematic. Several Western European countries (e.g., Austria, Denmark, The Netherlands, and Spain) also had difficulty in categorizing themselves in either Group 4a or Group 4b, suggesting that they often "scored differently for the different items" and, therefore, were "somewhere in between." In the African region, the respondent from South Africa proposed another subcategory within Group 4 to further refine the typology.

Conclusion

We have demonstrated that it is possible to map and measure levels of palliative care development, country by country, throughout the world. Our purpose is to facilitate cross-national comparative analysis and stimulate advocacy, policy making, and service development. To provide a more refined view of existing levels of palliative care development, the mapping exercise from 2006 was updated, new data were collected, and the typology was amended. The strong association between the categorization of palliative care development and human development provides an indication that the typology has an element of validity and reliability. Limitations to the study included the absence of data for some countries, problems in the counting and categorization of services, self-reporting by key persons who may have been subject to bias or inaccuracy, and respondents' difficulty in choosing between the newly divided categories.

In 2011, 136 of the world's 234 countries (58%) had one or more hospice-palliative care services established, an increase of 21 countries (+9%) from 2006. A regional analysis of palliative care development between 2006 and 2011 indicates that the most significant gains have been made in Africa. Although there are indications of interest in palliative care on the part of national governments and policy makers, advanced integration of palliative care with wider health services has been achieved in only 20 countries globally (8.5%). Despite increasing calls for palliative care to be recognized as a human right, there remains much to be done before palliative care is accessible equitably and globally.

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References

1. Clark D, Centeno C. Palliative care in Europe: an emerging approach to comparative analysis. Clin Med 2006;6:197–201.

2. Clark D, ten Have H, Janssens R. Common threads? Palliative care service developments in seven European countries. Palliat Med 2000;14: 479–490.

3. Clark D, Wright M. Transitions in end of life care. Hospice and related developments in Eastern Europe and Central Asia. Buckingham: Open University Press, 2003.

4. Centeno C, Clark D, Lynch T, et al. EAPC atlas of palliative care in Europe. Houston: IAHPC Press, 2007.

5. Jaspers B, Schindler J. Status of Palliative Care and Hospice Care in Germany compared to selected other States: Belgium, France, Great Britain, Netherlands, Norway, Austria, Poland, Sweden, Switzerland and Spain. [in German] In: Client: Study Commission of the Bundestag "Ethics and Law in Modern Medicine", 2004. Available from http://www.dgpalliativmedizin.de/pdf/Gutachten%20Jaspers-Schindler%20Endfassung%2050209.pdf. Accessed February 10, 2010.

6. Gronemeyer R, Fink M, Globish M, Schumann F. Project on hospice and palliative care in Europe: Helping people at the end of their lives. Berlin: Lit Verlag (English edition), 2005.

7. Wright M, Wood J, Lynch T, Clark D. Mapping levels of palliative care development: a global view. J Pain Symptom Manage 2008;35:469–485.

8. Martin-Moreno J, Harris M, Gorgojo L, et al. Palliative care in the European Union. European Parliament Economic and Scientific Policy Department, 2008. Available from http://www.europarl.europa.eu/activities/committees/studies/download.do?file=21421. Accessed January 11, 2011.

9. Economist Intelligence Unit. The quality of death: ranking end-of-life care across the world. A report commissioned by the Lien Foundation. 2010. Available from http://www.eiu.com/site_info.asp?info_name=qualityofdeath_lienfoundation&page=noads. Accessed July 2, 2012.

10. Human Rights Watch. Global state of pain treatment. Available from http://www.hrw.org/reports/2011/06/01/global-state-pain-treatment-0. Accessed November 16, 2011.

11. United Nations. International human development indicators. Available from http://hdr.undp.org/en/statistics/. Accessed November 24, 2011.

12. World Health Organization. Countries. Available from http://www.who.int/countries/en/. Accessed November 12, 2011.

13. Central Intelligence Agency. The world fact book. Available from https://www.cia.gov/library/publications/the-world-factbook. Accessed November 16, 2011.

Speaker: Jason Baker, M.D.
Date: March 8, 2021
Time: 5:00pm to 6:00pm
Title: Diabetes in the Developing World

Zoom info: https://weillcornell.zoom.us/j/92191714192 **Meeting ID**: 921 9171 4192 **Passcode**: 096379

Summary: Focus on the similarities and differences between the methods of diagnosis, treatment and prevention of diabetes in developed vs developing nations

Suggested Readings:

https://www.marjoriesfund.org/

https://ifl-usa.org/

https://idf.org/

Case Study:

Marjorie was 3 years old when she was diagnosed with type 1 diabetes in Uganda, and just 29 years old when she died, having succumbed to diabetes-related kidney failure. Unlike so many people with type 1 diabetes in Uganda and other parts of the developing world, Marjorie was one of the lucky ones.

Marjorie had been provided with enough insulin and glucose testing supplies to allow her to survive. Yet, Uganda is starved for resources that would have allowed Marjorie to keep her blood sugar levels under good enough control to avoid diabetic complications. While she awaited a kidney transplant – a treatment she never received – Marjorie relied on weekly dialysis treatments to stay alive. More often than not, Marjorie could not afford such treatments, and faced a preventable slow and painful death.

Throughout this painful time, Marjorie continued her efforts to educate both patients and healthcare providers on how to better manage type 1 diabetes, in hopes of preventing others from suffering her fate. Speaking at various medical conferences, Marjorie recounted her story, and fought to change a system, which had limited her own care because of a lack of resources. Marjorie's passed away, but others need not. Sadly there are many more Marjorie's in the world, and much work is needed to improve global diabetes care to allow everyone a change to thrive with diabetes.

Speaker: Kirk Deitsch, M.D.
Date: March 15, 2021
Time: 1:00pm – 2:00pm
Title: The Persistent Problem of Malaria in the Developing World

Zoom info: https://weillcornell.zoom.us/j/93864661904 **Meeting ID**: 938 6466 1904 **Passcode**: 652267

Summary: Focus on explaining the difficulties in reducing malaria transmission in places like sub-Saharan Africa, I have chosen to discuss several papers that are somewhat dated now, but that provide a possible explanation for the difficulties confronting the global health community. It is hoped that these papers will provide an opportunity to introduce and discuss the underlying topics of pathogenesis, host/parasite interactions, immunity to parasitic infections, the dynamics of vector-borne diseases and disease intervention. I will also provide a description of the basic molecular and cellular biology of these parasites.

Suggested Readings:

World Malaria Report 2019, World Health Organization

Trape, J.-F., & Rogier, C. (1996). Combating malaria morbidity and mortality by reducing transmission. *Parasitology Today*, *12*(6), 236–240. https://doi.org/10.1016/0169-4758(96)10015-6.

Case Study:

Aponte, J. J., Aide, P., Renom, M., Mandomando, I., Bassat, Q., Sacarlal, J., Manaca, M. N., Lafuente, S., Barbosa, A., Leach, A., Lievens, M., Vekemans, J., Sigauque, B., Dubois, M.-C., Demoitié, M.-A., Sillman, M., Savarese, B., McNeil, J. G., Macete, E., … Alonso, P. L. (2007). Safety of the RTS,S/AS02D candidate malaria vaccine in infants living in a highly endemic area of Mozambique: a double blind randomised controlled phase I/IIb trial. *The Lancet*, *370*(9598), 1543–1551. https://doi.org/10.1016/s0140-6736(07)61542-6.

mate choice by males? *Anim. Behav.* 40, 870–876
42 Burley, N. and Moran, N. (1979) **The significance of age and reproductive experience in the preferences of feral pigeons, *Columba livia*.** *Anim. Behav.* 27, 686–698
43 Owens, I.P.F. *et al.* (1994) **Sex differences, sex ratios and sex roles.** *Proc. R. Soc. London Ser. B* 258, 93–99
44 Combes, C. *et al.* (1987) **Les schistosomes.** *Pour la Science* 116, 80–88
45 Southgate, V.R. (1978) **On factors possibly restricting the distribution of *Schistosoma intercalatum* Fisher, 1934.** *Z. Parasitenkunde* 56, 183–193
46 Doumenge, J.P. *et al.* (1987) *Atlas of the Global Distribution of Schistosomiasis*, pp 41–49. CEGET-CNRS-WHO, Presses Universitaires de Bordeaux
47 De Clercq, D. *et al.* (1994) **Schistosomiasis in Dogon country, Mali: identification and prevalence of the species responsible for infection in the local community.** *Trans. R. Soc. Trop. Med. Hyg.* 88, 653–656
48 Woolhouse, M.E.J. (1991) **On the application of mathematical models of schistosome transmission dynamics. I. Natural transmission.** *Acta Trop.* 49, 241–270
49 May, R.M. and Woolhouse, M.E.J. (1993) **Biased sex ratios and parasite mating probabilities.** *Parasitology* 107, 287–295
50 Basch, P.F. (1990) *Schistosomes: Development, Reproduction, and Host Relations*, pp 152–153, Oxford University Press

Focus

Combating Malaria Morbidity and Mortality by Reducing Transmission

J-F. Trape and C. Rogier

Jean-François Trape and Christophe Rogier present epidemiological data and an analysis of the relationship between transmission, morbidity and mortality from malaria which suggest that any intervention aiming to reduce transmission will not, on a long-term basis, reduce the burden of malaria in the majority of epidemiological contexts observed in tropical Africa.

Malaria control in tropical Africa is principally based on the presumptive treatment of fever cases using anti-malarial drugs. In the past decade, the rapid spread of chloroquine resistance has stimulated the exploration of other control methods. Several studies have now shown that insecticide-impregnated bednets can reduce morbidity and mortality[1–4], and this method is generally considered to be an efficient means of combatting malaria. Aided by substantial funding from several international agencies, intervention programmes based on insecticide-impregnated bednets and curtains are either under way, or being planned, in many African countries. Other strategies aimed at reducing malaria transmission (such as the genetic manipulation of mosquito vectors[5] or the development of a transmission-blocking vaccine[6]) are also actively being explored.

Generally speaking, can we hope that interventions that aim to reduce malaria transmission can reduce, on a long-term basis, malaria morbidity and mortality whatever the epidemiological context? The answer lies within the general framework of relationships between the entomological inoculation rate, the incidence rate of malaria attacks and the frequency of severe forms of the disease. The average level of transmission varies considerably with the endemic area, from about 10^{-2} to 10^{3} infective bites per person per year. The degree of acquired immunity in individuals living all their lives in a given endemic area depends on transmission intensity and age. This has marked consequences for the absolute and relative importance of the burden of malaria at a given age[7], but also, probably, on the immediate and delayed evolution of the incidence of malaria morbidity and mortality after a reduction in transmission.

Jean-François Trape is at the Laboratoire de Paludologie, ORSTOM, BP 1386, Dakar, Sénégal. Christophe Rogier is at the Service d'Epidémiologie, Institut Pasteur, BP 220, Dakar, Sénégal. **Tel: +221 32 09 62, Fax: +221 32 16 75, e-mail: trape@belair.orstom.sn**

Transmission and mortality

The results of a large study covering the 500 000 inhabitants of Brazzaville (Congo) provide an initial indication that extreme differences in malaria transmission may be associated with only minor differences in malaria mortality rates[8–11]. This study is the only published comparison of malaria mortality rates between populations that were identical in their genetic and socio-cultural backgrounds and that benefited from equal opportunities for therapeutic care, while differing dramatically in their exposure to malaria. Depending on the district of Brazzaville, the entomological inoculation rate varied from more than 100 infective bites per person per year to less than one infective bite per person every three years, which represents almost the entire scale of malaria transmission rates observed in Africa[9]. Despite this, the incidence of severe malaria cases was essentially identical for all the districts, the only significant difference being the younger average age of severe malaria attacks in the high-transmission districts (Fig. 1). It is important to note that the parasite rate in schoolchildren varied from 3% to 81%, depending on the district of the town, and that two-thirds of the schoolchildren from the low-transmission districts had no detectable anti-*Plasmodium* antibodies at the age of seven, which clearly indicated that the circulation of children between different districts was limited and could not, therefore, explain the homogeneity of the risk of severe malaria[11]. Recently, other studies have compared severe malaria rates in areas with different entomological inoculation rates. Similar levels of severe malaria were observed in two areas of markedly different malaria transmission in East Africa: one in

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Tanzania, where transmission reached 300 infective bites per person per year; the other in Kenya, where transmission was about 10 infective bites per person per year[12]. As in the case of Brazzaville, the only important differences concerned the age distribution and the clinical patterns of the severe forms of the disease. Similarly, the incidence of severe malaria was not associated with transmission level at nine different sites in the Kilifi District in Kenya[13]. Finally, comparison of malaria mortality rates observed in 28 studies in Africa revealed that these estimated rates were generally of only limited variability and showed no relationship with the transmission level in the 11 studies where entomological data were available[14].

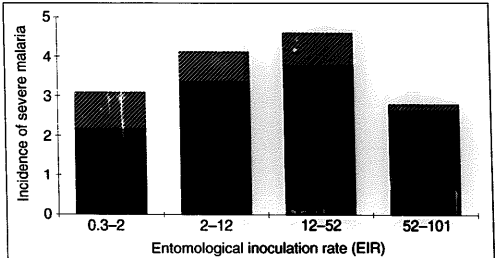

Fig. 1. Incidence of severe malaria as the number of cases per 10 000 people per year of observation in children aged 0–14 years living in Brazzaville (Congo) according to the entomological inoculation rate (EIR) in the district of residence. Cases occurring before age five are shown in black, and those occurring after age five are hatched.

Transmission and morbidity

If the level of transmission is not an important risk factor for malaria mortality in Africa, is the same true for malaria morbidity? In highly malaria-endemic areas, distinguishing malaria from other causes of fever poses difficult methodological problems because of the high frequency of asymptomatic infections and the lack of specificity of the signs and symptoms of the disease[15]. It is only recently that methods have been developed that permit a precise estimation of the incidence of malaria attacks in areas of moderate and high transmission[15–18]. By using these methods, we have compared the malaria morbidity of three Senegalese populations (from Dakar, Ndiop and Dielmo) exposed to approximately 1, 20 and 200 infective bites per person per year, respectively.

In Dakar, among individuals that have lived since birth in a district of the town where the transmission intensity was about one infective bite per person per year, the clinical incidence rate was identical to the parasitological incidence rate in children aged seven to 11 (Ref. 7) and was three times less than the parasitological incidence rate in adults (J-F. Trape and L. Konate, unpublished). These observations show that a high proportion of infections are symptomatic in individuals of all ages exposed since birth to about one infective bite each year. By the age of 60, these individuals have probably accumulated an average of 27 to 30 malaria attacks since birth, of which about half will have occurred in adulthood.

Since 1990 (Dielmo village) and 1993 (Ndiop village), we have uninterruptedly followed up the population of two villages in Senegal where malaria transmission intensity differs considerably[19,20]. In the first village, transmission is intense and perennial due to the presence of a stream which serves as a permanent breeding site for *Anopheles gambiae* s.l. and *An. funestus*. In the second village, transmission is about ten times lower, as the *Anopheles*-breeding sites only exist during the rainy season, which lasts about four months. For these two populations, identical and strict clinical surveillance programs have been carried out. These include a daily home visit to each person and the presence, night and day, of a medical team in the village to diagnose and treat any pathological episode. As shown in Fig. 2, these two populations differ markedly in terms of the pattern of age-dependent variations in malaria attack incidence rates. From these data, it can be estimated that, at the age of 60, the Dielmo inhabitants, who are exposed to about 200 infective bites per person per year, average a total of 43 attacks since birth, with only 23% of these arising during adulthood. For the Ndiop inhabitants, who are exposed to about 20 infective bites per person per year, one can estimate an average total of 62 malaria attacks by the age of 60 of which 41% occur during adulthood.

The comparison of these three Senegalese populations suggests that there is little difference in the total number of attacks over an entire lifetime in individuals residing in areas that vary by as much as a factor of 200 in transmission intensity. If this is correct, how do we explain the decrease in malaria morbidity and mortality following the implementation of bednets programmes which has been observed in most studies in Africa? Figure 3 compares the fluctuations of the entomological inoculation rate and the incidence density of malaria attacks in chidren in Dielmo. Clearly, these fluctuations are closely correlated, and a tenfold decrease or increase in malaria transmission is associated, in the following weeks, with a twofold decrease or increase in malaria morbidity. The decrease of malaria transmission in Dielmo each year at the end of the rainy season can be compared to the implementation of a bednet programme, as a tenfold reduction of transmission is close to the maximum reduction in malaria transmission that has been achieved by impregnated bednets in tropical Africa. In the short term, it is followed by a decrease of malaria morbidity. There are no existing data on the medium- and long-term efficacy of bednet trials. However, they can be predicted using data from areas where malaria transmission is lower because of natural conditions.

Relationships between transmission, morbidity and mortality

We have attempted to quantify the relationships between transmission, the incidence of clinical attacks

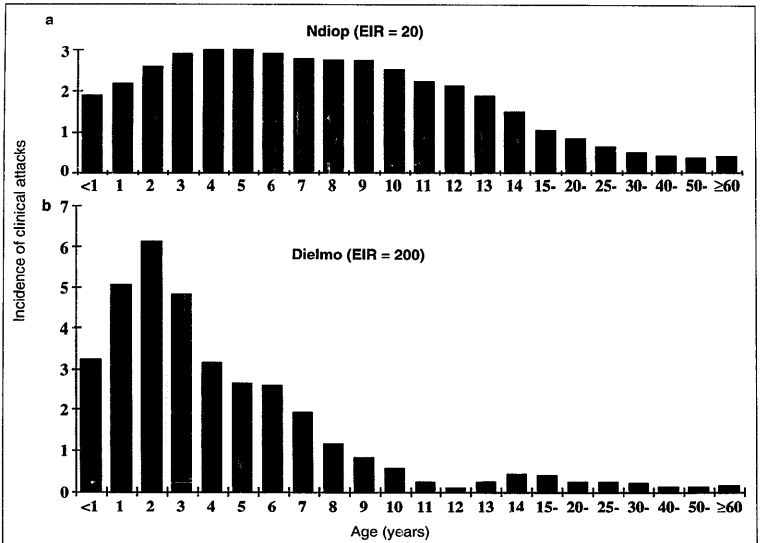

Fig. 2. Annual incidence of malaria attacks according to age in permanent residents of two Senegalese villages with markedly different *P. falciparum* transmission: Ndiop (EIR: 20 infective bites per person per year) (a), and Dielmo (EIR: 200 infective bites per person per year) (b).

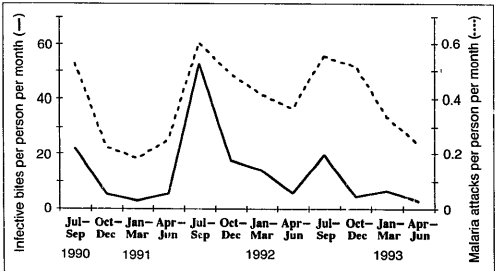

Fig. 3. Entomological inoculation rate and incidence of malaria attacks in children under seven years old in Dielmo (Senegal), 1990–1993.

and potential malaria mortality, on the basis of available data for six different levels of transmission representing, on a logarithmic scale, the complete range of epidemiological situations observed in endemic areas (Table 1). At least half of the bites from an *Anopheles* which carries sporozoites of *Plasmodium falciparum* in its salivary glands will give a blood infection followed by a clinical attack in non-immune subjects[21], and it is generally acknowledged that protective immunity, which is acquired by a person exposed to malaria, is lost after several years without exposure. Thus, for low levels of transmission, ie. 0.01 and 0.1 infective bites per person per year, the incidence of malaria attacks is probably directly proportional to the level of transmission, in adults as in children. For levels of transmission of 1, 10, 100 and 1000 infective bites per person per year, the data that we have collected in Senegal suggest that global malaria morbidity, which is always very high, varies at maximum by a factor of two to three according to the level of transmission (Table 1).

Quantifying the relationship between transmission levels and potential malaria mortality is a much more uncertain exercise as almost all of available data, even old data, deal with populations who had access, albeit varying, to antimalarial drugs. For populations benefitting from identical possibilities of treatment, we have previously seen that all available data in Africa suggest that there is no marked variation in malaria mortality according to transmission when this is transmission of at least one infective bite per person per year. In the case of populations with

Table 1. Annual number of malaria attacks and malaria deaths according to the level of transmission in an imagined population of 10 000 people (125 individuals per year of age 0–79 years) who would have no available means of treatment

	Entomological inoculation rate (EIR) (no. infective bites per person per year)					
	0.01	0.1	1	10	100	1000
Number of attacks	100	1000	3700[a]	8800[a]	5800[a]	?
Number of malaria deaths	2–20	⩾20	25[b]	25[b]	25[c]	25[c]

[a]Estimated figure based on studies carried out in Pikine[7], Ndiop[20] and Dielmo[19,20].
[b]Hypothesis: no more than 20% of newborns are at risk of death from malaria.
[c]Maximum estimate derived from previous field studies in holoendemic areas of central Africa[27] and from the prevalence of sickle-cell trait in these areas[28].

no access to antimalarial drugs, we have attempted to estimate the maximum or minimum malaria mortality rates at different levels of transmission. In people without immunity, such as tourists, cases of severe or complicated malaria (always fatal without treatment) are observed in 1% to 5% of clinical infections. However, historical data suggest that the complications of untreated malaria in a non-immune subject often occur several weeks after the onset of clinical symptoms[22], and it is relatively infrequent nowadays that a diagnosis would be so delayed. To our knowledge, the most documented data on malaria mortality in non-immune populations with little or no access to anti-malaria drugs are those of the epidemics of Mauritius in 1867 (Refs 23,24), Rio Grande do Norte and Ceara (Brazil) in 1938 (Ref. 25), and Ethiopia in 1958 (Ref. 26). Data from these three epidemics are consistent in suggesting that in the absence of any treatment, lethality due to *P. falciparum* in non-immune people occurs between 5% and 20% of cases. This latter rate is close to the maximum estimates of global malaria mortality that were reported in the most highly endemic regions of Central Africa[27] or which are derived from the frequency of the carriers of the sickle-cell gene in these areas[28]. For these populations exposed since birth to numerous malaria infections, there is strong evidence that genetically determined factors protecting against the severe forms of malaria have been selected and that in that way the risk of death following a malaria attack may vary considerably according to individuals. However, even in retaining the low hypothesis that only 2% of malaria attacks are potentially lethal in a non-immune African population[29] and that this lethality is in fact concentrated in only 20% of genetically susceptible individuals, Table 1 suggests that it is necessary to reduce transmission to very low levels – probably one infective bite per person every 10 years, or even less – to hope to obtain a long-term impact on potential malaria mortality.

In this succinct quantitative approach of the relationships between transmission, morbidity and mortality from malaria, several data and hypotheses that we used were approximate or uncertain. Furthermore, the real populations' age structure and the competing causes of death within these populations are also to be considered, because they are fundamental to ascertaining the number of potential deaths due to malaria in high- and moderate-transmission areas. However, whatever hypothesis is considered, it appears clearly that variations of the burden of morbidity and potential mortality from malaria are weak compared with the considerable range of transmission levels.

Concluding comments

It is generally estimated that over 80% of the deaths due to malaria in the world occur in tropical Africa, although this region represents only one quarter of those populations exposed to *P. falciparum*[30]. Clearly, a huge mortality from malaria exists in tropical Africa, and is often attributed to the very high transmission levels, since the entomological inoculation rate ranges generally from five to 1000 infective bites per person per year in rural areas, whereas in other endemic areas in the world (except in New Guinea) the entomological inoculation rate is almost always less than one.

Our analysis suggests that in most epidemiological contexts observed in tropical Africa, only a considerable reduction of transmission (much higher than that which it is presently possible to obtain on a large scale, or to maintain for more than several years) would be able to reduce, on a long-term basis, the burden of malaria for the whole community.

The health sectors in African countries have few means at their disposal, are often badly managed and their staff frequently lack motivation. Hoping to work round these difficulties, the main funding agencies are now strongly encouraging the setting up of programmes to combat malaria with insecticide-impregnated bednets, basing such programmes on the results of short-term studies, and thus reflecting the general disarray with regard to the continual aggravation of the problem posed by chemoresistance. We believe that the only effective ways of fighting malaria in Africa with currently available means are (1) improvements in health services, and (2) health education to facilitate better use of antimalarial drugs.

Acknowledgements
We thank Pierre Druilhe, David Fidock and Louis Molineaux for helpful suggestions and Guy Charmot for supplying helpful historical documents.

References

1 Rozendaal, J.A. (1989) **Impregnated mosquito nets and curtains for self-protection and vector control.** *Trop. Dis. Bull.* 86, R1–R41
2 Alonso, P.L. *et al.* (1991) **The effect of insecticide-treated bednets on mortality of Gambian children.** *Lancet* 337, 1499–1502
3 Bermejo, A. and Veeken, H. (1992) **Insecticide-impregnated bed nets for malaria control: a review of the field trials.** *Bull. WHO* 70, 293–296
4 D'Alessandro, U. *et al.* (1995) **Mortality and morbidity from malaria in Gambian children after introduction of an impregnated bednet programme.** *Lancet* 345, 479–483
5 Spielman, A. (1994) **Why entomological antimalaria research should not focus on transgenic mosquitoes.** *Parasitology Today* 10, 374–376
6 Meuwissen, J.H.E.T. (1989) **Current studies related to the development of transmission-blocking malaria vaccines: a review.** *Trans. R. Soc. Trop. Med. Hyg.* 83 (Suppl.), 57–60
7 Trape, J-F. *et al.* (1993) **Malaria morbidity among children**

exposed to low seasonal transmission in Dakar, Senegal, and its implications for malaria control in tropical Africa. *Am. J. Trop. Med. Hyg.* 48, 748–756

8 Trape, J-F. *et al.* (1987) **Malaria and urbanization in Central Africa: the example of Brazzaville. V. Pernicious attacks and mortality.** *Trans. R. Soc. Trop. Med. Hyg.* 81 (Suppl. 2), 34–42

9 Trape, J-F. and Zoulani, A. (1987) **Malaria and urbanization in Central Africa: the example of Brazzaville. II. Results of entomological surveys and epidemiological analysis.** *Trans. R. Soc. Trop. Med. Hyg.* 81 (Suppl. 2), 10–18

10 Trape, J-F. and Zoulani, A. (1987) **Malaria and urbanization in Central Africa: the example of Brazzaville. III. Relationships between urbanization and the intensity of malaria transmission.** *Trans. R. Soc. Trop. Med. Hyg.* 81 (Suppl. 2), 19–25

11 Trape, J-F. (1987) **Malaria and urbanization in Central Africa: the example of Brazzaville. IV. Parasitological and serological surveys in urban and surrounding rural areas.** *Trans. R. Soc. Trop. Med. Hyg.* 81 (Suppl. 2), 26–33

12 Snow, R.W. *et al.* (1994) **Severe childhood malaria in two areas of markedly different *falciparum* transmission in East Africa.** *Acta Trop.* 57, 289–300

13 Mbogo, C.N.M. *et al.* (1995) **Relationships between *Plasmodium falciparum* transmission by vector populations and the incidence of severe disease at nine sites on the Kenyan coast.** *Am. J. Trop. Med. Hyg.* 52, 201–206

14 Snow, R.W. and Marsh, K. (1995) **Will reducing *Plasmodium falciparum* transmission alter malaria transmission among African children?** *Parasitology Today* 11, 188–190

15 Trape, J-F., Peelman, P. and Morault-Peelman, B. (1985) **Criteria for diagnosing clinical malaria among a semi-immune population exposed to intense and perennial transmission.** *Trans. R. Soc. Trop. Med. Hyg.* 79, 435–442

16 Armstrong Schellenberg, J.R.M. *et al.* (1994) **What is clinical malaria? Finding cases definitions for field research in highly endemic areas.** *Parasitology Today* 10, 439–442

17 Rogier, C., Commenges, D. and Trape, J-F. **Evidence for an age-dependent pyrogenic threshold of *Plasmodium falciparum* parasitaemia in highly endemic populations.** *Am. J. Trop. Med. Hyg.* (in press)

18 Smith, T., Armstrong Schellenberg, J.R.M. and Hayes, R. (1994) **Attributable fraction estimates and case definitions for malaria in endemic areas.** *Stat. Med.* 13, 2345–2358

19 Trape, J-F. *et al.* (1994) **The Dielmo Project: a longitudinal study of natural malaria infection and the mechanisms of protective immunity in a community living in a holoendemic area of Senegal.** *Am. J. Trop. Med. Hyg.* 51, 123–137

20 Rogier, C. and Trape, J-F. (1996) **Étude de l'acquisition de la prémunition en zones d'holo et mésoendémie palustre à Dielmo et à Ndiop (Sénégal).** *Med. Trop.* 55 (Suppl.), 71–76

21 Rickman, L.S. *et al.* (1990) ***Plasmodium falciparum*-infected *Anopheles stephensi* inconsistently transmit malaria to humans.** *Am. J. Trop. Med. Hyg.* 43, 441–445

22 Chauliac, G. (1964) *Contribution à l'Etude Médico-Militaire de l'Expédition de Madagascar en 1895*, Tananarive

23 Davidson, A. (1892) *Geographical Pathology*, Y.J. Pentland

24 Julvez, J. (1993) *Anthropisation et Paludisme*, University of Toulouse

25 Soper, F.L. and Wilson, D.B. (1943) Anopheles gambiae *in Brazil, 1930 to 1940*, Rockefeller Foundation

26 Fontaine, R.E., Najjar, A.E. and Prince, J.S. (1961) **The 1958 malaria epidemic in Ethiopia.** *Am. J. Trop. Med. Hyg.* 10, 795–803

27 Duren, A.N. (1951) **Essai d'étude sur l'importance du paludisme dans la mortalité au Congo Belge.** *Ann. Soc. Belge Med. Trop.* 31, 129–147

28 Molineaux, L. (1985) in *La Lutte Contre La Mort* (Vallin, J. and Lopez A. eds), pp 11–40, Presses Universitaires de France

29 Sudre, P., Breman, J.G. and Koplan, J.P. (1990) **Delphi survey of malaria mortality and drug resistance in Africa.** *Lancet* 335, 722

30 WHO (1993) **World malaria situation in 1991.** *Weekly Epidemiol. Rec.* 68, 245–252

Control of Lymphatic Filariasis by Annual Single-dose Diethylcarbamazine Treatments

E. Kimura and J.U. Mataika

It has long been stressed that diethylcarbamazine citrate must be given at a total dosage of 72 mg per kilogram of body weight in 12 divided doses of 6 mg kg^{-1} to obtain maximum effect against Wuchereria bancrofti. *However, recent studies revealed that only a single dose at 6 mg kg^{-1} could reduce microfilaria (Mf) counts by 90%, and that the effect would persist for 12–18 months. The annual repeat of the single-dose mass treatment was shown to be effective in reducing Mf prevalence and density in large-scale, long-term field trials. The scheme is simple and economic, and could be sustainable in many endemic areas, where health manpower and resources are often not sufficient. Annual single-dose mass treatments can be an effective weapon against human lymphatic filariasis, as discussed here by Eisaku Kimura and Jona Mataika.*

There are an estimated 78.6 million cases of lymphatic filariasis in the world[1], and only a small proportion of them is fortunate enough to be treated with the first drug of choice, diethylcarbamazine citrate (DEC). For more than 40 years, DEC has been used, worldwide, as the most effective and safest drug. The standard treatment scheme recommended by WHO[2] is to administer the drug at a dosage of 6 mg per kilogram of body weight daily, weekly or monthly for a total of 12 times in order to obtain the required overall dose of 72 mg kg^{-1} for the treatment of *Wuchereria bancrofti* infection, or a total dose of 36–72 mg kg^{-1} for *Brugia* spp infections. The standard treatment can effectively reduce filariasis and suppress its transmission, but ensuring that 12 doses are given poses considerable practical difficulties in a large-scale campaign. Recently, annual single-dose treatments with DEC at 6 mg kg^{-1} were reported to be effective in reducing the microfilaria (Mf) prevalence and density. The effect of each single dose is not very strong but is steadily progressive in a course of repeated treatments. In a filariasis control campaign in Samoa involving 160 000 people over eight years, three single-dose treatments decreased the Mf prevalence from 5.6% to 2.5%, showing that single-dose chemotherapy is a practical strategy for filariasis control.

Eisaku Kimura is at the Department of Parasitology, Aichi Medical University, Nagakute-cho, Aichi-ken, Japan 480-11. Jona Mataika is at the Wellcome Virus Laboratory, Tamavua Hospital, Suva, Fiji. **Tel: +81 561 623311, Fax: +81 561 633645, e-mail: kimura@amugw.aichi-med-u.ac.jp**

What is the aim?

Annual single dose is given for mass treatment, eliminating the laborious and costly step of blood

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WORLD MALARIA REPORT

2019

World Health Organization

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Contents

Foreword

Dr Tedros Adhanom Ghebreyesus
Director-General
World Health Organization

Leaving no one behind in the march to a malaria-free world

The scourge of malaria continues to strike hardest against pregnant women and children in Africa. The *World malaria report 2019* includes a special section focused on the burden and consequences of the disease among these two most at-risk groups. It delivers a clear message: we must all do more to protect the most vulnerable in the fight against a disease that continues to claim more than 400 000 lives every year.

Malaria in pregnancy compromises the mother's health and puts her at greater risk of death. It impacts the health of the fetus, leading to prematurity and low birthweight, major contributors to neonatal and infant mortality. Last year, some 11 million pregnant women in sub-Saharan Africa were infected with malaria and, consequently, nearly 900 000 children were born with a low birthweight.

To protect pregnant women in Africa, WHO recommends the use of insecticide-treated mosquito nets (ITNs) and preventive antimalarial medicines. This report shows progress on both fronts. Still, nearly 40% of pregnant woman did not sleep under an ITN in 2018 and two thirds did not receive the recommended three or more doses of preventive therapy.

Among children, efforts to expand access to preventive antimalarial medicines are bearing fruit. In Africa's Sahel sub-region, WHO recommends seasonal malaria chemoprevention during the peak transmission season. More than 60% of children living in areas eligible for this preventive therapy received it in 2018.

Sierra Leone is to be commended for becoming the first country in Africa to roll out intermittent preventive treatment in infants, another WHO-recommended approach for protecting young children in malaria-affected areas.

Still, access to care for children showing signs of a fever remains too low. Country surveys show that nearly 40% of febrile children in sub-Saharan Africa are not taken for care with a trained medical provider.

At least 10 countries that are part of the WHO "E-2020 initiative" are on track to reach the 2020 elimination milestone of our global malaria strategy. In 2015, all of these countries were malaria endemic; now they have either achieved zero indigenous malaria cases or are nearing the finish line.

However, in recent years, global progress in reducing new malaria cases has levelled off. Most worrying of all, malaria is on the rise across some high-burden countries in Africa.

Critical milestones of our global malaria strategy are likely to be missed.

In 2018, WHO and the RBM Partnership to End Malaria launched "High burden to high impact", a new approach to prevent disease and save lives in the countries hardest hit by malaria. Replacing a "one size fits all" strategy, the approach calls for using the most effective tools in a more targeted way. I am very pleased to note that two countries – India and Uganda – have reported substantial reductions in malaria cases in 2018 over the previous year.

In September, I issued a "Malaria Challenge", calling for greater investment in the research and development of transformative new tools, technologies and approaches to accelerate progress in beating back this disease.

Through a WHO-coordinated pilot progamme, Ghana, Kenya and Malawi recently introduced the world's first malaria vaccine in selected areas. Evidence and experience from the programme will inform policy decisions on the vaccine's potential wider use in Africa. With support from the Global Fund to Fight AIDS, Tuberculosis and Malaria and from Unitaid, other promising tools are being tested, such as new types of ITNs and tools that target outdoor-biting mosquitoes.

Achieving our common vision of a malaria-free world will also require enhanced action in other critical areas. We need affordable, people-centred health services. We need reliable and accurate surveillance and response systems. We need strategies that are tailored to local malaria-transmission settings.

Stepped-up financing for the malaria response is essential. In 2018, total funding for malaria control and elimination reached an estimated US$ 2.7 billion, falling far short of the US$ 5 billion funding target of our global strategy.

Through resolute, robust financing, political leadership and universal health coverage, we can defeat this disease once and for all.

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[1] https://map.ox.ac.uk/

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Abbreviations

ACT	artemisinin-based combination therapy
AIDS	acquired immunodeficiency syndrome
AL	artemether-lumefantrine
ANC	antenatal care
AQ	amodiaquine
AS	artesunate
AS-SP	artesunate-sulfadoxine-pyrimethamine
AS-AQ	artesunate-amodiaquine
AS-MQ	artesunate-mefloquine
AS-PY	artesunate-pyronaridine
CHW	community health worker
CI	confidence interval
CQ	chloroquine
DHA	dihydroartemisinin
DHIS2	District Health Information Software2
DHS	demographic and health survey
E-2020	eliminating countries for 2020
Global Forum	Global Forum of Malaria-Eliminating Countries
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
GMP	Global Malaria Programme
GMS	Greater Mekong subregion
GPW13	WHO's 13th General Programme of Work
GTS	*Global technical strategy for malaria 2016–2030*
Hb	haemoglobin
HBHI	high burden to high impact
HIV	human immunodeficiency virus
HMIS	health management information system
HRP2	histidine-rich protein 2
iCCM	integrated community case management
iDES	integrated drug efficacy surveillance
IPTi	intermittent preventive treatment in infants
IPTp	intermittent preventive treatment in pregnancy
IQR	interquartile range
IRS	indoor residual spraying
ITN	insecticide-treated mosquito net
LBW	low birthweight
LLIN	long-lasting insecticidal net
MEOC	Malaria Elimination Oversight Committee
MIS	malaria indicator survey
MPAC	Malaria Policy Advisory Committee
NMP	national malaria programme
OECD	Organisation for Economic Co-operation and Development
P.	*Plasmodium*
PBO	piperonyl butoxide
PPQ	piperaquine
PQ	primaquine
RAcE	Rapid Access Expansion Programme
R&D	research and development
RBM	Roll Back Malaria
RDT	rapid diagnostic test
SDG	Sustainable Development Goal
SMC	seasonal malaria chemoprevention
SP	sulfadoxine-pyrimethamine
TES	therapeutic efficacy study
UNICEF	United Nations Children's Fund
United Kingdom	United Kingdom of Great Britain and Northern Ireland
USA	United States of America
WHO	World Health Organization

This year's report at a glance

REGIONAL AND GLOBAL TRENDS IN BURDEN OF MALARIA CASES AND DEATHS

Malaria cases

- In 2018, an estimated 228 million cases of malaria occurred worldwide (95% confidence interval [CI]: 206–258 million), compared with 251 million cases in 2010 (95% CI: 231–278 million) and 231 million cases in 2017 (95% CI: 211–259 million).
- Most malaria cases in 2018 were in the World Health Organization (WHO) African Region (213 million or 93%), followed by the WHO South-East Asia Region with 3.4% of the cases and the WHO Eastern Mediterranean Region with 2.1%.
- Nineteen countries in sub-Saharan Africa[1] and India carried almost 85% of the global malaria burden. Six countries accounted for more than half of all malaria cases worldwide: Nigeria (25%), the Democratic Republic of the Congo (12%), Uganda (5%), and Côte d'Ivoire, Mozambique and Niger (4% each).
- The incidence rate of malaria declined globally between 2010 and 2018, from 71 to 57 cases per 1000 population at risk. However, from 2014 to 2018, the rate of change slowed dramatically, reducing to 57 in 2014 and remaining at similar levels through to 2018.
- The WHO South-East Asia Region continued to see its incidence rate fall – from 17 cases of the disease per 1000 population at risk in 2010 to five cases in 2018 (a 70% decrease). In the WHO African Region, case incidence levels also declined from 294 in 2010 to 229 in 2018, representing a 22% reduction. All other WHO regions recorded either little progress or an increase in incidence rate. The WHO Region of the Americas recorded a rise, largely due to increases in malaria transmission in the Bolivarian Republic of Venezuela.
- Between 2015 and 2018, only 31 countries, where malaria is still endemic, reduced case incidence significantly and were on track to reduce incidence by 40% or more by 2020. Without accelerated change, the *Global technical strategy for malaria 2016–2030* (GTS) milestones for morbidity in 2025 and 2030 will not be achieved.
- *Plasmodium falciparum* is the most prevalent malaria parasite in the WHO African Region, accounting for 99.7% of estimated malaria cases in 2018, as well as in the WHO South-East Asia Region (50%), the WHO Eastern Mediterranean Region (71%) and the WHO Western Pacific Region (65%).
- Globally, 53% of the *P. vivax* burden is in the WHO South-East Asia Region, with the majority being in India (47%). *P. vivax* is the predominant parasite in the WHO Region of the Americas, representing 75% of malaria cases.

Malaria deaths

- In 2018, there were an estimated 405 000 deaths from malaria globally, compared with 416 000 estimated deaths in 2017, and 585 000 in 2010.
- Children aged under 5 years are the most vulnerable group affected by malaria. In 2018, they accounted for 67% (272 000) of all malaria deaths worldwide.

[1] The full list of sub-Saharan countries is available at https://unstats.un.org/unsd/methodology/m49; for all analyses conducted in this report and pertaining to malaria endemic sub-Saharan countries, Sudan is also included.

- The WHO African Region accounted for 94% of all malaria deaths in 2018. Although this region was home to the highest number of malaria deaths in 2018, it also accounted for 85% of the 180 000 fewer global malaria deaths reported in 2018 compared with 2010.
- Nearly 85% of global malaria deaths in 2018 were concentrated in 20 countries in the WHO African Region and India; Nigeria accounted for almost 24% of all global malaria deaths, followed by the Democratic Republic of the Congo (11%), the United Republic of Tanzania (5%), and Angola, Mozambique and Niger (4% each).
- In 2018, only the WHO African Region and the WHO South-East Asia Region showed reductions in malaria deaths compared with 2010. The WHO African Region had the largest absolute reduction in malaria deaths, from 533 000 in 2010 to 380 000 in 2018. Despite these gains, the malaria mortality reduction rate has also slowed since 2016.

MATERNAL, INFANT AND CHILD HEALTH CONSEQUENCES OF MALARIA

- In 2018, about 11 million pregnancies in moderate and high transmission sub-Saharan African countries would have been exposed to malaria infection.
- In 2018, prevalence of exposure to malaria infection in pregnancy was highest in the West African subregion and Central Africa (each with 35%), followed by East and Southern Africa (20%). About 39% of these were in the Democratic Republic of the Congo and Nigeria.
- The 11 million pregnant women exposed to malaria infections in 2018 delivered about 872 000 children with low birthweight (16% of all children with low birthweight in these countries), with West Africa having the highest prevalence of low birthweight children due to malaria in pregnancy.
- Between 2015 and 2018 in 21 moderate to high malaria burden countries in the WHO African Region, the prevalence of anaemia in children under 5 years with a positive rapid diagnostic test (RDT) was double that of children with a negative RDT. In the children who were positive for malaria, 9% had severe anaemia and 54% had moderate anaemia; in contrast, in the children without malaria, only 1% had severe anaemia and 31% had moderate anaemia.
- The countries with the highest percentage of severe anaemia among children aged under 5 years who were positive for malaria were Senegal (26%), Mali (16%), Guinea (14%) and Mozambique (12%). For most other countries, severe anaemia ranged from 5% to 10%.
- Overall, about 24 million children were estimated to be infected with *P. falciparum* in 2018 in sub-Saharan Africa, and an estimated 1.8 million of them were likely to have severe anaemia.

HIGH BURDEN TO HIGH IMPACT APPROACH

- There were about 155 million malaria cases in the 11 high burden to high impact (HBHI) countries in 2018, compared with 177 million in 2010. The Democratic Republic of the Congo and Nigeria accounted for 84 million (54%) of total cases.
- Of the 10 highest burden countries in Africa, Ghana and Nigeria reported the highest absolute increases in cases of malaria in 2018 compared with 2017. The burden in 2018 was similar to that of 2017 in all other countries, apart from in Uganda and India, where there were reported reductions of 1.5 and 2.6 million malaria cases, respectively, in 2018 compared with 2017.
- Malaria deaths reduced from about 400 000 in 2010 to about 260 000 in 2018, the largest reduction being in Nigeria, from almost 153 000 deaths in 2010 to about 95 000 deaths in 2018.

- By 2018, in all of the 11 HBHI countries, at least 40% of the population at risk were sleeping under long-lasting insecticidal nets (LLINs), the highest percentage being in Uganda (80%) and the lowest in Nigeria (40%).
- Only Burkina Faso and the United Republic of Tanzania were estimated as having more than half of pregnant women receiving three doses of intermittent preventive treatment in pregnancy (IPTp3) in 2018. In Cameroon, Nigeria and Uganda, the estimated coverage was about 30% or less.
- Six countries in Africa's Sahel subregion implemented seasonal malaria chemoprevention (SMC) in 2018; a mean total of 17 million children, out of the 26 million targeted, were treated per SMC cycle.
- The percentage of children aged under 5 years with fever seeking treatment varied from 58% in Mali to 82% in Uganda. In the Democratic Republic of the Congo and Mali, more than 40% of children were not brought for care at all. Testing was also worryingly low in children who were brought for care, with 30% or less being tested in Cameroon, the Democratic Republic of the Congo and Nigeria.
- Except for India, direct domestic investment remains very low relative to international funding in the HBHI countries.

MALARIA ELIMINATION AND PREVENTION OF RE-ESTABLISHMENT

- Globally, the elimination net is widening, with more countries moving towards zero indigenous cases: in 2018, 49 countries reported fewer than 10 000 such cases, up from 46 countries in 2017 and 40 countries in 2010. The number of countries with fewer than 100 indigenous cases – a strong indicator that elimination is within reach – increased from 17 countries in 2010, to 25 countries in 2017 and 27 countries in 2018.
- Paraguay and Uzbekistan were awarded WHO certification of elimination in 2018, with Algeria and Argentina achieving certification in early 2019. In 2018, China, El Salvador, Iran, Malaysia and Timor-Leste reported zero indigenous cases.
- One of the key GTS milestones for 2020 is elimination of malaria in at least 10 countries that were malaria endemic in 2015. At the current rate of progress, it is likely that this milestone will be reached.
- In 2016, WHO identified 21 countries with the potential to eliminate malaria by the year 2020. WHO is working with the governments in these countries – known as "E-2020 countries" – to support their elimination acceleration goals.
- Although 10 E-2020 countries remain on track to achieve their elimination goals, Comoros and Costa Rica reported increases in indigenous malaria cases in 2018 compared with 2017.
- In the six countries of the Greater Mekong subregion (GMS) – Cambodia, China (Yunnan Province), Lao People's Democratic Republic, Myanmar, Thailand and Viet Nam – the reported number of malaria cases fell by 76% between 2010 and 2018, and malaria deaths fell by 95% over the same period. In 2018, Cambodia reported no malaria related deaths for the first time in the country's history.

INVESTMENTS IN MALARIA PROGRAMMES AND RESEARCH

- In 2018, an estimated US$ 2.7 billion was invested in malaria control and elimination efforts globally by governments of malaria endemic countries and international partners – a reduction from the US$ 3.2 billion that was invested in 2017. The amount invested in 2018 fell short of the US$ 5.0 billion estimated to be required globally to stay on track towards the GTS milestones.
- Nearly three quarters of investments in 2018 were spent in the WHO African Region, followed by the WHO Region of the Americas (7%), the WHO South-East Asia Region (6%), and the WHO Eastern Mediterranean Region and the WHO Western Pacific Region (5% each).
- In 2018, 47% of total funding for malaria was invested in low-income countries, 43% in lower-middle-income countries and 11% in upper-middle-income countries. International funding represented the major source of funding in low-income and lower-middle-income countries, at 85% and 61%, respectively. Domestic funding has remained stable since 2010.
- Of the US$ 2.7 billion invested in 2018, US$ 1.8 billion came from international funders. Governments of malaria endemic countries contributed 30% of total funding (US$ 900 million) in 2018, a figure unchanged from 2017. Two thirds of domestically sourced funds were invested in malaria control activities carried out by national malaria programmes (NMPs), with the remaining share estimated as the cost of patient care.
- As in previous years, the United States of America (USA) was the largest international source of malaria financing, providing US$ 1.0 billion (37%) in 2018. Country members of the Development Assistance Committee together accounted for US$ 300 million (11%). The United Kingdom of Great Britain and Northern Ireland contributed around US$ 200 million (7%).
- Of the US$ 2.7 billion invested in 2018, US$ 1.0 billion was channelled through the Global Fund to Fight AIDS, Tuberculosis and Malaria.
- Although funding for malaria has remained relatively stable since 2010, the level of investment in 2018 is far from what is required to reach the first two milestones of the GTS; that is, a reduction of at least 40% in malaria case incidence and mortality rates globally by 2020, compared with 2015 levels.
- US$ 663 million was invested in basic research and product development for malaria in 2018, an increase of US$ 18 million compared with 2017.
- Funding for drug research and development (R&D) increased to the highest level ever recorded, from US$ 228 million in 2017 to US$ 252 million in 2018. This increase was a result of private sector industry investment in several Phase II trials of new chemical entities with the potential for single-exposure radical cure.

Deliveries of malaria commodities

Insecticide-treated mosquito nets

- Between 2016 and 2018, a total of 578 million insecticide-treated mosquito nets (ITNs), mainly LLINs, were reported by manufacturers as having been delivered globally, with 50% going to Côte d'Ivoire, the Democratic Republic of the Congo, Ethiopia, Ghana, India, Nigeria, Uganda and the United Republic of Tanzania.
- In 2018 about 197 million ITNs were delivered by manufacturers, of which more than 87% were delivered to countries in sub-Saharan Africa.
- Globally, 80% of ITNs were distributed through mass distribution campaigns, 10% in antenatal care facilities and 6% as part of immunization programmes.

Rapid diagnostic tests

- An estimated 412 million RDTs were sold globally in 2018.
- In 2018, 259 million RDTs were distributed by NMPs. Most RDTs (64%) were tests that detected *P. falciparum* only and were supplied to sub-Saharan Africa.

Artemisinin-based combination therapy

- An estimated 3 billion treatment courses of artemisinin-based combination therapy (ACT) were procured by countries over the period 2010–2018. An estimated 63% of these procurements were reported to have been made for the public sector.
- In 2018, 214 million ACT treatment courses were delivered by NMPs, of which 98% were in the WHO African Region.

PREVENTING MALARIA

Vector control

- Half of people at risk of malaria in sub-Saharan Africa are sleeping under an ITN; in 2018, 50% of the population were protected by this intervention, an increase from 29% in 2010. Furthermore, the percentage of the population with access to an ITN increased from 33% in 2010 to 57% in 2018. However, coverage has improved only marginally since 2015 and has been at a standstill since 2016.
- Households with at least one ITN for every two people increased to 72% in 2018, from 47% in 2010. However, this figure represents only a modest increase over the past 3 years, and remains far from the target of universal coverage.
- Fewer people at risk of malaria are being protected by indoor residual spraying (IRS), a prevention method that involves spraying the inside walls of dwellings with insecticides. Globally, IRS protection declined from a peak of 5% in 2010 to 2% in 2018, with declining trends seen across all WHO regions apart from the WHO Eastern Mediterranean Region.
- Although IRS coverage dropped from 180 million people at risk protected globally in 2010 to 93 million in 2018, the 2018 figure was a decrease of 13 million compared with 2017.
- The declines in IRS coverage may be due to the switch from pyrethroids to more expensive insecticides in response to increasing pyrethroid resistance, or changes in operational strategies (e.g. at-risk populations decreasing in countries aiming for elimination of malaria).

Preventive therapies

- To protect women in areas of moderate and high malaria transmission in Africa, WHO recommends IPTp with the antimalarial drug sulfadoxine-pyrimethamine (SP). Among 36 African countries that reported on IPTp coverage levels in 2018, an estimated 31% of eligible pregnant women received the recommended three or more doses of IPTp, compared with 22% in 2017 and 2% in 2010, indicating considerable improvements in country uptake.
- About 18% of women who use antenatal care services at least once do not receive any IPTp, representing a missed opportunity that, if harnessed, could considerably and rapidly improve IPTp coverage.
- In 2018, 19 million children in 12 countries in Africa's Sahel subregion were protected through SMC programmes. All targeted children received treatment in Cameroon, Guinea, Guinea-Bissau and Mali. However, about 12 million children who could have benefited from this intervention were not covered, mainly due to a lack of funding.

DIAGNOSTIC TESTING AND TREATMENT

Accessing care

- Prompt diagnosis and treatment is the most effective way to prevent a mild case of malaria from developing into severe disease and death. Based on national household surveys completed in 20 countries in sub-Saharan Africa between 2015 and 2018, a median of 42% (interquartile range [IQR]: 34–49%) of children with a fever (febrile) were taken to a trained medical provider for care in the public sector compared with 10% (IQR: 8–22%) in the formal private sector and 3% (IQR: 2–7%) in the informal private sector.
- A high proportion of febrile children did not receive any medical attention (median: 36%, IQR: 28–45%). Poor access to health care providers or lack of awareness of malaria symptoms among caregivers are among the contributing factors.

Diagnosing malaria

- The percentage of patients suspected of having malaria who are seen in public health facilities and tested with either an RDT or microscopy, rose from 38% in 2010 to 85% in 2018.
- In 71% of moderate to high transmission countries in sub-Saharan Africa, the percentage of suspected cases tested with any parasitological test was greater than 80% in 2018.
- According to 19 nationally representative household surveys conducted between 2015 and 2018 in sub-Saharan Africa, the median percentage of febrile children brought for care who received a finger or heel stick (suggesting that a malaria diagnostic test may have been performed) was greater in the public sector (median: 66%, IQR: 49–75%) than in the formal private sector (median: 40%, IQR: 16–46%) or the informal private sector (median: 9%, IQR: 5–22%).
- According to 61 surveys conducted in 29 sub-Saharan African countries between 2010 and 2018, the percentage of children with a fever that received a diagnostic test before antimalarial treatment in the public health sector increased from a median of 48% (IQR: 30–62%) in 2010–2013 to a median of 76% (IQR: 60–86%) in 2015–2018.

Treating malaria

- Based on 20 household surveys conducted in sub-Saharan Africa in 2015–2018, the median percentage of febrile children who were treated with any antimalarial drug was higher in the public sector (median: 48%, IQR: 30–69%) than in the formal private sector (median: 40%, IQR: 21–51%) or the informal private sector (median: 18%, IQR: 10–29%).
- Data from 20 national surveys conducted in sub-Saharan Africa show that for the period 2015–2018, an estimated 47% (IQR: 29–69%) of febrile children brought for treatment for malaria in the public health sector received antimalarial drugs, compared with 59% (IQR: 53–84%) among those visiting a community health worker and 49% (IQR: 19–55%) in the formal medical private sector.
- Based on 19 surveys, antimalarial treatments among febrile children who received antimalarial medicine were slightly more likely to be ACTs if treatment was sought in the public sector (median: 80%, IQR: 45–94%) than in the formal private sector (median: 77%, IQR: 43–87%) or the informal private sector (median: 60%, IQR: 40–84%).
- To bridge the treatment gap among children, WHO recommends the uptake of integrated community case management (iCCM). This approach promotes integrated management of common life-threatening conditions in children – malaria, pneumonia and diarrhoea – at health facility and community levels. In 2018, 30 countries were implementing iCCM at different levels, with only a few implementing nationally.

MALARIA SURVEILLANCE SYSTEMS

- Pillar 3 of the GTS is to transform malaria surveillance into a core intervention. To understand whether malaria surveillance systems are fit for purpose, WHO recommends the regular monitoring and evaluation of surveillance systems.
- The Global Malaria Programme (GMP), in collaboration with the University of Oslo, has developed standardized malaria modules in District Health Information Software2 (DHIS2) for aggregate and case-based collection of routine data with associated data elements, dashboards of key epidemiological and data quality indicators, reports and a curriculum for facility-level data analysis to facilitate data analysis and interpretation.
- As of October 2019, 23 countries have installed the WHO aggregate malaria module and another six installations are planned over the next year. Five countries have already developed and integrated their own malaria module into DHIS2.
- WHO has been working in coordination with national health management information systems (HMIS) departments of ministries of health, in particular the HBHI countries, to establish structured dynamic databases known as data repositories. The GMP has developed an easily adaptable repository structure in DHIS2, with guidance on relevant data elements and indicators, their definitions and computation to cover key thematic areas. So far, work to develop these databases has started in Gambia, Ghana, Mozambique, Nigeria, Uganda and the United Republic of Tanzania.
- WHO also encourages countries to implement surveillance system assessments. An example of such an assessment and its role in improving surveillance systems is illustrated through a case study of Mozambique.

RESPONDING TO BIOLOGICAL THREATS TO THE FIGHT AGAINST MALARIA

Pfhrp2/3 gene deletions

- Deletions in the *pfhrp2* and *pfhrp3* (*pfhrp2/3*) genes of the parasite renders parasites undetectable by RDTs based on histidine-rich protein 2 (HRP2). The prevalence of dual *pfhrp2* and *pfhrp3* among symptomatic patients reached as high as 80% in Eritrea and Peru.
- WHO has recommended that countries with reports of *pfhrp2/3* deletions or neighbouring countries should conduct representative baseline surveys among suspected malaria cases to determine whether the prevalence of *pfhrp2/3* deletions causing false negative RDT results has reached a threshold for RDT change (>5% *pfhrp2* deletions causing false negative RDT results).
- WHO is tracking published reports of *pfhrp2/3* deletions using the Malaria Threat Map mapping tool. To date, 28 countries have reported *pfhrp2* deletions.

Drug resistance

- *PfKelch13* mutations have been identified as molecular markers of partial artemisinin resistance. *PfKelch13* mutations associated with artemisinin resistance are widespread in the GMS, and have also been detected at a significant prevalence (over 5%) in Guyana, Papua New Guinea and Rwanda. In the case of Rwanda, the presence of *PfKelch13* mutations does not affect efficacy of first-line treatment.
- In the WHO Western Pacific Region, artemisinin resistance has been confirmed in Cambodia, Lao People's Democratic Republic and Viet Nam through several studies conducted between 2001

and 2018. Treatment efficacy for *P. vivax* remains high across all countries where treatment failure rates are below 10%.

- In the WHO African Region the efficacy rates of artemether-lumefantrine (AL), artesunate-amodiaquine (AS-AQ) and dihydroartemisinin-piperaquine (DHA-PPQ) for *P. falciparum* were more than 98%, and efficacy has remained high over time.
- Treatment efficacy with first-line treatment remains high for *P. falciparum* and *P. vivax* in the WHO Region of the Americas.
- In the WHO South-East Asia Region, the presence of molecular markers of artemisinin resistance has been reported in Bangladesh, India, Myanmar and Thailand. With the exception of Myanmar, failure rates of *P. falciparum* to first-line ACTs were found to be above 10% and were as high as 93% in Thailand. For *P. vivax* most countries continue to demonstrate high efficacy of chloroquine (CQ), except for Myanmar and Timor-Leste.
- In the WHO Eastern Mediterranean Region, high failure rates of treatment with artesunate-sulfadoxine-pyrimethamine (AS-SP) for *P. falciparum* in Somalia and Sudan led to a change in first-line treatment policy to AL. For *P. vivax* there is high treatment efficacy with AL and CQ in all countries where a therapeutic efficacy study (TES) has been conducted.

Insecticide resistance

- From 2010 through 2018, some 81 countries reported data on insecticide resistance monitoring to WHO.
- Of the 81 malaria endemic countries that provided data for 2010–2018, resistance to at least one of the four insecticide classes in one malaria vector from one collection site was detected in 73 countries, an increase of five countries compared with the previous reporting period 2010–2017. In 26 countries, resistance was reported to all main insecticide classes.
- Resistance to pyrethroids – the only insecticide class currently used in ITNs – is widespread and was detected in at least one malaria vector in more than two thirds of the sites tested, and was highest in the WHO African Region and in the WHO Eastern Mediterranean Region.
- Resistance to organochlorines was detected for at least one malaria vector in almost two thirds of the sites. Resistance to carbamates and organophosphates was less prevalent and was detected in 31% and 26% of the tested sites, respectively. Prevalence was highest for carbamates in the WHO South-East Asia Region and for organophosphates in the WHO South-East Asia Region and in the WHO Western Pacific Region.
- All the standard insecticide resistance data reported to WHO are included in the WHO Global Insecticide Resistance database, and are available for exploration via the Malaria Threats Map. This online tool was extended in 2019 to cover invasive mosquito species, and currently shows the geographical extent of reports on the detection of *Anopheles stephensi*.
- To guide resistance management, countries should develop and implement a national plan for insecticide-resistance monitoring and management, drawing on the WHO *Framework for a national plan for monitoring and management of insecticide resistance in malaria vector*. In 2018, a total of 45 countries reported having completed plans for resistance monitoring and management and 36 were currently in the process of developing them.
- NMPs and their partners should consider the deployment of pyrethroid-piperonyl butoxide nets in geographical areas where the main malaria vectors meet the criteria recommended by WHO in 2017, rather than being based on whether the whole country meets the criteria.

Avant-propos

Dr Tedros Adhanom Ghebreyesus
Directeur général
de l'Organisation mondiale de la Santé (OMS)

N'oublier personne sur la voie d'un monde sans paludisme

Le fléau du paludisme continue de toucher plus lourdement les femmes enceintes et les enfants en Afrique. Le *Rapport sur le paludisme dans le monde 2019* comporte donc une section spéciale sur le poids de cette maladie et ses conséquences sur ces deux groupes les plus à risque. Le message qu'il délivre est très clair : nous devons tous faire davantage pour protéger les plus vulnérables contre une maladie responsable de plus de 400 000 décès chaque année.

Le paludisme pendant la grossesse nuit à la santé de la mère et l'expose à un risque accru de décès. Il a un impact sur la santé du fœtus, entraînant prématurité et insuffisance pondérale à la naissance qui sont les principales causes de mortalité néonatale et infantile. L'an passé, environ 11 millions de femmes enceintes en Afrique subsaharienne ont présenté une infection palustre et, par conséquent, près de 900 000 enfants un faible poids à la naissance.

Pour protéger les femmes enceintes en Afrique, l'OMS recommande l'utilisation de moustiquaires imprégnées d'insecticide (MII) et de médicaments antipaludiques préventifs. Ce rapport fait état de progrès sur les deux fronts. Pourtant, près de 40 % des femmes enceintes n'ont pas dormi sous MII en 2018 et les deux tiers n'ont pas reçu le minimum de trois doses de traitement préventif comme il est recommandé.

En ce qui concerne les enfants, les efforts déployés pour améliorer l'accès aux médicaments antipaludiques préventifs portent leurs fruits. En Afrique, dans la sous-région du Sahel, l'OMS recommande la chimioprévention du paludisme saisonnier durant la période de pic de transmission. Plus de 60 % des enfants vivant dans des zones éligibles à ce traitement préventif en ont bénéficié en 2018.

La Sierra Leone peut être citée en exemple ; en effet, elle est devenue le premier pays d'Afrique à déployer le traitement préventif intermittent chez les nourrissons, une autre approche recommandée par l'OMS pour protéger les enfants en bas âge dans les zones touchées par le paludisme.

Chez les enfants présentant des signes de fièvre, l'accès aux soins reste néanmoins trop faible. En Afrique subsaharienne, les enquêtes nationales indiquent que près de 40 % des enfants ayant eu de la fièvre n'ont pas été orientés vers un prestataire médical formé.

Au moins 10 pays participant à l'« Initiative E-2020 » de l'OMS sont en passe d'atteindre l'objectif d'élimination du paludisme d'ici à 2020 défini dans notre stratégie mondiale de lutte contre le paludisme. En 2015, la maladie était endémique dans tous ces pays ; aujourd'hui, soit ils n'enregistrent aucun cas de paludisme indigène, soit ils sont tout proches de l'objectif.

Toutefois, les progrès réalisés au niveau mondial en termes de baisse de l'incidence du paludisme ont ralenti ces dernières années. Plus préoccupant encore, le paludisme progresse dans quelques pays d'Afrique où il pèse déjà lourdement.

Il est probable que des objectifs essentiels de notre stratégie mondiale de lutte contre le paludisme ne seront pas atteints.

En 2018, l'OMS et le Partenariat RBM pour en finir avec le paludisme ont lancé « *High burden to high impact* » (« D'une charge élevée à un fort impact »), une nouvelle approche visant à prévenir la maladie et à sauver des vies dans les pays les plus durement touchés par le paludisme. Se substituant à une stratégie « universelle », cette approche encourage l'utilisation des outils les plus efficaces de façon plus ciblée. Je suis ravi de constater que deux pays, l'Inde et l'Ouganda, ont rapporté une baisse substantielle du nombre de cas de paludisme en 2018 par rapport à l'année précédente.

En septembre, j'ai publié un « Malaria Challenge », préconisant d'investir davantage dans la recherche et le développement d'outils, de technologies et d'approches de transformation innovants afin d'accélérer les progrès réalisés pour vaincre cette maladie.

Grâce à un programme pilote coordonné par l'OMS, le Ghana, le Kenya et le Malawi ont récemment introduit dans certaines régions le premier vaccin antipaludique au monde. Les données et les expériences tirées de ce programme éclaireront les décisions politiques sur une utilisation éventuellement plus large du vaccin en Afrique. Grâce au soutien du Fonds mondial de lutte contre le sida, la tuberculose et le paludisme et d'Unitaid, d'autres outils prometteurs sont en phase de test, notamment de nouveaux types de moustiquaires imprégnées d'insecticide, ainsi que des outils ciblant les moustiques exophages.

Pour concrétiser notre vision commune d'un monde sans paludisme, nous allons également devoir renforcer notre action dans d'autres domaines essentiels. Nous avons besoin de services de santé abordables et axés sur les populations. Nous avons également besoin de systèmes de surveillance et de riposte qui soient fiables et précis. Enfin, nous devons définir des stratégies parfaitement adaptées aux conditions locales de transmission du paludisme.

Augmenter le financement de la lutte contre le paludisme est également indispensable. En 2018, le financement total du contrôle et de l'élimination du paludisme a atteint US$ 2,7 milliards, bien en deçà de l'objectif de US$ 5 milliards défini dans le cadre de notre stratégie mondiale.

Grâce à un financement solide et résolu, à un véritable leadership politique et à une couverture de santé universelle, nous pourrons venir à bout de cette maladie une fois pour toutes.

Le rapport de cette année en un clin d'œil

POIDS DU PALUDISME AU NIVEAU MONDIAL ET RÉGIONAL : ÉVOLUTION DU NOMBRE DE CAS ET DE DÉCÈS

Cas de paludisme

- Au niveau mondial, le nombre de cas de paludisme est estimé à 228 millions en 2018 (intervalle de confiance [IC] de 95 % : 206-258 millions), contre 251 millions en 2010 (IC de 95 % : 231-278 millions) et 231 millions en 2017 (IC de 95 % : 211-259 millions).
- La plupart des cas (213 millions ou 93 %) ont été enregistrés en 2018 dans la région Afrique de l'OMS, loin devant la région Asie du Sud-Est (3,4 %) et la région Méditerranée orientale (2,1 %).
- Dix-neuf pays d'Afrique subsaharienne[1] et l'Inde ont concentré quasiment 85 % du nombre total de cas de paludisme dans le monde. Six pays, à eux seuls, ont enregistré plus de la moitié des cas : le Nigéria (25 %), la République démocratique du Congo (12 %), l'Ouganda (5 %), ainsi que la Côte d'Ivoire, le Mozambique et le Niger (4 % chacun).
- Au niveau mondial, l'incidence du paludisme a reculé entre 2010 et 2018, passant de 71 cas pour 1 000 habitants exposés au risque de paludisme à 57 pour 1 000. Néanmoins, cette baisse a considérablement ralenti entre 2014 et 2018, l'incidence ayant diminué à 57 pour 1 000 en 2014 pour rester à un niveau similaire jusqu'en 2018.
- Dans la région Asie du Sud-Est de l'OMS, l'incidence du paludisme continue à baisser, de 17 cas pour 1 000 habitants exposés au risque de paludisme en 2010 à 5 pour 1 000 en 2018 (soit une baisse de 70 %). De même, l'incidence du paludisme a diminué dans la région Afrique de l'OMS, avec 294 cas pour 1 000 en 2010 contre 229 en 2018 (-22 %). Toutes les autres régions de l'OMS ont enregistré des progrès très modestes, voire une hausse de l'incidence. Dans la région Amériques de l'OMS, l'incidence du paludisme a augmenté, principalement à cause d'une transmission accrue au Venezuela (République bolivarienne du).
- Seuls 31 pays dans lesquels le paludisme est encore endémique ont réduit l'incidence du paludisme de manière significative entre 2015 et 2018 et étaient donc en passe d'atteindre une baisse de l'incidence égale à au moins 40 % d'ici 2020. À moins d'un changement rapide, les objectifs de morbidité définis pour 2025 et 2030 dans la *Stratégie technique de lutte contre le paludisme 2016-2030* ([le] GTS) ne seront pas atteints.
- *P. falciparum* est le parasite du paludisme le plus prévalent dans la région Afrique de l'OMS ; il est en effet à l'origine de 99,7 % des cas de paludisme estimés en 2018, tout comme dans les régions Asie du Sud-Est (50 %), Méditerranée orientale (71 %) et Pacifique occidental (65 %).
- Au niveau mondial, 53 % des cas de paludisme à *P. vivax* sont enregistrés dans la région Asie du Sud-Est de l'OMS, avec une majorité des cas en Inde (47 %). *P. vivax* prédomine dans la région Amériques de l'OMS, représentant 75 % des cas de paludisme.

Mortalité associée

- Au niveau mondial, le nombre de décès dus au paludisme a été estimé à 405 000 en 2018, contre 416 000 en 2017 et 585 000 en 2010.
- Les enfants de moins de 5 ans sont les plus vulnérables face au paludisme. En 2018, ils ont représenté 67 % (272 000) des décès associés au paludisme dans le monde.
- À elle seule, la région Afrique de l'OMS a enregistré 94 % des décès liés au paludisme dans le monde en 2018. Pourtant, elle a aussi représenté 85 % des 180 000 décès en moins dus à la maladie par rapport à 2010.

[1] La liste des pays d'Afrique subsaharienne est disponible à l'adresse https://unstats.un.org/unsd/methodology/m49 ; pour toutes les analyses présentées dans ce rapport et liées aux pays d'endémie du paludisme en Afrique subsaharienne, le Soudan est également inclus.

- Près de 85 % des décès dus au paludisme dans le monde en 2018 ont été concentrés dans 20 pays de la région Afrique de l'OMS et en Inde. Le Nigéria a représenté à lui seul près de 24 % de ces décès, suivi par la République démocratique du Congo (11 %), la République-Unie de Tanzanie (5 %), ainsi que l'Angola, le Mozambique et le Niger (4 % chacun).
- Par rapport à 2010, la mortalité liée au paludisme n'a diminué en 2018 que dans les régions Afrique et Asie du Sud-Est de l'OMS. La baisse la plus prononcée du nombre de décès dus au paludisme, en valeur absolue, a été observée dans la région Afrique de l'OMS, qui est passée de 533 000 décès en 2010 à 380 000 en 2018. Malgré ces progrès, la baisse de la mortalité liée au paludisme a ralenti depuis 2016.

CONSÉQUENCES DU PALUDISME SUR LA SANTÉ MATERNELLE ET INFANTILE

- En 2018, près de 11 millions de femmes enceintes vivant dans des zones de transmission modérée à élevée en Afrique subsaharienne auraient été exposées à une infection palustre.
- Cette même année, la prévalence de l'exposition à l'infection palustre durant la grossesse a été plus forte dans les sous-régions Afrique de l'Ouest et Afrique centrale (chacune avec 35 %), suivies par la sous-région Afrique de l'Est et Afrique australe (20 %). Près de 39 % de cette prévalence a été concentrée en République démocratique du Congo et au Nigéria.
- Les 11 millions de femmes enceintes exposées à une infection palustre en 2018 ont donné naissance à quelque 872 000 enfants présentant un faible poids à la naissance (soit 16 % de tous les enfants avec un faible poids à la naissance dans ces pays). L'Afrique de l'Ouest a enregistré la plus forte prévalence d'insuffisance pondérale (liée au paludisme pendant la grossesse) chez le nouveau-né.
- Entre 2015 et 2018, dans 21 pays de la région Afrique de l'OMS où la transmission du paludisme est modérée à élevée, la prévalence de l'anémie chez les enfants de moins de 5 ans avec un résultat positif à un test de diagnostic rapide (TDR) était deux fois plus élevée que chez les enfants avec un résultat de TDR négatif. Parmi les enfants avec un résultat de test positif, 9 % souffraient d'anémie grave et 54 % d'anémie modérée. À titre de comparaison, 1 % seulement des enfants non infectés par le paludisme souffraient d'anémie grave et 31 % d'anémie modérée.
- Les pays où l'anémie grave chez les enfants de moins de 5 ans présentant un résultat positif à un test de dépistage du paludisme était la plus prévalente étaient les suivants : le Sénégal (26 %), le Mali (16 %), la Guinée (14 %) et le Mozambique (12 %). Dans la plupart des autres pays, l'anémie grave atteignait entre 5 % et 10 %.
- Selon les estimations, près de 24 millions d'enfants d'Afrique subsaharienne ont souffert d'infections palustres à *P. falciparum* en 2018, avec un risque d'anémie grave pour 1,8 million d'entre eux.

APPROCHE « HIGH BURDEN TO HIGH IMPACT » (D'UNE CHARGE ÉLEVÉE À UN FORT IMPACT)

- Les 11 pays où le paludisme sévit le plus (pays de l'approche HBHI) ont enregistré près de 155 millions de cas en 2018, contre 177 millions en 2010. La République démocratique du Congo et le Nigéria ont cumulé 84 millions de ces cas (54 %).
- Parmi les 10 pays africains de l'approche HBHI, le Ghana et le Nigéria ont rapporté les plus fortes augmentations, en valeur absolue, du nombre de cas en 2018 par rapport à 2017. En 2018, le poids du paludisme dans les autres pays est resté à un niveau similaire à celui de 2017, à l'exception de l'Ouganda et de l'Inde, qui ont rapporté respectivement 1,5 million et 2,6 millions de cas en moins.
- Les décès dus au paludisme ont diminué, passant de près de 400 000 en 2010 à environ 260 000 en 2018. La plus forte baisse a été enregistrée au Nigéria, avec 153 000 décès en 2010 et 95 000 décès en 2018.
- En 2018, dans les 11 pays de l'approche HBHI, au moins 40 % de la population à risque avait dormi sous moustiquaire imprégnée d'insecticide longue durée (MILD). Le pourcentage le plus élevé a été enregistré en Ouganda (80 %), et le plus faible au Nigéria (40 %).

- Selon les estimations, c'est uniquement au Burkina Faso et en République-Unie de Tanzanie que plus de 50 % des femmes enceintes ont reçu trois doses de traitement préventif intermittent pendant la grossesse (TPIp3) en 2018. Au Cameroun, au Nigéria et en Ouganda, le taux de couverture a atteint environ 30 %, voire moins.
- Six pays de la sous-région sahélienne ont mis en œuvre la chimioprévention du paludisme saisonnier (CPS) en 2018. En moyenne, 17 millions d'enfants sur les 26 millions ciblés ont été traités par cycle de CPS.
- Le pourcentage des enfants de moins de 5 ans ayant de la fièvre et sollicitant des soins a varié entre 58 % au Mali et 82 % en Ouganda. En République démocratique du Congo et au Mali, plus de 40 % des enfants n'ont sollicité aucun soin. Tout aussi préoccupant, le taux de dépistage du paludisme a été très faible chez les enfants sollicitant des soins, avec 30 % ou moins d'enfants testés au Cameroun, en République démocratique du Congo et au Nigéria.
- Dans tous les pays de l'approche HBHI à l'exception de l'Inde, les investissements nationaux directs restent très peu élevés par rapport au financement international.

ÉLIMINATION DU PALUDISME ET PRÉVENTION DE SA RÉAPPARITION

- Au niveau mondial, l'élimination du paludisme progresse. En effet, de plus en plus de pays tendent vers un nombre de cas de paludisme indigène égal à zéro. En 2018, 49 pays ont rapporté moins de 10 000 cas de paludisme indigène, alors qu'ils n'étaient que 46 en 2017 et 40 en 2010. Le nombre de pays comptant moins de 100 cas de paludisme indigène, un bon indicateur que l'élimination de la maladie est proche, est passé de 17 en 2010 à 25 en 2017, puis à 27 en 2018.
- Le Paraguay et l'Ouzbékistan ont été certifiés exempts de paludisme par l'OMS en 2018, alors que l'Algérie et l'Argentine ont obtenu cette certification début 2019. En 2018, la Chine, El Salvador, l'Iran, la Malaisie et le Timor-Leste ont rapporté zéro cas de paludisme indigène.
- Éliminer le paludisme dans au moins 10 pays où il était encore endémique en 2010 est l'un des principaux objectifs intermédiaires du GTS pour 2020. Compte tenu du rythme de progression actuel, il est probable que cet objectif sera atteint.
- En 2016, l'OMS a identifié 21 pays ayant le potentiel pour éliminer le paludisme d'ici 2020. L'OMS travaille avec les gouvernements de ces pays appelés « E-2020 » pour les aider à atteindre leurs objectifs d'élimination.
- Même si 10 de ces pays restent en bonne voie pour atteindre leurs objectifs, les Comores et le Costa Rica ont rapporté une augmentation des cas de paludisme indigène en 2018 par rapport à 2017.
- En revanche, dans les six pays de la sous-région du Grand Mékong (Cambodge, Chine [province du Yunnan], République démocratique populaire lao, Myanmar, Thaïlande et Viet Nam), le nombre de cas de paludisme rapportés a diminué de 76 % entre 2010 et 2018, alors que le nombre de décès dus au paludisme a chuté de 95 % sur la même période. En 2018, le Cambodge n'a rapporté aucun décès dû au paludisme pour la première fois de son histoire.

INVESTISSEMENTS DANS LES PROGRAMMES ET LA RECHERCHE ANTIPALUDIQUES

- En 2018, US$ 2,7 milliards ont été investis au total par les gouvernements des pays d'endémie et les partenaires internationaux pour le contrôle et l'élimination du paludisme, soit une baisse par rapport aux US$ 3,2 milliards investis en 2017. Les investissements de 2018 sont bien inférieurs aux

US$ 5 milliards estimés nécessaires à l'échelle mondiale pour rester sur la voie des objectifs du GTS.

- Près des trois quarts des investissements réalisés en 2018 ont été dirigés vers la région Afrique de l'OMS, suivie par les régions Amériques (7 %), Asie du Sud-Est (6 %), Méditerranée orientale et Pacifique occidental (5 % chacune).
- En 2018, 47 % du financement total a été investi dans des pays à faible revenu, 43 % dans des pays à revenu intermédiaire de la tranche inférieure et 11 % dans des pays à revenu intermédiaire de la tranche supérieure. Les fonds internationaux ont représenté la principale source de financement dans les pays à faible revenu et à revenu intermédiaire de la tranche inférieure (respectivement 85 % et 61 %). Les financements nationaux stagnent depuis 2010.
- Sur les US$ 2,7 milliards investis en 2018, US$ 1,8 milliard provenaient de bailleurs de fonds internationaux. En 2018, les gouvernements des pays d'endémie ont contribué à hauteur de 30 % du financement total (US$ 900 millions), un chiffre inchangé par rapport à 2017. Deux tiers des financements nationaux ont été investis dans des activités de contrôle menées par les programmes nationaux de lutte contre le paludisme (PNLP), le tiers restant étant estimé correspondre aux coûts des soins dispensés aux patients.
- Comme les années précédentes, les États-Unis ont été le premier bailleur de fonds international pour les programmes de lutte contre le paludisme, avec US$ 1 milliard en 2018 (37 % du total). Les pays membres du Comité d'aide au développement ont investi au total US$ 300 millions (11 %). Le Royaume-Uni de Grande-Bretagne et d'Irlande du Nord a contribué à hauteur d'environ US$ 200 millions (7 %).
- Sur les US$ 2,7 milliards investis en 2018, US$ 1 milliard ont transité par le Fonds mondial de lutte contre le sida, la tuberculose et le paludisme.
- Même si le financement de la lutte contre le paludisme est relativement stable depuis 2010, les investissements consentis en 2018 sont loin d'atteindre le niveau requis pour réaliser les deux premiers objectifs intermédiaires du GTS, à savoir réduire d'au moins 40 % l'incidence du paludisme et la mortalité associée au plan mondial par rapport à 2015.
- Au total, US$ 663 millions ont été investis en 2018 dans la recherche fondamentale et le développement de produits contre le paludisme, soit une hausse de US$ 18 millions par rapport à 2017.
- Les fonds dédiés à la recherche et au développement (R&D) de médicaments ont atteint un niveau record, passant de US$ 228 millions en 2017 à US$ 252 millions en 2018. Cette augmentation est due aux investissements du secteur industriel privé dans plusieurs essais de phase II sur de nouveaux composants chimiques offrant le potentiel d'une guérison radicale en une prise unique.

Livraison de produits antipaludiques

Moustiquaires imprégnées d'insecticide

- Les fabricants de moustiquaires imprégnées d'insecticide (MII) ont indiqué en avoir livré 578 millions dans le monde entre 2016 et 2018, principalement des MILD, dont 50 % en Côte d'Ivoire, en République démocratique du Congo, en Éthiopie, au Ghana, en Inde, au Nigéria, en Ouganda et en République-Unie de Tanzanie.
- En 2018, ces fabricants ont livré environ 197 millions de MII, dont plus de 87 % en Afrique subsaharienne.
- Au niveau mondial, 80 % des MII ont été distribuées gratuitement par le biais de campagnes de distribution de masse, 10 % via des établissements de soins prénataux et 6 % dans le cadre de programmes de vaccination.

Tests de diagnostic rapide

- En 2018, 412 millions de TDR ont été vendus dans le monde.
- En 2018, 259 millions de TDR ont été distribués par les PNLP. La plupart de ces TDR (64 %) étaient des tests livrés en Afrique subsaharienne et pouvant uniquement détecter le parasite *P. falciparum*.

Combinaisons thérapeutiques à base d'artémisinine

- Entre 2010 et 2018, les pays ont acheté 3 milliards de traitements par combinaison thérapeutique à base d'artémisinine (ACT). Au total, 63 % de ces achats auraient été effectués pour le secteur public de la santé.
- En 2018, 214 millions de traitements par ACT ont été distribués par les PNLP, dont 98 % dans la région Afrique de l'OMS.

PRÉVENTION DU PALUDISME

Lutte antivectorielle

- En Afrique subsaharienne, la moitié de la population à risque dort sous MII : en 2018, 50 % de la population a donc été protégée par cette intervention, contre 29 % en 2010. Par ailleurs, la part de la population ayant accès à une MII est passée de 33 % en 2010 à 57 % en 2018. Le taux de couverture n'a cependant que très peu augmenté depuis 2015 et il s'est même stabilisé depuis 2016.
- Le pourcentage des ménages disposant d'au moins une MII pour deux membres du foyer est passé de 47 % en 2010 à 72 % en 2018. Ce pourcentage ne représente néanmoins qu'une augmentation très modeste au cours des trois dernières années et reste bien loin de l'objectif de couverture universelle.
- La part de la population à risque protégée par pulvérisation intradomiciliaire d'insecticides à effet rémanent (PID), une mesure préventive qui consiste à pulvériser d'insecticides les murs intérieurs des habitations, a diminué. Au niveau mondial, le taux de couverture de cette intervention a diminué, passant d'un pic de 5 % en 2010 à 2 % en 2018, avec des tendances à la baisse dans toutes les régions de l'OMS, hormis la région Méditerranée orientale.
- Même si la population à risque couverte par cette intervention a chuté de 180 millions en 2010 à 93 millions en 2018, elle est pour 2018 inférieure de 13 millions au niveau de 2017.
- Ce recul de la couverture en PID est sans doute lié au passage des pyréthoïdes à des insecticides plus onéreux en réponse à la résistance aux pyréthoïdes ou à des changements de stratégies opérationnelles (baisse de la population à risque dans les pays en voie d'élimination du paludisme).

Traitements préventifs

- En Afrique, pour protéger les femmes vivant dans des zones de transmission modérée à élevée, l'OMS recommande le traitement préventif intermittent pendant la grossesse (TPIp) par sulfadoxine-pyriméthamine (SP). Sur 36 pays africains ayant communiqué des données de couverture en TPIp en 2018, 31 % des femmes enceintes éligibles ont reçu au moins trois doses de TPIp (comme recommandé par l'OMS), contre 22 % en 2017 et 2 % en 2010, ce qui traduit des progrès considérables en termes de mise en œuvre au niveau national.
- Toutefois, environ 18 % des femmes s'étant présentées au moins une fois dans un établissement de soins prénataux n'ont reçu aucune dose de TPIp. Si elles avaient été exploitées, ces opportunités de traitement auraient permis d'améliorer considérablement et rapidement la couverture en TPIp.
- En 2018, 19 millions d'enfants vivant dans 12 pays d'Afrique sahélienne ont été protégés par des programmes de CPS. Tous les enfants ciblés ont reçu un traitement au Cameroun, en Guinée, en Guinée-Bissau et au Mali. Cependant, quelque 12 millions d'enfants qui auraient pu bénéficier de cette intervention n'ont pas été couverts, principalement à cause d'un manque de financements.

DIAGNOSTIC ET TRAITEMENT

Accès aux soins

- Un diagnostic précoce et un traitement rapide sont les moyens les plus efficaces de prévenir l'aggravation des cas de paludisme et les décès associés. D'après les enquêtes nationales réalisées dans 20 pays d'Afrique subsaharienne entre 2015 et 2018, une médiane de 42 % (écart interquartile [ÉI] : 34 %-49 %) des enfants ayant eu de la fièvre ont sollicité des soins auprès d'un prestataire formé dans un établissement public, contre une médiane de 10 % (ÉI : 8 %-22 %) dans un établissement privé formel et de 3 % (ÉI : 2 %-7 %) dans le secteur privé informel.
- Une part importante des enfants n'ont pas reçu de soins médicaux (médiane de 36 %, ÉI : 28 %-45 %), ce qui s'explique en partie par un accès limité aux prestataires de santé ou un manque de connaissances de la part du personnel soignant.

Diagnostic

- Le pourcentage de patients suspectés de paludisme et soumis à un test de diagnostic par TDR ou microscopie dans un établissement public est passé de 38 % en 2010 à 85 % en 2018.
- Dans 71 % des pays d'Afrique subsaharienne où la transmission est modérée à élevée, le pourcentage des cas suspectés de paludisme ayant été soumis à un test parasitologique a dépassé 80 % en 2018.
- Sur les 19 enquêtes nationales réalisées auprès des ménages en Afrique subsaharienne entre 2015 et 2018, le pourcentage médian d'enfants fiévreux ayant subi un prélèvement sanguin au doigt ou au talon (laissant penser qu'un test de dépistage du paludisme a été réalisé) a été plus élevé dans le secteur public (médiane de 66 %, ÉI : 49 %-75 %) que dans les établissements privés formels (médiane de 40 %, ÉI : 16 %-46 %) ou dans le secteur privé informel (médiane de 9 %, ÉI : 5 %-22 %).
- Sur 61 enquêtes menées dans 29 pays d'Afrique subsaharienne entre 2010 et 2018, le pourcentage des enfants fiévreux soumis à un test de diagnostic préalablement à tout traitement antipaludique dans un établissement public a augmenté, passant d'une médiane de 48 % (ÉI : 30 %-62 %) sur la période 2010-2013 à une médiane de 76 % (ÉI : 60 %-86 %) sur la période 2015-2018.

Traitement

- Sur 20 enquêtes nationales réalisées auprès des ménages en Afrique subsaharienne entre 2015 et 2018, le pourcentage médian des enfants fiévreux et ayant reçu un médicament antipaludique a été plus important dans le secteur public (médiane de 48 %, ÉI : 30 %-69 %) que dans le secteur privé formel (médiane de 40 %, ÉI : 21 %-51 %) ou le secteur privé informel (médiane de 18 %, ÉI : 10 %-29 %).
- Entre 2015 et 2018, les données collectées à partir de 20 enquêtes nationales menées en Afrique subsaharienne montrent que 47 % (ÉI : 29 %-69 %) des enfants fiévreux ayant sollicité des soins dans le secteur public ont reçu un traitement antipaludique, contre 59 % (ÉI : 53 %-84 %) auprès d'un agent de santé communautaire et 49 % (ÉI : 19 %-55 %) dans un établissement privé formel.
- D'après 19 enquêtes, la probabilité que les traitements antipaludiques donnés aux enfants fiévreux soient des ACT est légèrement plus élevée si le traitement est sollicité dans le secteur public (médiane de 80 %, ÉI : 45 %-94 %) que s'il l'est dans le secteur privé formel (médiane de 77 %, ÉI : 43 %-87 %) ou le secteur privé informel (médiane de 60 %, ÉI : 40 %-84 %).
- Pour combler les écarts de traitement parmi les enfants, l'OMS recommande la prise en charge intégrée des cas dans la communauté (PEC-C). Cette approche favorise la gestion intégrée des causes de mortalité infantile, à savoir paludisme, pneumonie et diarrhée, au niveau des établissements de santé et de la communauté. En 2018, 30 pays avaient des politiques de PEC-C en place à différents niveaux, mais la mise en œuvre n'était effective au niveau national que dans quelques-uns.

SYSTÈMES DE SURVEILLANCE DU PALUDISME

- Faire de la surveillance du paludisme une intervention de base est le pilier 3 du GTS. Pour savoir si les systèmes de surveillance du paludisme en place sont adaptés, l'OMS recommande un suivi et une évaluation à intervalles réguliers de ces systèmes.
- En collaboration avec l'Université d'Oslo, le Programme mondial de lutte antipaludique a développé des modules sur le paludisme uniformisés et intégrés à District Health Information Software2 (DHIS2). Ils permettent une collecte basée sur les cas et agrégée des données de routine, ainsi que la mise à disposition d'éléments associés, de tableaux de bord des principaux indicateurs épidémiologiques, d'indicateurs de qualité des données, de rapports et d'un programme d'analyse des données au niveau des établissements en vue de faciliter l'analyse et l'interprétation des données.
- En date du mois d'octobre 2019, 23 pays avaient installé le module agrégé de l'OMS sur le paludisme, et six autres installations étaient planifiées pour 2020. Cinq pays ont déjà développé leur propre module sur le paludisme et l'ont intégré à DHIS2.
- L'OMS travaille conjointement avec les départements chargés des systèmes de gestion de l'information sanitaire de différents ministères de la Santé, en particulier dans les pays de l'approche HBHI, pour établir des bases de données dynamiques structurées, appelées référentiels de données. Le Programme mondial de lutte antipaludique a ainsi développé une structure de référentiel facile à adapter dans DHIS2, ainsi que des directives sur des éléments de données et des indicateurs pertinents, leurs définitions et les calculs en vue de couvrir les domaines thématiques essentiels. À ce jour, le travail de développement de ces bases de données a commencé en Gambie, au Ghana, au Mozambique, au Nigéria, en Ouganda et en République-Unie de Tanzanie.
- L'OMS encourage également les pays à mettre en œuvre des évaluations de leur système de surveillance. L'étude de cas du Mozambique est un parfait exemple de ce genre d'évaluation et de son rôle pour améliorer les systèmes de surveillance.

RÉPONSES AUX MENACES BIOLOGIQUES EN MATIÈRE DE LUTTE CONTRE LE PALUDISME

Suppression du gène *pfhrp2/3*

- La suppression des gènes *pfhrp2* et *pfhrp3* (*pfhrp2/3*) du parasite rendent ces derniers indétectables par les TDR basés sur la protéine riche en histidine 2 (HRP2). La prévalence des deux gènes *pfhrp2* et *pfhrp3* chez les patients symptomatiques a atteint jusqu'à 80 % en Érythrée et au Pérou.
- L'OMS a recommandé aux pays rapportant des suppressions des gènes *pfhrp2/3* ou à leurs pays voisins de mener des études de référence représentatives sur les cas suspectés de paludisme, afin de déterminer si la prévalence des suppressions *pfhrp2/3* causant des résultats de TDR négatifs avait atteint un seuil qui nécessite un changement de TDR (suppressions du gène *pfhrp2* > 5 % causant des faux résultats de TDR négatifs).
- L'OMS effectue un suivi des rapports publiés sur les suppressions des gènes *pfhrp2/3* par le biais de l'outil de cartographie Carte des menaces du paludisme. À ce jour, 28 pays ont rapporté des suppressions du gène *pfhrp2*.

Résistance aux antipaludiques

- Des mutations du gène *PfKelch13* ont été identifiées en tant que marqueurs moléculaires de résistance partielle à l'artémisinine. Ces mutations *PfKelch13* associées à la résistance à l'artémisinine sont répandues dans la sous-région du Grand Mékong et ont également été détectées avec une forte prévalence (plus de 5 %) au Guyana, en Papouasie-Nouvelle-Guinée et au Rwanda. Dans le cas du Rwanda, la présence de mutations *PfKelch13* n'affecte pas l'efficacité des traitements de première intention.

- Dans la région Pacifique occidental de l'OMS, diverses études menées entre 2001 et 2018 ont confirmé une résistance à l'artémisinine au Cambodge, en République démocratique populaire lao et au Viet Nam. L'efficacité du traitement contre les infections à *P. vivax* reste élevée dans tous les pays où le taux d'échec au traitement est inférieur à 10 %.
- Dans la région Afrique de l'OMS, les taux d'efficacité des traitements à base d'artéméther-luméfantrine (AL), d'artésunate-amodiaquine (AS-AQ) et de dihydroartémisinine-pipéraquine (DHA-PPQ) contre les infections à *P. falciparum* ont été supérieurs à 98 %, et l'efficacité n'a jamais faibli au fil du temps.
- L'efficacité des traitements de première intention reste élevée contre les infections à *P. falciparum* et à *P. vivax* dans la région Amériques de l'OMS.
- Dans la région Asie du Sud-Est de l'OMS, la présence de marqueurs moléculaires de résistance à l'artémisinine a été rapportée au Bangladesh, en Inde, au Myanmar et en Thaïlande. À l'exception du Myanmar, les taux d'échec des ACT de première intention contre les infections à *P. falciparum* se sont avérés supérieurs à 10 % et ont même atteint 93 % en Thaïlande. Concernant les infections à *P. vivax*, la plupart des pays continuent d'enregistrer une grande efficacité de la chloroquine (CQ), sauf au Myanmar et au Timor-Leste.
- Dans la région Méditerranée orientale de l'OMS, les taux d'échec importants des traitements à base d'AS-SP contre les infections à *P. falciparum* en Somalie et au Soudan ont induit un changement dans la politique du traitement de première intention en faveur de l'AL. Concernant les infections à *P. vivax*, l'efficacité des traitements à base d'AL et de CQ est élevée dans tous les pays où une étude sur leur efficacité thérapeutique a été menée.

Résistance aux insecticides

- De 2010 à 2018, quelque 81 pays ont transmis à l'OMS des données de surveillance sur la résistance aux insecticides.
- Sur les 81 pays d'endémie palustre ayant fourni des données pour la période 2010-2018, la résistance à au moins une des quatre classes d'insecticides chez l'un des vecteurs du paludisme sur un site de collecte a été détectée dans 73 pays. Il s'agit là d'une augmentation de cinq pays par rapport à la période précédente de 2010-2017. Dans 26 pays, la résistance a été rapportée à toutes les principales classes d'insecticides.
- La résistance aux pyréthoïdes, la seule classe d'insecticides actuellement utilisés dans les MII, est répandue. Elle a été détectée chez au moins un des vecteurs du paludisme sur plus des deux tiers des sites testés et s'est avérée la plus élevée dans les régions Afrique et Méditerranée orientale de l'OMS.
- La résistance aux organochlorés a été détectée chez au moins un des vecteurs du paludisme sur près des deux tiers des sites. La résistance aux carbamates et aux organophosphorés a été moins prévalente, mais a été détectée, respectivement, sur 31 % et 26 % des sites testés. La résistance la plus prévalente aux carbamates a été détectée dans la région Asie du Sud-Est de l'OMS, et aux organophosphorés dans les régions Asie du Sud-Est et Pacifique occidental de l'OMS.
- Toutes les données standard sur la résistance aux insecticides rapportées à l'OMS sont intégrées à la base de données mondiales de l'OMS sur la résistance aux insecticides, et leur accès à des fins d'exploration est possible via la Carte des menaces du paludisme. Cet outil en ligne a été enrichi en 2019 pour couvrir les espèces de moustiques envahissantes et présente à l'heure actuelle la dimension géographique des rapports sur la détection des espèces *Anopheles stephensi*.
- Pour orienter la gestion de la résistance, les pays doivent développer et mettre en œuvre des plans nationaux de suivi et de gestion de la résistance aux insecticides, en se basant sur le *Cadre conceptuel d'un plan national de suivi et de gestion de la résistance aux insecticides chez les vecteurs du paludisme* élaboré par l'OMS. En 2018, 45 pays ont indiqué avoir établi un plan de suivi et de gestion de la résistance, et 36 en étaient encore à la phase de développement.
- Les PNLP et leurs partenaires devraient envisager de déployer des moustiquaires imprégnées de butoxyde de pipéronyle (PBO) dans les zones géographiques où les principaux vecteurs du paludisme répondent aux critères recommandés par l'OMS en 2017, plutôt qu'en partant du principe que tout le pays doit répondre à ces critères.

Prefacio

Dr Tedros Adhanom Ghebreyesus
Director General
Organización Mundial de la Salud (OMS)

No dejar a nadie atrás en la marcha hacia un mundo libre de malaria

El flagelo de la malaria continúa golpeando con más fuerza a las mujeres embarazadas y a los niños en África. El *Informe mundial sobre la malaria 2019* incluye una sección especial centrada en la carga y las consecuencias de la enfermedad entre estos dos grupos de mayor riesgo. Transmite un mensaje claro: todos debemos hacer más para proteger a los más vulnerables en la lucha contra una enfermedad que sigue cobrando más de 400 000 vidas cada año.

La malaria en el embarazo compromete la salud de la madre y la pone en mayor riesgo de muerte. Afecta la salud del feto, lo que lleva a la prematuridad y al bajo peso al nacer, los principales contribuyentes de la mortalidad neonatal e infantil. El año pasado, unos 11 millones de mujeres embarazadas en África subsahariana se infectaron con malaria y, en consecuencia, casi 900 000 niños nacieron con bajo peso al nacer.

Para proteger a las mujeres embarazadas en África, la OMS recomienda el uso de mosquiteros tratados con insecticidas (MTI) y medicamentos antimaláricos preventivos. Este informe muestra el progreso en ambos frentes. Aún así, casi el 40% de las mujeres embarazadas no durmieron bajo un MTI en 2018 y dos tercios no recibieron las tres o más dosis recomendadas de terapia preventiva.

En los niños, los esfuerzos para ampliar el acceso a los medicamentos antipalúdicos preventivos están dando frutos. En la subregión del Sahel de África, la OMS recomienda la quimio-prevención de la malaria estacional durante la temporada alta de transmisión. Más del 60% de los niños que viven en áreas elegibles para esta terapia preventiva la recibieron en 2018.

Se debe elogiar a Sierra Leona por convertirse en el primer país de África en implementar un tratamiento preventivo intermitente en infantes, otro enfoque recomendado por la OMS para proteger a los niños pequeños en las áreas afectadas por la malaria.

Aún así, el acceso a la atención de los niños que muestran signos de fiebre sigue siendo demasiado bajo. Las encuestas de países muestran que casi 40% de los niños febriles en África subsahariana no son atendidos por un proveedor de atención médica capacitado.

Al menos 10 países que forman parte de la "Iniciativa E-2020" de la OMS están en camino de alcanzar la eliminación en 2020, hito de nuestra estrategia mundial contra la malaria. En 2015, todos estos países eran endémicos de malaria; ahora han logrado cero casos autóctonos de malaria o se están acercando a ésta meta.

Sin embargo, en los últimos años, el progreso global de la reducción de nuevos casos de malaria se ha estabilizado. Lo más preocupante de todo es que la malaria está en aumento en algunos países de alta carga en África.

Es probable que se pierdan los hitos críticos de nuestra estrategia global contra la malaria.

En 2018, la OMS y la Alianza para Hacer Retroceder la Malaria lanzaron el nuevo enfoque de "Alta carga a alto impacto", para prevenir la enfermedad y salvar vidas en los países más afectados por la malaria. Reemplazando una estrategia de "talla única", el enfoque requiere el uso de las herramientas más efectivas de una manera más específica. Me complace observar que dos países, India y Uganda, han reportado reducciones sustanciales en los casos de malaria en 2018 comparado con el año anterior.

En septiembre, emití el "Reto de la malaria", que pedía una mayor inversión en investigación y el desarrollo de nuevas herramientas, tecnologías y enfoques transformadores para acelerar el progreso en la lucha contra esta enfermedad.

A través de un programa piloto coordinado por la OMS, Ghana, Kenia y Malawi introdujeron recientemente, en áreas seleccionadas, la primera vacuna contra la malaria del mundo. La evidencia y la experiencia del programa informarán las decisiones de política sobre el posible uso más amplio de la vacuna en África. Con el apoyo del Fondo Mundial para la lucha contra el VIH/SIDA, la tuberculosis y la malaria y del Unitaid, se están probando otras herramientas prometedoras, como nuevos tipos de mosquiteros tratados con insecticidas e intervenciones dirigidas a los mosquitos que pican fuera de las viviendas.

Lograr nuestra visión común de un mundo libre de malaria también requerirá mejorar acciones en otras áreas críticas. Necesitamos servicios de salud asequibles y centrados en las personas. Necesitamos sistemas de vigilancia y respuesta confiables y precisos. Necesitamos estrategias que se adapten a los entornos locales de transmisión de la malaria.

Acelerar el financiamiento para responder a la malaria es esencial. En 2018, el financiamiento total para el control y la eliminación de la malaria alcanzó un estimado de US $ 2.7 mil millones, muy por debajo del objetivo de financiamiento de US $ 5 mil millones de nuestra estrategia global.

A través de una financiación sólida y decidida, liderazgo político y cobertura de salud universal, podemos vencer esta enfermedad de una vez por todas.

El informe de este año de un vistazo

TENDENCIAS REGIONALES Y MUNDIALES SOBRE LA CARGA DE CASOS Y MUERTES POR MALARIA

Casos de malaria

- En 2018, se estima que hubo 228 millones de casos de malaria en todo el mundo (intervalo de confianza [IC] del 95%: 206–258 millones), en comparación con 251 millones de casos en 2010 (IC del 95%: 231–278 millones) y 231 millones de casos en 2017 (IC 95%: 211–259 millones).
- La mayoría de los casos de malaria en 2018 se produjeron en la Región de África de la Organización Mundial de la Salud (OMS) (213 millones o 93%), seguida de la Región de Asia Sudoriental con el 3,4% de los casos y la Región del Mediterráneo Oriental con el 2.1%.
- Diecinueve países en África subsahariana[1] e India sumaron casi el 85% de la carga mundial de malaria. Mas de la mitad de todos los casos de malaria en todo el mundo se concentró en seis países: Nigeria (25%), la República Democrática del Congo (12%), Uganda (5%) y Costa de Marfil, Mozambique y Níger (4% cada uno).
- La tasa de incidencia de la malaria disminuyó a nivel mundial entre 2010 y 2018, de 71 a 57 casos por 1000 habitantes en riesgo. Sin embargo, de 2014 a 2018, la tasa de cambio disminuyó drásticamente, reduciendo a 57 en 2014 y permaneciendo en niveles similares hasta 2018.
- En la Región de Asia Sudoriental de la OMS la tasa de incidencia continúo disminuyendo: de 17 casos por cada 1000 habitantes en riesgo en 2010 a cinco casos en 2018 (una disminución del 70%). En la Región de África, los niveles de incidencia de casos también disminuyeron de 294 en 2010 a 229 en 2018, lo que representa una reducción del 22%. Todas las demás regiones de la OMS registraron poco progreso o un aumento en la tasa de incidencia. La Región de las Américas de la OMS registró un aumento, en gran parte debido a los aumentos en la transmisión de la malaria en la República Bolivariana de Venezuela.
- Entre 2015 y 2018, solo 31 países endémicos redujeron significativamente la incidencia de casos y estaban en camino de reducir la incidencia en un 40% o más en el año 2020. Sin un cambio acelerado, los hitos de la Estrategia Técnica Mundial contra la malaria 2016–2030 (ETM) relacionados con la morbilidad en 2025 y 2030 no se van a lograr.
- *Plasmodium falciparum* es el parásito de la malaria más frecuente en la Región de África de la OMS, representando el 99.7% de los casos estimados de malaria en 2018, así como en la Región de Asia Sudoriental de la OMS (50%), Región del Mediterráneo Oriental (71%) y Región del Pacífico occidental (65%).
- A nivel mundial, el 53% de la carga de *P. vivax* se concentra en la Región de Asia Sudoriental de la OMS, con la mayoría en India (47%). *P. vivax* es el parásito predominante en la Región de las Américas, representando el 75% de los casos de malaria.

Muertes por malaria

- En 2018, se estimaron 405 000 muertes por malaria en todo el mundo, comparado con 416 000 muertes estimadas en 2017 y 585 000 en 2010.
- Los niños menores de 5 años son el grupo más vulnerable afectado por la malaria. En 2018, este grupo represento el 67% (272 000) de todas las muertes por malaria en todo el mundo.

[1] La lista completa de países del África subsahariana puede consultarse en https://unstats.un.org/unsd/methodology/m49; Sudan ha sido incluido como país subsahariano en todos los análisis llevados a cabo para este informe para esta región.

- El 94% de todas las muertes por malaria en 2018 se produjo en la Región de África de la OMS. A pesar de ser la región que albergó la mayor cantidad de muertes por malaria en 2018, también es la región donde se produjo 85% de la reducción de muertes conseguida globalmente en 2018, 180 000 muertes de menos en comparación con 2010.
- Casi el 85% de las muertes por malaria en el mundo en 2018 se concentraron en 20 países de la Región de África de la OMS y la India. Nigeria representó casi el 50% de todas las muertes por malaria en el mundo, seguida de la República Democrática del Congo (11%), la República Unida de Tanzania (5%) y Angola, Mozambique y Níger (4% cada uno).
- En 2018, solo la Región de África de la OMS y la Región de Asia Sudoriental mostraron reducciones en las muertes por malaria en comparación con 2010. La Región de África tuvo la mayor reducción absoluta en las muertes por malaria, de 533 000 en 2010 a 380 000 en 2018. Sin embargo, a pesar de estas ganancias, la tasa de reducción de la mortalidad por malaria en esta región también se ha desacelerado desde 2016.

CONSECUENCIAS DE LA MALARIA PARA LA SALUD MATERNA, DE LOS INFANTES Y LOS NIÑOS

- En 2018, alrededor de 11 millones de embarazos en países con transmisión de malaria moderada y alta en el África subsahariana, habrían estado expuestas a una infección por malaria.
- En 2018, la prevalencia de exposición a infección por malaria durante el embarazo fue más alta en la subregión de África occidental y África central (cada una con un 35%), seguida de África oriental y Suráfrica (20%). Alrededor del 39% de esta exposición se concentró en la República Democrática del Congo y Nigeria.
- Los 11 millones de mujeres embarazadas expuestas a infecciones por malaria en 2018 dieron a luz a unos 872 000 niños con bajo peso al nacer (16% de todos los niños con bajo peso al nacer en estos países), con África Occidental teniendo la mayor prevalencia de niños con bajo peso al nacer atribuido a malaria durante el embarazo.
- Entre 2015 y 2018 en 21 países con carga de malaria de moderada a alta en la Región de África de la OMS, la prevalencia de anemia en niños menores de 5 años con una prueba de diagnóstico rápido (PDR) positivo fue el doble que la de los niños con una PDR negativa. En los niños con malaria confirmada, el 9% tenía anemia severa y el 54% tenía anemia moderada; en contraste, en los niños sin malaria, solo el 1% tenía anemia severa y el 31% tenía anemia moderada.
- Los países con el mayor porcentaje de anemia severa entre los niños menores de 5 años con malaria confirmada fueron Senegal (26%), Malí (16%), Guinea (14%) y Mozambique (12%). Para la mayoría de los otros países, la anemia severa varió del 5% al 10%.
- En general, se estimó que alrededor de 24 millones de niños estaban infectados con *P. falciparum* en 2018 en África subsahariana, y se estima que 1.8 millones de ellos tenían anemia severa.

ENFOQUE DE ALTA CARGA A ALTO IMPACTO

- En 2018, hubo alrededor de 155 millones de casos de malaria en los 11 países incluidos en el enfoque alta carga a alto impacto (ACAI), en comparación con 177 millones en 2010. La República Democrática del Congo y Nigeria tuvieron 84 millones (54% del total de casos).
- De los 10 países con mayor carga de malaria en África, Ghana y Nigeria reportaron, en 2018, los aumentos absolutos de casos más altos en comparación con 2017. La carga en 2018 fue similar a la de 2017 en los otros países, exceptuando Uganda e India, donde, en 2018, se reportó una reducción de 1.5 y 2.6 millones de casos, respectivamente en comparación con 2017.

- Las muertes por malaria se redujeron de aproximadamente de 400 000 en 2010 a aproximadamente 260 000 en 2018. La mayor reducción se produjo en Nigeria, donde las casi 153 000 muertes en 2010 pasaron a aproximadamente 95 000 en 2018.
- Para el año 2018, en todos los 11 países del enfoque ACAI, al menos el 40% de la población en riesgo durmió bajo mosquiteros tratados con insecticida de larga duración (MILD), el porcentaje más alto lo tuvo Uganda (80%) y el más bajo Nigeria (40%).
- En Burkina Faso y la República Unida de Tanzania, se estimó que más de la mitad de las mujeres embarazadas recibieron tres dosis de tratamiento preventivo intermitente durante el embarazo (TPI) en 2018. En Camerún, Nigeria y Uganda, la cobertura estimada fue de alrededor del 30% o menos.
- Seis países de la subregión africana del Sahel implementaron la quimio-prevención estacional de malaria (QPE) en 2018; de los 26 millones de niños objetivo, un total de 17 millones de niños, fueron tratados con QPE.
- El porcentaje de niños menores de 5 años con fiebre que buscaron tratamiento varió del 58% en Malí al 82% en Uganda. En la República Democrática del Congo y Malí, más del 40% de los niños no fueron llevados a recibir tratamiento. El porcentaje de niños que fueron diagnosticados también fue preocupantemente bajo entre los niños que fueron sometidos a tratamiento, con un 30% o menos de niños que fueron diagnosticados en Camerún, la República Democrática del Congo y Nigeria.
- A excepción de la India, en los países ACAI la inversión interna directa sigue siendo muy baja en relación con la financiación internacional.

ELIMINACIÓN DE LA MALARIA Y PREVENCIÓN DEL RESTABLECIMIENTO

- A nivel mundial, la red de eliminación se está ampliando, con más países avanzando hacia el objetivo de cero casos autóctonos: en 2018, 49 países reportaron menos de 10 000 de estos casos, frente a 46 países en 2017 y 40 países en 2010. El número de países con menos de 100 casos autóctonos, -un fuerte indicador de que la eliminación está cerca-, aumentó de 17 países en 2010 a 25 países en 2017 y 27 países en 2018.
- Paraguay y Uzbekistán obtuvieron la certificación de eliminación de la OMS en 2018, y Argelia y Argentina lograron la certificación a principios de 2019. En 2018, China, El Salvador, Irán, Malasia y Timor-Leste reportaron cero casos autóctonos.
- Uno de los hitos clave de la ETM para 2020 es la eliminación de la malaria en al menos 10 países de los que eran endémicos de malaria en 2015. Al ritmo actual de progreso, es probable que se alcance este hito.
- En 2016, la OMS identificó 21 países con el potencial de eliminar la malaria para el año 2020. La OMS está trabajando con los gobiernos de estos países, conocidos como "países E-2020", para apoyar sus objetivos de aceleración de la eliminación.
- Aunque hay 10 países del E-2020 que están en el buen camino para lograr sus objetivos de eliminación, en 2018 Comoros y Costa Rica informaron de aumentos en los casos de malaria autóctonos en comparación con 2017.
- En los seis países de la subregión del Gran Mekong (GM) - Camboya, China (provincia de Yunnan), República Democrática Popular Laos, Myanmar, Tailandia y Vietnam - el número de casos de malaria disminuyó en un 76% entre 2010 y 2018, y las muertes por malaria disminuyeron en un 95% durante el mismo período. En 2018, Camboya, por primera vez en la historia, reportó de que no hubo muertes relacionadas con la malaria denle el país.

INVERSIONES EN LOS PROGRAMAS DE MALARIA E INVESTIGACIÓN

- En 2018, los gobiernos de los países endémicos de malaria y sus colaboradores internacionales invirtieron aproximadamente $ 2.700 millones en esfuerzos de control y eliminación de la malaria a nivel mundial, menos que los $ 3.200 millones que se invirtieron en 2017. La cantidad invertida en 2018 es insuficiente dado que se estima que se requieren $ 5.0 mil millones para continuar avanzando hacia el complimiento de los objetivos de la ETM.
- Casi tres cuartas partes de las inversiones en 2018 se gastaron en la Región de África de la OMS, seguidas por la Región de las Américas (7%), la Región de Asia Sudoriental (6%), la Región del Mediterráneo Oriental y la Región del Pacífico Occidental (5% cada uno).
- En 2018, el 47% de la financiación total para la malaria se invirtió en países de bajos ingresos, el 43% en países de ingresos bajo a medio y el 11% en países de ingresos medio a alto. La financiación internacional representó la principal fuente de financiación en los países de bajos y de bajo a medios ingresos, con 85% y 61% respectivamente. La financiación interna se ha mantenido estable desde 2010.
- De los $ 2.700 millones de dólares invertidos en 2018, $ 1.800 millones provienen de financiadores internacionales. Los gobiernos de los países endémicos contribuyeron con el 30% de la financiación total ($ 900 millones de dólares) en 2018, una cifra sin cambios desde 2017. Dos tercios de los fondos de origen nacional se invirtieron en actividades de control de la malaria llevadas a cabo por los programas nacionales de malaria (PNM), siendo el resto estimado como el costo de atención a los pacientes.
- Como en años anteriores, los Estados Unidos de América (EE. UU.) Fue la mayor fuente internacional de financiación de la malaria, proporcionando $ 1 mil millones de dólares (37%) en 2018. Los países miembros del Comité de Asistencia para el Desarrollo representaron $ 300 millones (11%). El Reino Unido de Gran Bretaña e Irlanda del Norte contribuyeron con alrededor de $ 200 millones (7%).
- De los $ 2.700 millones de dólares invertidos en 2018, $ 1.000 millones se canalizaron a través del Fondo Mundial de Lucha contra el SIDA, la Tuberculosis y la Malaria.
- Aunque la financiación para la malaria se ha mantenido relativamente estable desde 2010, el nivel de inversión en 2018 está lejos de lo que se requiere para alcanzar los dos primeros hitos de la ETM; es decir, conseguir, para el 2020, una reducción de al menos el 40% en la incidencia de casos de malaria y en las tasas de mortalidad a nivel mundial en comparación con los niveles de 2015.
- Se invirtieron $ 663 millones de dólares en investigación básica y desarrollo de productos para la malaria en 2018, un aumento de $ 18 millones en comparación con 2017.
- La financiación para investigación y desarrollo de medicamentos antimaláricos llego al nivel más alto jamás registrado, de $ 228 millones en 2017 a $ 252 millones de dólares en 2018. Este aumento fue el resultado de la inversión del sector privado en varios ensayos de Fase II de nuevos productos con potencial de curación radical con una dosis única.

Distribución de productos básicos contra la malaria

Mosquiteros tratados con insecticida

- Entre 2016 y 2018, de acuerdo con los fabricantes, se entregaron 578 millones de mosquiteros tratados con insecticida (MTI), principalmente MILD, con un 50% destinado a Costa de Marfil, República Democrática del Congo, Etiopía, Ghana, India, Nigeria, Uganda y la República Unida de Tanzania.
- En 2018, los fabricantes entregaron alrededor de 197 millones de MILD, de los cuales más del 87% fueron entregados a países del África subsahariana.
- A nivel mundial, el 85% de los MTI se distribuyeron a través de campañas gratuitas de distribución masiva, el 10% en centros de atención prenatal y el 6% como parte de los programas de inmunización.

Pruebas de diagnóstico rápido (PDR).

- Se estima que 412 millones de PDR se vendieron a nivel mundial en 2018.
- En 2018, los PNM distribuyeron 259 millones de PDR. La mayoría de las PDR (64%) fueron pruebas para detectar *P. falciparum* y se suministraron al África subsahariana.

Terapia combinada basada en artemisinina

- Se estima que 3,000 millones de tratamientos de terapia combinada basada en artemisinina (TCA) fueron adquiridos por los países durante el período 2010-2018 y que el 63% fue adquirido por el sector público.
- En 2018, los PNM distribuyeron 214 millones de tratamientos con TCA, el 98% fueron en la Región de África de la OMS.

PREVENCIÓN DE LA MALARIA

Control de vectores

- La mitad de las personas en riesgo de malaria en África están durmiendo bajo un MTI; en 2018, el 50% de la población estaba protegida por esta intervención, un aumento del 29% comparado con 2010. Además, el porcentaje de la población con acceso a un MTI aumentó del 33% en 2010 al 57% en 2018. Sin embargo, la cobertura mejoró solo marginalmente desde 2015 y se ha estancado desde 2016.
- El porcentaje de hogares con al menos un MTI por cada dos personas aumentaron a 72% en 2018, de 47% en 2010. Sin embargo, esta cifra representa solo un aumento modesto en los últimos 3 años, y sigue estando lejos del objetivo de cobertura universal.
- El número de personas en riesgo de contraer malaria protegidas por el rociado residual intradomiciliar (RRI), un método de prevención que implica el rociado de insecticidas en las paredes interiores de las viviendas, está disminuyendo. A nivel mundial, la protección del RRI disminuyó de un pico del 5% en 2010 al 2% en 2018, año en el que se observaron disminuciones en todas las regiones de la OMS, salvo en la Región del Mediterráneo Oriental.
- Aunque la cobertura del RRI en la Región de África de la OMS cayo de 180 millones de personas en riesgo protegidas en 2010 a 93 millones en 2018, la cobertura disminuyó de 13 millones de personas entre 2017 y 2018.
- La disminución de la cobertura del RRI puede deberse los cambios en los insecticidas usados, la transición de piretroides a insecticidas más caros en respuesta al aumento de la resistencia a los piretroides; o a cambios en las estrategias operativas (por ejemplo, la disminución de las poblaciones en riesgo en los países en vías de eliminación de la malaria).

Terapias preventivas

- Para proteger a las mujeres en áreas de transmisión de malaria moderada y alta en África, la OMS recomienda TPI con el antimalárico sulfadoxina-pirimetamina (SP). Entre los 36 países africanos que informaron sobre los niveles de cobertura de TPI en 2018, se estima que el 31% de las mujeres embarazadas elegibles recibieron las tres o más dosis recomendadas de TPI, en comparación con el 22% en 2017 y el 0% en 2010, lo que indica mejoras considerables en la implementación de esta intervención en los países.
- Alrededor del 18% de las mujeres que utilizaron los servicios de atención prenatal al menos una vez, no recibieron ninguna dosis de TPI, lo que representa una oportunidad perdida que, si se aprovecha, podría mejorar considerablemente y rápidamente la cobertura de TPI.
- En 2018, 19 millones de niños en 12 países de la subregión del Sahel de África fueron protegidos a través de programas de quimio-prevención estacional (QPE). Todos los niños seleccionados recibieron tratamiento en Camerún, Guinea, Guinea-Bissau y Malí. Sin embargo, unos 12 millones de niños que podrían haberse beneficiado de esta intervención no lo hicieron. Esto es debido principalmente a la falta de fondos.

PRUEBAS DE DIAGNÓSTICO Y TRATAMIENTO

Acceso a la atención médica

- El diagnóstico y el tratamiento oportunos son la forma más efectiva de evitar que un caso leve de malaria se convierta en enfermedad grave y que cause la muerte. Según las encuestas nacionales de hogares realizadas en 20 países del África subsahariana entre 2015 y 2018, una mediana del 42% (rango inter-cuartil [RI]: 34-49%) de los niños con fiebre (febriles) fueron trasladados a un proveedor de atención médica capacitado en el sector público, comparado con el 10% (RI: 8–22%) en el sector privado formal y el 3% (RI: 2–7%) en el sector privado informal.
- Una alta proporción de niños febriles no recibió atención médica (mediana: 36%, RI: 28–45%). El pobre acceso a los proveedores de atención médica o la falta de conocimiento de los síntomas de la malaria entre los cuidadores son algunos de los factores que contribuyen a esta falta de atención médica.

Diagnóstico de la malaria

- El porcentaje de pacientes con sospecha de malaria, que son atendidos en centros de salud pública y examinados con una PDR o microscopía, aumentó del 38% en 2010 al 85% en 2018.
- En 2018, en el 71% de los países con transmisión moderada a alta en el África subsahariana, el porcentaje de casos con sospecha de malaria a quienes se les realizó una prueba parasitológica fue superior al 80%.
- Según 19 encuestas de hogares a nivel nacional, realizadas entre 2015 y 2018 en África subsahariana, el porcentaje promedio de niños febriles que fueron atendidos y recibieron un pinchazo en el dedo o el talón (lo que sugiere que pudo haberse realizado una prueba de diagnóstico de malaria) fue mayor en el sector público (mediana: 66%, RI: 49–75%) que en el sector privado formal (mediana: 40%, RI: 16–46%) o el sector privado informal (mediana: 9%, RI: 5– 22%).
- Según 61 encuestas de hogares realizadas en 29 países del África subsahariana entre 2010 y 2018, el porcentaje de niños con fiebre que recibieron una prueba de diagnóstico antes de recibir tratamiento antimalárico en el sector de la salud pública aumentó de una mediana del 48% (RI: 30 –62%) en 2010–2013, a una mediana del 76% (RI: 60–86%) en 2015–2018.

Tratamiento de la malaria

- Según 20 encuestas de hogares realizadas en África subsahariana en 2015–2018, el porcentaje medio de niños febriles que fueron tratados con algún medicamento antimalárico fue mayor en el sector público (mediana: 48%, RI: 30–69%) que en el sector privado formal (mediana: 40%, RI: 21–51%) o el sector privado informal (mediana: 18%, RI: 10–29%).
- Los datos de 20 encuestas nacionales realizados en África subsahariana muestran que, para el período 2015–2018, el 47% (RI: 29–69%) de los niños febriles que recibieron tratamiento para la malaria en el sector de la salud pública recibieron tratamiento antimalárico, en comparación con 59% (RI: 53–84%) entre quienes visitan a un trabajador de salud comunitario y 49% (RI: 19–55%) en el sector privado formal.
- Con base en 19 encuestas de hogares, los tratamientos antimaláricos dados a los niños febriles fueron más frecuentemente un TCA cuando se buscó tratamiento en el sector público (mediana: 80%, RI: 45-94%) que en el sector privado formal (mediana: 77%, RI: 43–87%) o el sector privado informal (mediana: 60%, RI: 40–84%).
- Para cerrar la brecha de tratamiento a los niños, la OMS recomienda la adopción del manejo integrado de casos por la comunidad (MICC). Este enfoque promueve el manejo integrado de condiciones de salud que comúnmente amenazan la vida de los niños (malaria, neumonía y diarrea) a nivel de centros de salud y comunitarios. En 2018, 30 países implementaron el MICC en diferentes niveles, con solo unos pocos implementando ésta a nivel nacional.

SISTEMAS DE VIGILANCIA DE LA MALARIA

- El pilar 3 de la Estrategia Mundial de malaria (ETM) es transformar la vigilancia de malaria en una intervención principal. Para comprender si los sistemas de vigilancia de la malaria son adecuados para su propósito, la OMS recomienda el monitoreo y la evaluación regulares de los sistemas de vigilancia.
- El Programa Global contra la Malaria (PGM), en colaboración con la Universidad de Oslo, ha desarrollado módulos estandarizados de vigilancia de malaria basados en el Software de Información de Salud del Distrito-2 (DHIS2) para la recogida de datos epidemiológicos de rutina, datos de casos individuales y datos de vigilancia entomológica y monitoria de intervenciones de control vectorial. Estos modules incluyen elementos de datos, indicadores de monitoria y de calidad de los datos, tableros estandarizados de interpretación de los datos e informes.
- Hasta octubre de 2019, 23 países han instalado el módulo agregado de malaria de la OMS, otras ocho instalaciones están planificadas para el próximo año y otros cinco países ya han desarrollado e integrado su propio módulo para la vigilancia de malaria en DHIS2.
- La OMS ha estado trabajando en coordinación con los departamentos de Sistemas de Información de Gestión de Salud (SIGS) de los ministerios de salud, en particular de los países ACAI, para establecer bases de datos dinámicas estructuradas conocidas como repositorios de datos. El PGM ha desarrollado una estructura de repositorio standard basada en DHIS2 y fácilmente adaptable, que contiene los elementos de datos e indicadores más relevantes, sus definiciones y computación para cubrir las áreas temáticas clave. Hasta ahora, el trabajo para desarrollar estas bases de datos ha comenzado en Gambia, Ghana, Mozambique, Nigeria, Uganda y la República Unida de Tanzania.
- La OMS también alienta a los países a implementar evaluaciones del sistema de vigilancia. Un ejemplo de estudio de caso de Mozambique ilustra tal evaluación y su papel en la mejora de los sistemas de vigilancia.

RESPONDIENDO A LOS DESAFÍOS BIOLÓGICAS EN LA LUCHA CONTRA LA MALARIA

Supresión del gen *Pfhrp2 / 3*

- La supresión de los genes *pfhrp2* y *pfhrp3* (*pfhrp2 / 3*) del parásito hacen que los parásitos sean indetectables por las PDR que se basan en la detección del HRP2. La supresión doble *pfhrp2* y *pfhrp3* entre pacientes sintomáticos ha alcanzado una prevalencia de hasta el 80% en Eritrea y Perú.
- La OMS ha recomendado a los países con evidencia de supresiones de *pfhrp2 / 3*, o los países vecinos, que realicen encuestas representativas entre los casos sospechosos de malaria para determinar si la prevalencia de supresión de *pfhrp2 / 3*, que causan falsos negativos en las PDR, ha alcanzado un umbral que indique la necesidad de cambio de PDR (> 5 % de deleciones en *pfhrp2* causan resultados de falsos negativos en PDR).
- La OMS está rastreando los informes publicados de supresiones *pfhrp2 / 3* utilizando la herramienta de mapeo del Mapa de los Desafíos de la Malaria. Hasta la fecha, 28 países han reportado supresiones de *pfhrp2*.

Resistencia a los medicamentos antimaláricos

- Las mutaciones de *PfKelch13* se han identificado como marcadores moleculares de resistencia parcial a la artemisinina. Las mutaciones de *PfKelch13* asociadas con la resistencia a la artemisinina están muy extendidas en la subregión del Gran Mekong (GM) y también se han detectado con una prevalencia significativa (más del 5%) en Guyana, Papua Nueva Guinea y Ruanda. En el caso de Ruanda, se ha visto que la presencia de mutaciones *PfKelch13* no afecta la eficacia del tratamiento de primera línea.

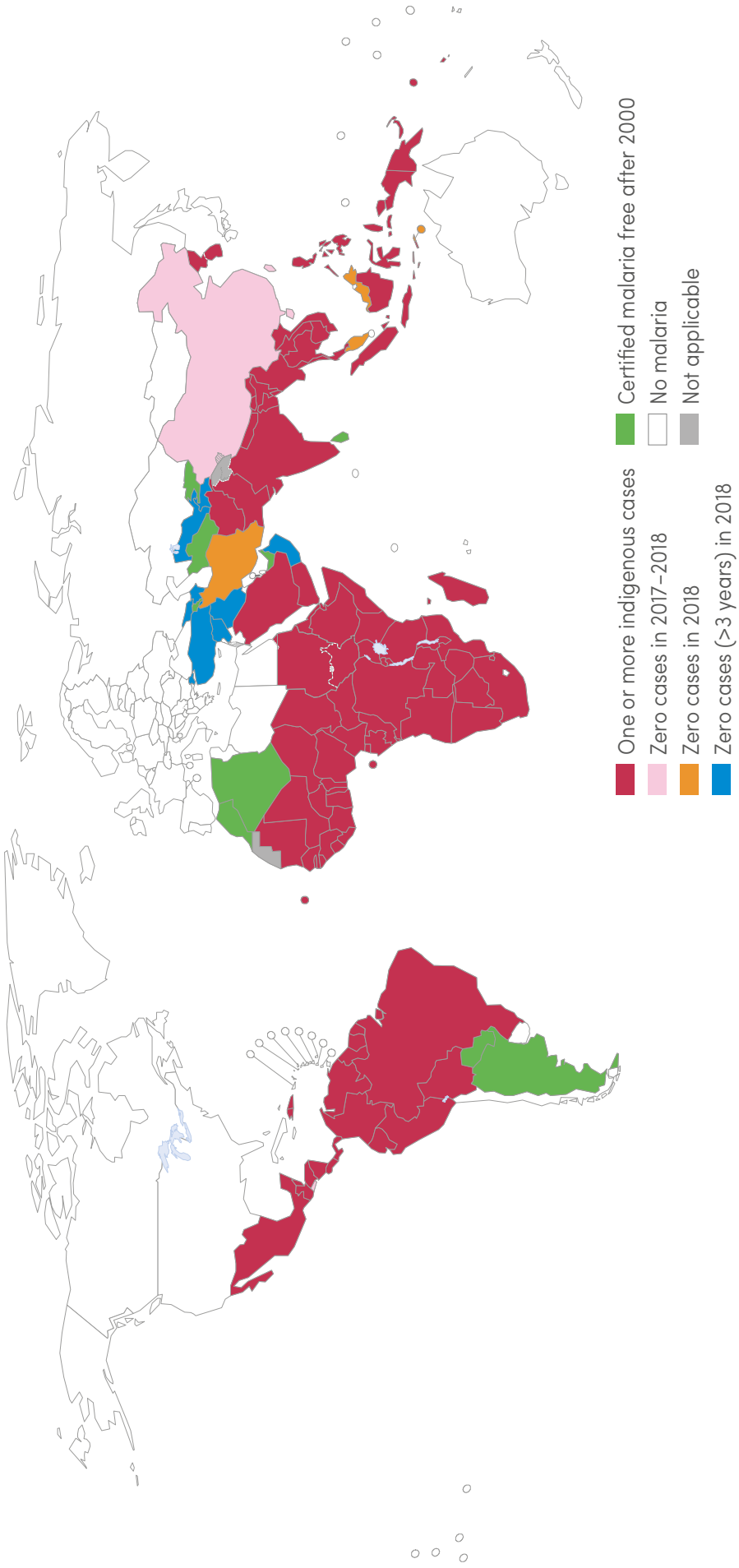
- En la Región del Pacífico Occidental de la OMS, la resistencia a la artemisinina se ha confirmado en Camboya, República Democrática Popular Lao y Vietnam a través de varios estudios realizados entre 2001 y 2018. La eficacia del tratamiento para *P. vivax* sigue siendo alta en todos los países, las tasas de fallo del tratamiento son inferiores al 10 %.
- En la Región de África, las tasas de eficacia de arteméter-lumefantrina (AL), artesunato-amodiaquina (AS-AQ) y dihidroartemisinina-piperaquina (DHA-PPQ) para *P. falciparum* fueron más del 98%, y la eficacia se ha mantenido alta a lo largo del tiempo.
- En la Región de las Américas, la eficacia del tratamiento para *P. falciparum*, contratamientos de primera línea, sigue siendo alta.
- En la Región de Asia Sudoriental, se han encontrado marcadores moleculares de resistencia a la artemisinina en Bangladesh, India, Myanmar y Tailandia. Con excepción de Myanmar, las tasas de fallo de los TCA de primera línea para *P. falciparum* fueron mayores que 10% y llegaron hasta el 93% en Tailandia. Con base a los estudios de eficacia terapéutica reportados, la cloroquina (CQ) sigue siendo altamente eficaz contra *P. vivax* en la mayoría de los países, excepto en Myanmar y Timor-Leste.
- En la Región del Mediterráneo Oriental, las altas tasas de fallo del tratamiento con AS-SP contra P. falciparum detectadas en Somalia y Sudán llevaron a un cambio en la política de tratamiento de primera línea que ahora es AL. Los estudios de eficacia terapéutica (EET) realizados con AL y CQ contra *P. vivax* indican una alta eficacia de estos tratamientos.

Resistencia a los insecticidas

- Desde 2010 hasta 2018, unos 81 países informaron datos a la OMS sobre el monitoreo de la resistencia a los insecticidas.
- De los 81 países endémicos de malaria que proporcionaron datos para 2010–2018, 73 confirmaron la resistencia a al menos una de las cuatro clases de insecticidas en al menos un vector de malaria y un sitio de recolección, un aumento de cinco países en comparación con el período del informe anterior 2010-2017. 26 países, confirmaron la resistencia a las cuatro clases principales de insecticidas.
- La resistencia a los piretroides, la única clase de insecticidas actualmente utilizada en los MTI, es generalizada y se detectó en al menos un vector de malaria en más de dos tercios de los sitios analizados, y fue más alta en la Región de África de la OMS y en la Región del Mediterráneo Oriental.
- La resistencia a los organoclorados fue confirmada en casi un tercio de los sitios de recolección en al menos un vector de malaria. La resistencia a los carbamatos y los organofosforados fue menos prevalente, siendo confirmada en el 31% y 26% de los sitios de recolección testados, respectivamente. La resistencia a los carbamatos fue más prevalente en la región de Asia sudoriental, mientras que la resistencia a los organofosforados fue más prevalente en la región de Asia sudoriental y el Pacifico Oriental.
- Todos los datos estándar de resistencia a los insecticidas proporcionados a la OMS están incluidos en la Base de datos Mundial de Resistencia a los Insecticidas en los Vectores de Malaria de la OMS y están disponibles para su consulta a través del Mapa de los Desafíos de la Malaria. Esta herramienta en línea se extendió en 2019 para cubrir los movimientos de las especies de mosquitos invasoras, y actualmente muestra el alcance geográfico de los informes sobre la detección de *Anopheles stephensi*.
- Para guiar el manejo de la resistencia, los países deben desarrollar e implementar un plan nacional para el monitoreo y manejo de la resistencia a los insecticidas, basándose en el documento *Estructura general de un plan nacional de monitoreo y manejo de la resistencia a insecticidas en vectores del paludismo* de la OMS. En 2018, un total de 45 países informaron haber completado el plan para el monitoreo y manejo de la resistencia y 36 estaban en proceso de desarrollarlo.
- Los PNM y sus socios deberían considerar la distribución de mosquiteros con piretroide y butóxido de piperonilo (PBO) en áreas geográficas concretas donde los principales vectores de la malaria cumplen con los criterios recomendados por la OMS en 2017, en lugar de basarse en si todo el país cumple los criterios.

FIG. 1.1.

Countries with indigenous cases in 2000 and their status by 2018 Countries with zero indigenous cases over at least the past 3 consecutive years are considered as having eliminated malaria. In 2018, China and El Salvador reported zero indigenous cases for the second consecutive year, and Iran (Islamic Republic of), Malaysia and Timor-Leste reported zero indigenous cases for the first time. *Source: WHO database.*



WHO: World Health Organization.

1 Introduction

The World Health Organization's (WHO's) *World malaria report 2019* summarizes global progress in the fight against malaria up to the end of 2018. This is the fourth world malaria report since the launch of the *WHO Global technical strategy for malaria 2016–2030* (GTS) (*1*). Key indicators are tracked across several countries (**Fig. 1.1**) and WHO regions against the milestones outlined in the GTS (**Table 1.1**).

TABLE 1.1.

GTS: global targets for 2030 and milestones for 2020 and 2025 *Source: GTS* (*1*).

Vision – A world free of malaria

Pillars	
Pillar 1	Ensure universal access to malaria prevention, diagnosis and treatment
Pillar 2	Accelerate efforts towards elimination and attainment of malaria free status
Pillar 3	Transform malaria surveillance into a core intervention

Goals	Milestones		Targets
	2020	2025	2030
1. Reduce malaria mortality rates globally compared with 2015	At least 40%	At least 75%	At least 90%
2. Reduce malaria case incidence globally compared with 2015	At least 40%	At least 75%	At least 90%
3. Eliminate malaria from countries in which malaria was transmitted in 2015	At least 10 countries	At least 20 countries	At least 35 countries
4. Prevent re-establishment of malaria in all countries that are malaria free	Re-establishment prevented	Re-establishment prevented	Re-establishment prevented

GTS: *Global technical strategy for malaria 2016–2030.*

FIG. 1.2.

Malaria and the SDGs 2016–2030 Reducing the burden of malaria will contribute to or benefit from progress towards the SDG goals. *Sources: United Nations* (*3*) and *Swiss Malaria Group* (*5*).

17

Goal 17: Partnership for the Goals. The many **multisectoral partnerships** in place to reduce and eliminate malaria have a positive collateral effect, and also bring progress to other **domains of development**.

1

Goal 1: No Poverty. Sustained investment in health and malaria unlocks the potential of human capital to **generate growth**. A 10% reduction in malaria has been associated with a 0.3% rise in annual GDP. At household level, **reducing malaria protects household income** from lost earnings and the costs of seeking care.

2

Goal 2: Zero Hunger. Sustainable agricultural practices help reduce malaria. People who suffer less from malaria work their fields more consistently, resulting in better harvests and **improved food security**. Well-nourished people, especially children, are better able to fight malaria.

3

Goal 3: Good Health and Well-being. The scale-up of malaria interventions **averted at least 670 million bouts of malaria illness and 4.3 million malaria deaths** between 2001 and 2013. Preventing malaria in pregnancy **reduces maternal mortality and gives newborns a far healthier start in life.** Lowering the burden of malaria makes a substantial contribution to **improvements in child health**, and thus often to a decline in fertility rates, and an associated increase in the investment that parents can make in their children.

10 16

Goals 10, 16: Reduce Inequality. Promote Peace and Justice. A targeted response to malaria actively improves the health of the poorest, enabling vulnerable families to **break the vicious cycle of disease and poverty**, and helping to make sure that no one is left behind. Investing in malaria reduction contributes to the creation of more **cohesive, inclusive societies**. Stable countries are more likely to attract international investment and overseas development aid.

4

Goal 4: Quality Education. Reducing malaria enables children to **attend school regularly and learn more effectively.** This significantly improves their school performance, and later wage-earning capacity. As a mother's or caregiver's level of education increases, so do the chances that their children will access malaria prevention and treatment services and survive childhood.

13

Goal 13: Climate Action. Given that climate change is predicted to increase the range and intensity of malaria transmission, plans to **mitigate the effects of climate change** are likely to include an increased commitment to controlling and eliminating malaria, and vice versa.

5

Goal 5: Gender Equality. Freeing women and school-age girls from the burden of caring for family members when they fall sick with malaria increases their likelihood of completing school, entering and remaining in the workforce, and participating in public decision-making.

9 11 15

Goals 9, 11, 15: Infrastructure, Sustainable Cities and Life on Land. By ensuring that major construction and development projects do not introduce or increase malaria transmission, the benefits of progress can be reaped, while also **protecting human health and ecosystems. Well-planned infrastructure and improved housing** help reduce exposure to mosquitoes, and facilitate greater access to health and malaria services.

6

Goal 6: Clean Water and Sanitation. Drainage of standing water leads to decreased mosquito breeding and a reduction in the rate of malaria transmission. It also improves water quality, generating further health benefits.

7

Goal 7: Affordable and Clean Energy. In resource-constrained malaria endemic regions, **access to sustainable energy will stimulate prosperity** and increase the adoption of more sophisticated personal protection measures. It will also mean greater access to electric lighting and cooling, enabling people to increase time spent indoors, where vectors are more easily controlled through insecticides, bet nets and temperature. These developments are likely to result in a reduced burden of malaria.

8 12

Goal 8, 12: Decent Work, Economic Growth and Responsible Production. Reducing malaria creates **healthier, more productive workforces** which can help to attract trade and commerce. When combined with pro-poor policies, these factors **drive job creation, inclusive growth and shared prosperity.** Enterprises that invest in their workers reduce the costs of doing business, increase their **competitiveness** and enhance their reputation.

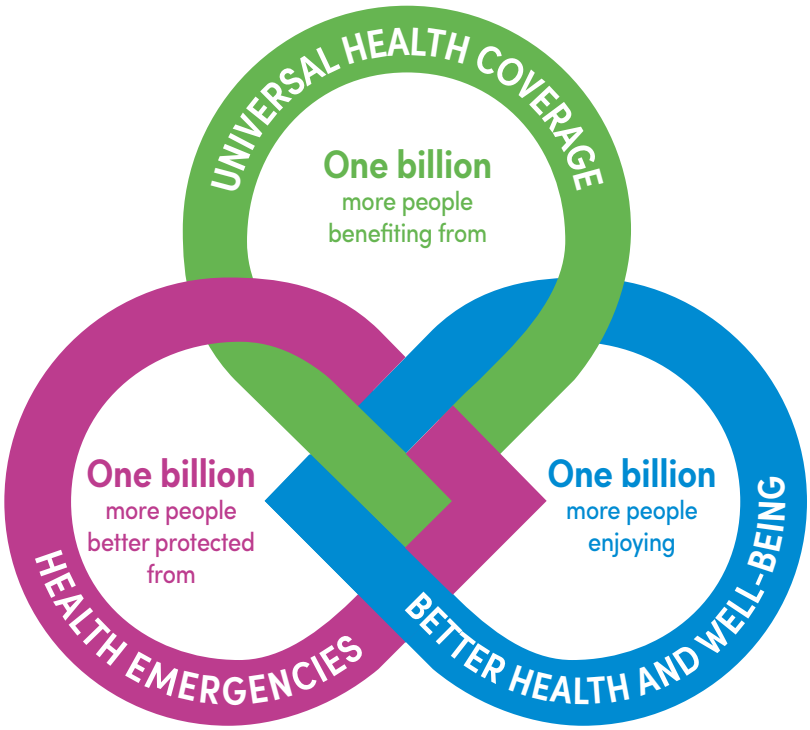
GDP: gross domestic product; SDG: Sustainable Development Goal.

The report also tracks a set of indicators outlined in the Roll Back Malaria (RBM) advocacy plan, *Action and investment to defeat malaria 2016–2030* (AIM) (*2*) and the Sustainable Development Goals (SDGs) (*3*) – a set of interconnected global goals seen as a plan of action for people, the planet and prosperity (**Fig. 1.2**). The report highlights the various ways investment in the fight against malaria contributes to the SDGs and the aligned WHO "triple billion" targets of the 13th General programme of work (GPW13) (*4*) (**Fig. 1.3**).

The main results, presented in **Sections 2–10**, cover the period 2010–2018. **Section 2** describes the global trends in malaria morbidity and mortality burden. Estimates of the burden of anaemia and its association with malaria – and for the first time in the world malaria report, burden and consequences of malaria during pregnancy – are presented in **Section 3**. The "high burden to high impact" (HBHI) approach and related control activities and funding are described in **Section 4**, while progress towards elimination is presented in **Section 5**. **Section 6** dwells on total funding for malaria control and elimination, for malaria research and for the supply of key commodities to endemic countries. The population-level coverage achieved through these investments is presented in **Section 7** and **Section 8**. **Section 9** focuses on surveillance as an intervention, and **Section 10** describes the threats posed by *Plasmodium falciparum* parasite histidine-rich protein 2 (HRP2) deletions, and by drug and insecticide resistance. The main text is followed by annexes that contain data sources and methods, regional profiles and data tables. Country profiles are presented online (*6*).

FIG. 1.3.

The WHO triple billion targets and the contribution of the fight against malaria These interconnected targets articulated in the GPW13 aim for one billion more people benefiting from universal health coverage; one billion more people better protected from health emergencies; and one billion more people enjoying better health and well-being. *Source: WHO (2018)* (*4*).



WHO: World Health Organization.

2 Regional and global trends in burden of malaria cases and deaths

Assessing progress in reducing the burden of malaria, to track the targets and milestones of the GTS (*1*), is a key mandate of the WHO Global Malaria Programme (GMP). This section of the report reviews the total number of cases and deaths estimated to have occurred between 2010 and 2018. There are several methods for estimating the burden of malaria cases and deaths; the method used depends on the quality of the national surveillance systems and the availability of data over time (**Section 9.1** and **Annex 1**).

2.1 ESTIMATED NUMBER OF MALARIA CASES BY WHO REGION, 2000–2018

An estimated 228 million cases of malaria occurred worldwide in 2018 (95% confidence interval [CI]: 206–258 million) compared with 251 million cases in 2010 (95% CI: 231–278 million) and 231 million cases in 2017 (95% CI: 211–259 million) (**Table 2.1**).

The WHO African Region still bears the largest burden of malaria morbidity, with 213 million cases (93%) in 2018, followed by the WHO South-East Asia Region (3.4%) and the WHO Eastern Mediterranean Region (2.1%) (**Table 2.1**). Globally, 3.3% of all estimated cases were caused by *P. vivax*, with 53% of the vivax burden being in the WHO South-East Asia Region (**Table 2.2**). *P. vivax* is the predominant parasite in the WHO Region of the Americas (75%), and is responsible for 50% of cases in the WHO South-East Asia Region and 29% in the WHO Eastern Mediterranean Region (**Table 2.2**).

TABLE 2.1.

Estimated malaria cases by WHO region, 2010–2018 Estimated cases are shown with 95% upper and lower CIs. *Source: WHO estimates.*

	Number of cases (000)								
	2010	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**
African									
Lower 95% CI	199 000	194 000	190 000	185 000	181 000	184 000	189 000	192 000	191 000
Estimated total	**218 000**	**213 000**	**209 000**	**204 000**	**197 000**	**199 000**	**206 000**	**212 000**	**213 000**
Upper 95% CI	245 000	237 000	233 000	229 000	218 000	219 000	229 000	240 000	244 000
Americas									
Lower 95% CI	744	566	541	520	445	525	640	880	867
Estimated total	**814**	**611**	**580**	**562**	**477**	**566**	**691**	**944**	**929**
Upper 95% CI	894	666	627	613	512	611	749	1 026	1 007
Eastern Mediterranean									
Lower 95% CI	3 300	3 400	3 200	3 000	3 100	3 000	3 800	3 800	3 700
Estimated total	**4 300**	**4 500**	**4 200**	**3 900**	**4 000**	**3 800**	**4 800**	**5 000**	**4 900**
Upper 95% CI	6 300	6 500	6 000	5 300	5 500	5 200	6 400	6 800	6 800
South-East Asia									
Lower 95% CI	19 800	17 700	14 700	10 900	10 400	10 700	10 500	8 800	5 800
Estimated total	**25 000**	**21 100**	**18 400**	**13 700**	**13 000**	**13 600**	**14 000**	**11 300**	**7 900**
Upper 95% CI	33 900	23 300	24 400	18 000	17 400	18 200	19 700	15 400	10 700
Western Pacific									
Lower 95% CI	1 045	922	914	1 305	1 588	1 115	1 318	1 392	1 495
Estimated total	**1 839**	**1 576**	**1 761**	**2 027**	**2 345**	**1 445**	**1 733**	**1 854**	**1 980**
Upper 95% CI	2 779	2 340	3 009	2 925	3 339	1 852	2 228	2 420	2 588
World									
Lower 95% CI	231 000	222 000	214 000	205 000	202 000	203 000	210 000	211 000	206 000
Estimated total	**251 000**	**241 000**	**234 000**	**224 000**	**217 000**	**219 000**	**227 000**	**231 000**	**228 000**
Upper 95% CI	278 000	267 000	260 000	250 000	238 000	240 000	251 000	260 000	258 000
Estimated *P. vivax*									
Lower 95% CI	11 700	10 600	9 400	7 200	6 300	5 900	6 400	6 200	5 900
Estimated total	**16 300**	**15 700**	**14 200**	**10 900**	**8 700**	**8 000**	**8 300**	**7 700**	**7 500**
Upper 95% CI	23 700	24 100	22 300	17 200	12 300	10 900	10 900	9 800	9 300

CI: confidence interval; *P. vivax*: *Plasmodium vivax*; WHO: World Health Organization.

TABLE 2.2.

Estimated *P. vivax* malaria cases by WHO region, 2018 Estimated cases are shown with 95% upper and lower CI. *Source: WHO estimates.*

	Number of cases (000)					
	African	**Americas**	**Eastern Mediterranean**	**South-East Asia**	**Western Pacific**	**World**
Estimated *P. vivax*						
Lower 95% CI	91	657	1 171	2 860	556	5 900
Estimated total	**704**	**700**	**1 414**	**3 947**	**690**	**7 500**
Upper 95% CI	1 813	758	1 738	5 390	858	9 300
Percentage of *P. vivax* cases	0.3	75.4	28.9	50.0	34.8	3.3

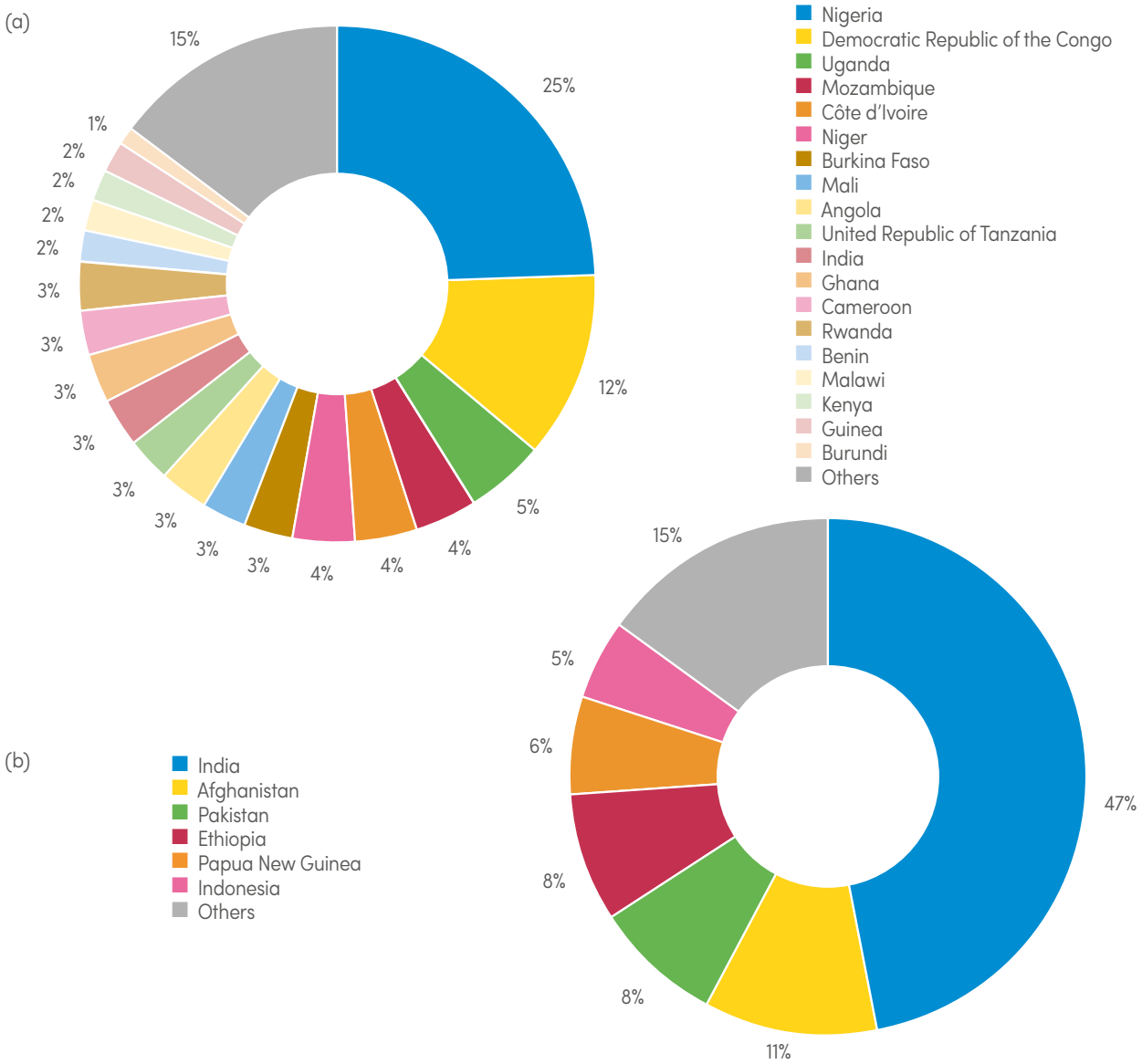
CI: confidence interval; *P. vivax*: *Plasmodium vivax*; WHO: World Health Organization.

Almost 85% of all malaria cases globally were in 19 countries: India and 18 African countries (**Fig. 2.1a**). Over 50% of all cases globally were accounted for by Nigeria (25%), followed by the Democratic Republic of the Congo (12%), Uganda (5%), and Côte d'Ivoire, Mozambique and Niger (4% each). Of these 19 countries, India reported the largest absolute reductions in cases, with 2.6 million fewer cases in 2018 than in 2017, followed by Uganda (1.5 million fewer cases) and Zimbabwe (0.6 million fewer cases). Notable increases were seen in Ghana (8% increase, 0.5 million more cases) and Nigeria (6% increase, 3.2 million more cases). Changes in the remaining 14 countries were generally small, suggesting a similar burden of cases in 2017 and 2018.

More than 85% of estimated vivax malaria cases in 2018 occurred in just six countries, with India accounting for 47% of all vivax cases globally (**Fig. 2.1b**).

FIG. 2.1.

Estimated country share of (a) total malaria cases and (b) *P. vivax* malaria cases, 2018 *Source: WHO estimates.*



P. vivax: *Plasmodium vivax*; WHO: World Health Organization.

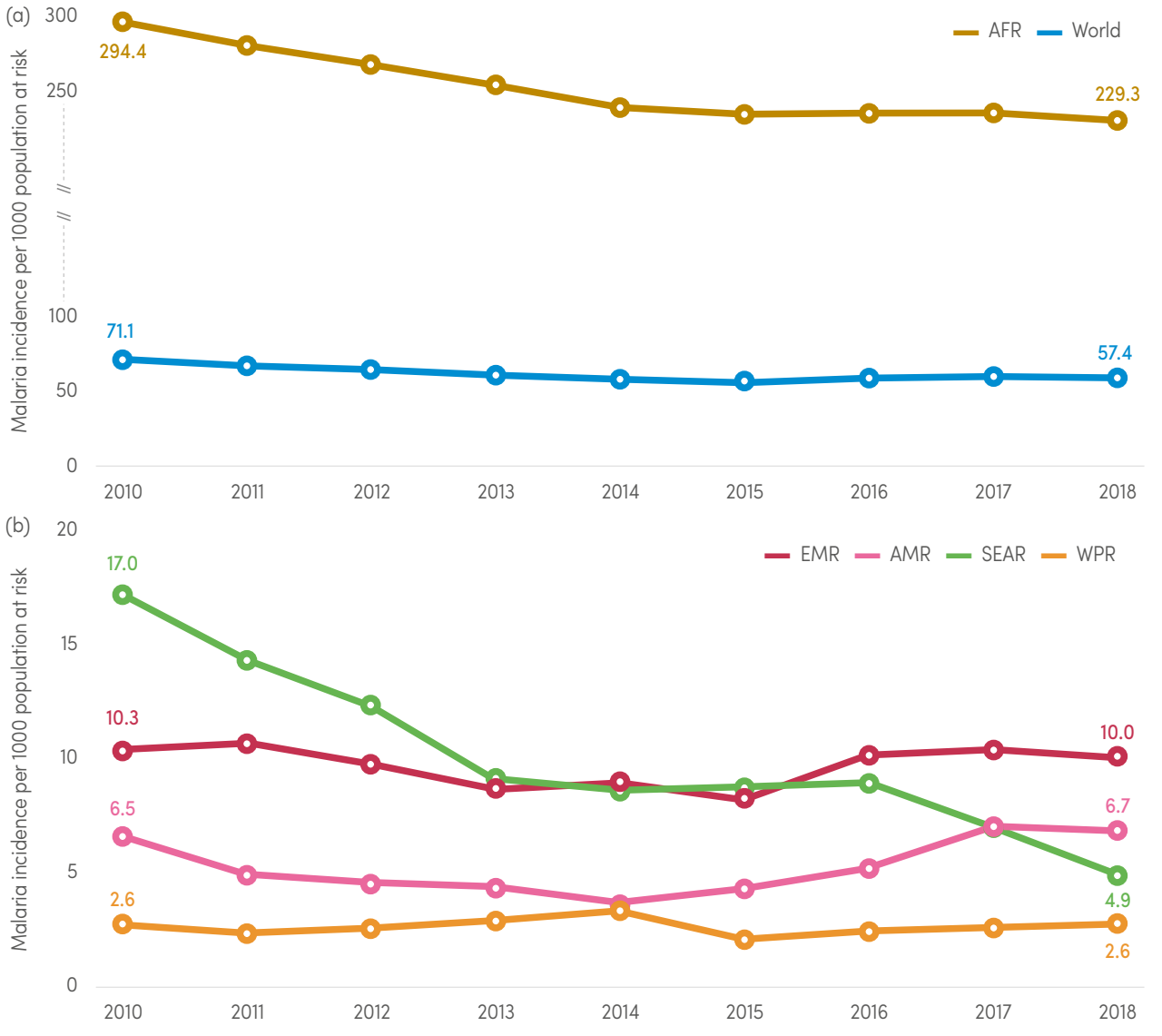
2.2 MALARIA CASE INCIDENCE RATE

The global incidence rate (i.e. the number of cases per 1000 population) of malaria reduced between 2010 and 2018; it fell from 71 in 2010 to 57 in 2018 (**Fig. 2.2a**). However, from 2014 to 2018, the rate of change slowed dramatically, reducing from 60 in 2013 to 57 in 2014 and remaining at similar levels through to 2018. In the WHO African Region, case incidence levels declined from 294 in 2010 to 229 in 2018, representing a 22% reduction in incidence, although the rate of change also appeared to slow from 2014.

The WHO Eastern Mediterranean Region and WHO Western Pacific Region saw a slight increase in case incidence between 2010 and 2018, while the WHO Region of the Americas saw a moderate increase, largely due to an increase in cases in Venezuela (Bolivarian Republic of). The highest reductions in incidence, however, were seen in the WHO South-East Asia Region, mainly owing to reductions in India, Indonesia and countries in the Greater Mekong subregion (GMS) (**Fig. 2.2b**). The geographic distribution of malaria case incidence by country is shown in **Fig. 2.3**.

FIG. 2.2.

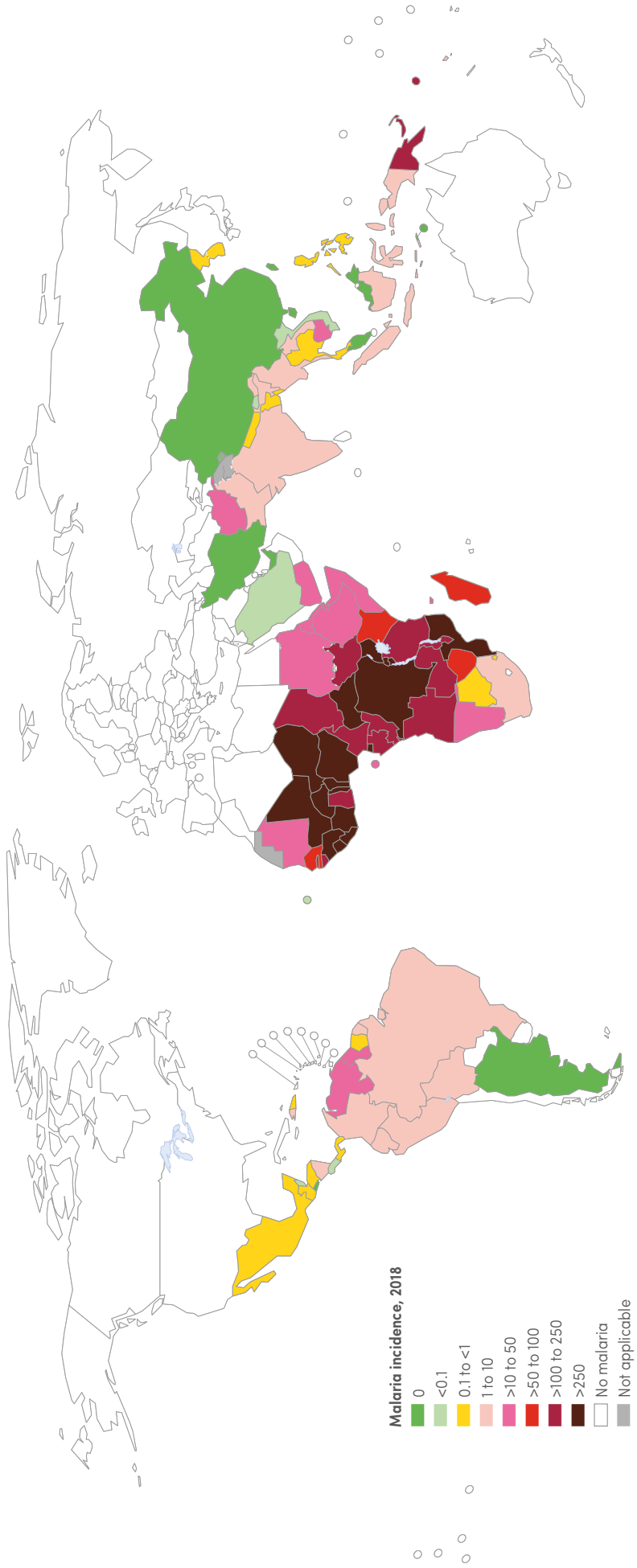
Trends in malaria case incidence rate (cases per 1000 population at risk) globally and by WHO region, 2010–2018 The WHO European Region has reported zero indigenous cases since 2015. *Source: WHO estimates.*



AFR: WHO African Region; AMR: WHO Region of the Americas; EMR: WHO Eastern Mediterranean Region; SEAR: WHO South-East Asia Region; WHO: World Health Organization; WPR: WHO Western Pacific Region.

FIG. 2.3.

Map of malaria case incidence rate (cases per 1000 population at risk) by country, 2018 *Source: WHO estimates.*

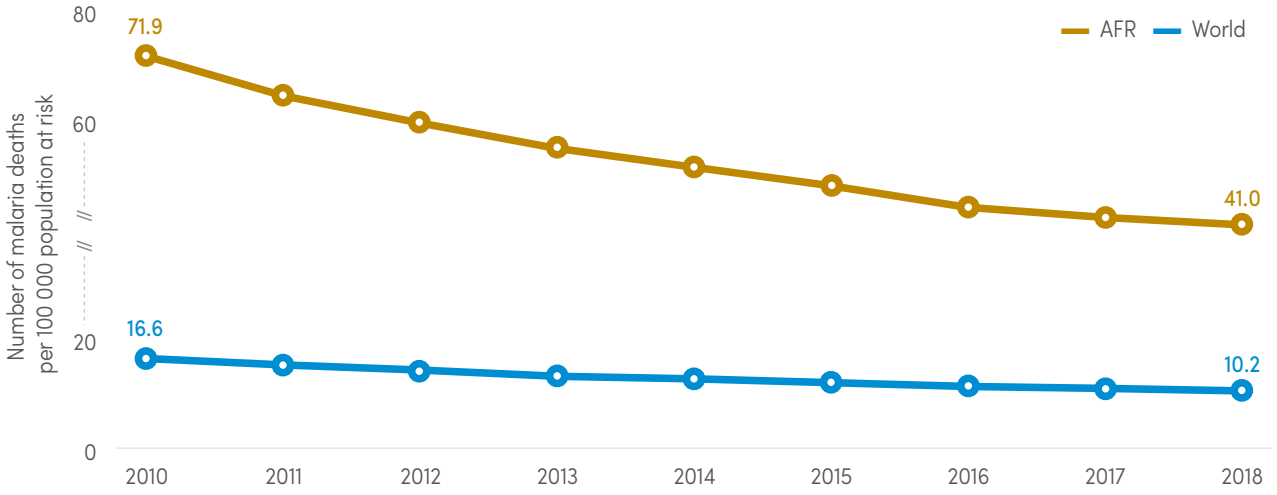


2.3 ESTIMATED NUMBER OF MALARIA DEATHS AND MORTALITY RATE BY WHO REGION, 2010–2018

Between 2010 and 2018, estimated deaths due to malaria globally declined from 585 000 to 405 000 cases (**Table 2.3**). Declines were recorded in all regions apart from the WHO Region of the Americas due to increases in malaria in Venezuela (Bolivarian Republic of) and the WHO Eastern Mediterranean Region due to increases in Somalia, Sudan and Yemen. Estimates of the malaria mortality rate (i.e. deaths per 100 000 population at risk) show that, compared with 2010, only the WHO African Region and the WHO South-East Asia Region had recorded notable reductions by 2018 (**Fig. 2.4** and **Fig. 2.5**). The highest absolute reduction in malaria deaths occurred in the WHO African Region, from 533 000 deaths in 2010 to 380 000 deaths in 2018. The rate of reduction of malaria mortality was slower in the period 2016–2018 than in the period 2010–2015.

FIG. 2.4.

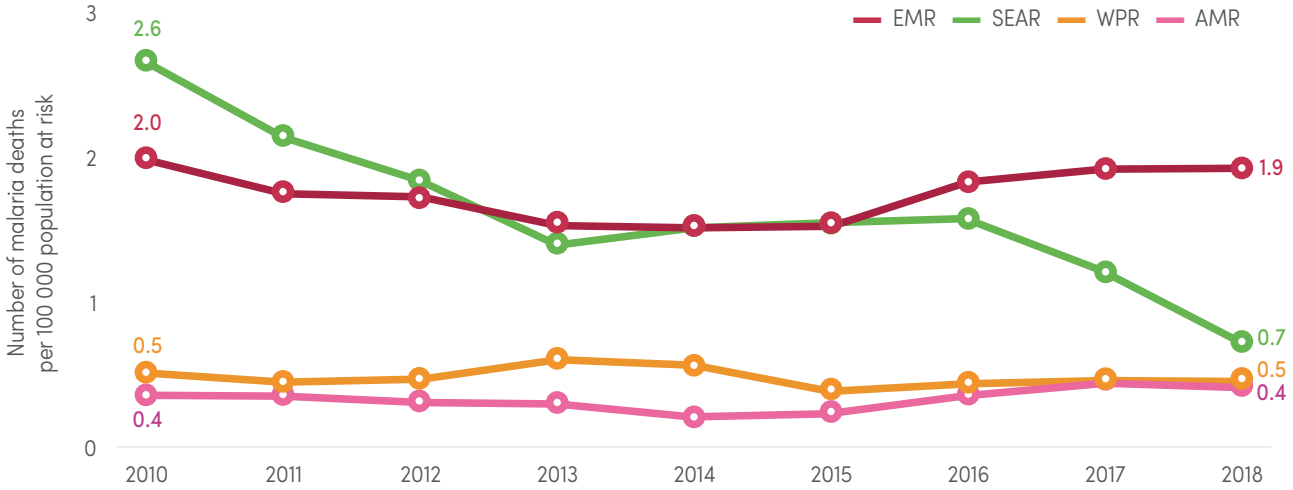
Trends in malaria mortality rate (deaths per 100 000 population at risk), globally and in the WHO African Region, 2010–2018 *Source: WHO estimates.*



AFR: WHO African Region; WHO: World Health Organization.

FIG. 2.5.

Trends in malaria mortality rate (deaths per 100 000 population at risk) in WHO regions, 2010–2018 *Source: WHO estimates.*



AMR: WHO Region of the Americas; EMR: WHO Eastern Mediterranean Region; SEAR: WHO South-East Asia Region; WHO: World Health Organization; WPR: WHO Western Pacific Region.

Globally, 272 000 (67%) malaria deaths were estimated to be in children aged under 5 years (**Table 2.3**).

Almost 85% of all deaths in 2018 occurred in 20 countries in the WHO African Region and India, and almost 50% of all malaria deaths globally were accounted for by Nigeria (24%) followed by the Democratic Republic of the Congo (11%), the United Republic of Tanzania (5%), and Niger, Mozambique and Angola (4% each) (**Fig. 2.6**).

TABLE 2.3.

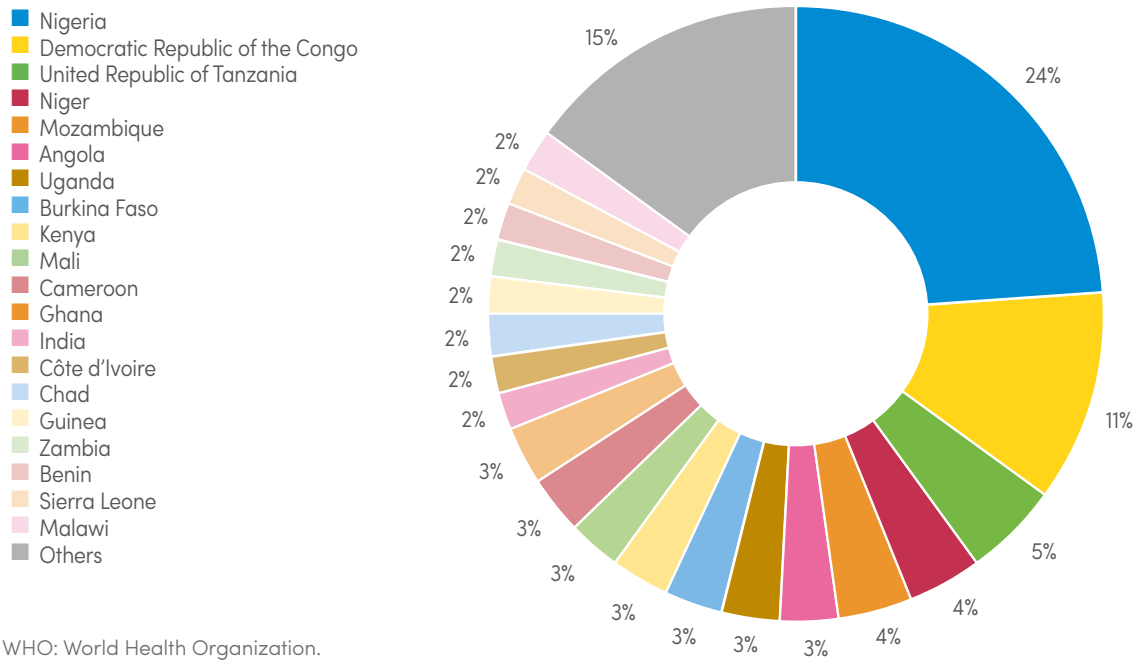
Estimated number of malaria deaths by WHO region, 2010–2018 *Source: WHO estimates.*

	Number of deaths								
	2010	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**
African	533 000	493 000	469 000	444 000	428 000	411 000	389 000	383 000	380 000
Americas	459	444	392	391	289	324	474	620	577
Eastern Mediterranean	8 300	7 500	7 600	6 900	6 900	7 100	8 600	9 200	9 300
European	0	0	0	0	0	0	0	0	0
South-East Asia	39 000	32 000	28 000	21 000	24 000	25 000	25 000	20 000	12 000
Western Pacific	3 800	3 300	3 600	4 600	4 400	2 800	3 500	3 600	3 600
World (total)	**585 000**	**536 000**	**508 000**	**477 000**	**463 000**	**446 000**	**427 000**	**416 000**	**405 000**
World (children aged under 5 years)	**450 000**	**406 000**	**377 000**	**348 000**	**334 000**	**311 000**	**290 000**	**278 000**	**272 000**

WHO: World Health Organization.

FIG. 2.6.

Percentage of estimated malaria deaths attributable to the 21 countries with nearly 85% of malaria deaths globally in 2018 *Source: WHO estimates.*



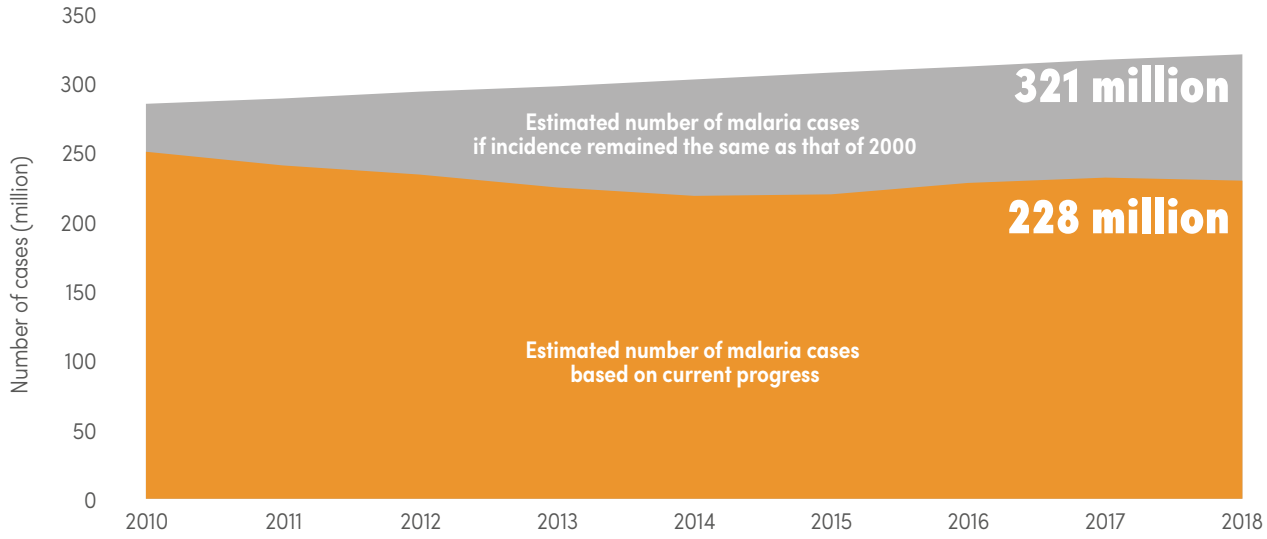
WHO: World Health Organization.

2.4 PROGRESS TOWARDS THE GTS MILESTONES FOR MALARIA MORBIDITY AND MORTALITY

The GTS aims for a reduction of 40% of malaria morbidity incidence and mortality rate by 2020 from a 2015 baseline (*1*). To illustrate the level of progress made so far, our analysis shows that if malaria case incidence and mortality rate remained the same as those in 2000, globally there would be 321 million cases and nearly 1 million malaria deaths in 2018 (**Fig. 2.7** and **Fig. 2.8**). Instead, there were an estimated 228 million malaria cases (**Table 2.1**) and 405 000 malaria deaths (**Table 2.3**) in 2018. These represent about 29% fewer cases and 60% fewer deaths in 2018 than would have been the case had levels of malaria incidence and malaria death remained similar to those in 2000.

FIG. 2.7.

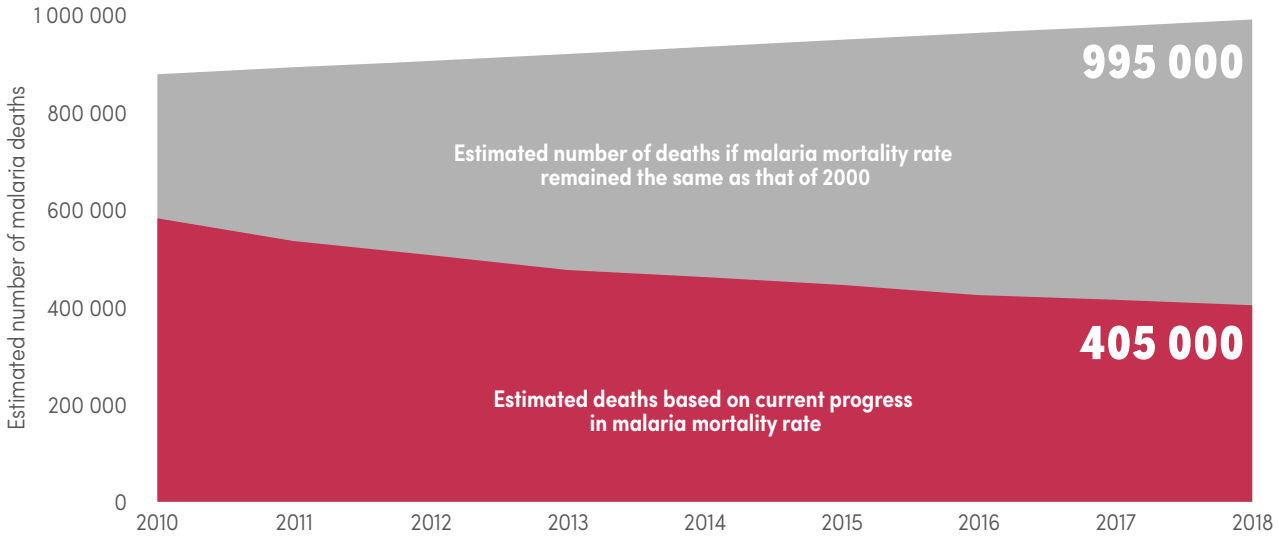
Comparison of current estimated malaria cases with expected cases had malaria incidence remained at 2000 levels globally *Source: WHO estimates.*



WHO: World Health Organization.

FIG. 2.8.

Comparison of current estimated malaria deaths with expected deaths had malaria incidence remained at 2000 levels globally *Source: WHO estimates.*

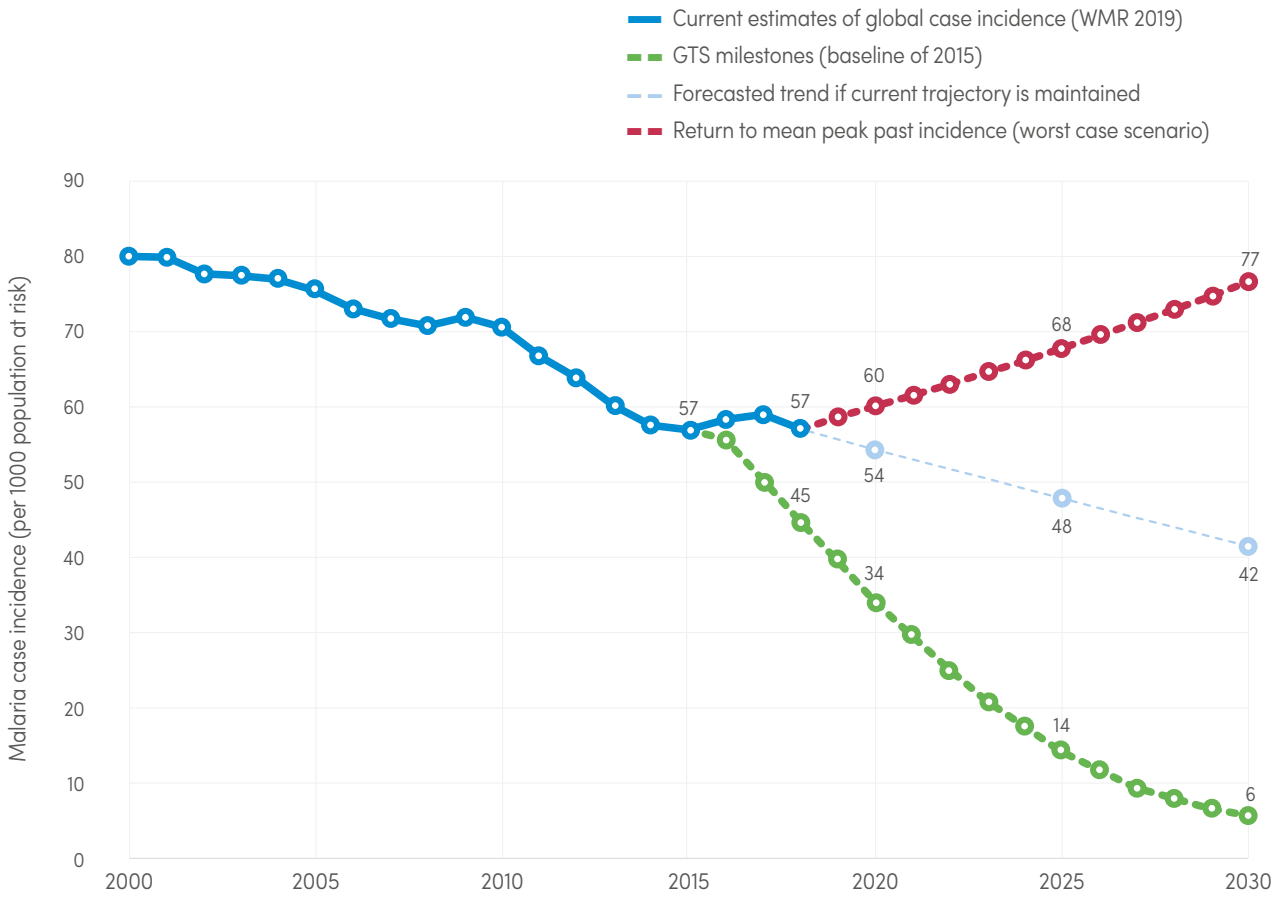


WHO: World Health Organization.

While the gains to date are impressive, the global malaria challenge remains enormous and the level of progress is slowing down. For example, on the current trajectory, globally, the 2020 GTS milestones for morbidity will not be achieved, and without accelerated change, the 2025 and 2030 milestones will not be achieved. A global malaria case incidence of 45 per 1000 population at risk in 2018 would have been required to get the world on target for the 2020 milestones, but current estimated incidence is at 57 cases per 1000 population at risk. If the current trend in incidence is maintained, estimated malaria case incidence (per 1000 population at risk) would be 54 in 2020, 48 in 2025 and 42 in 2030, instead of the 34, 14 and 6 required to achieve the GTS milestones (**Fig. 2.9**).

FIG. 2.9.

Comparison of progress in malaria case incidence considering three scenarios: current trajectory maintained (blue), GTS targets achieved (green) and worst case scenario, that is a return to mean peak past incidence in the period 2000–2007 (red) *Source: WHO estimates.*



GTS: *Global technical strategy for malaria 2016–2030*; WHO: World Health Organization; WMR: *World Malaria Report*.

3 Maternal, infant and child health consequences of malaria

Malaria infection during pregnancy is a significant public health problem, with substantial risks for the pregnant woman, her fetus and the newborn child. The symptoms and complications of malaria in pregnancy vary according to malaria transmission intensity in the given geographical area, and the individual's level of acquired immunity (*7*). Malaria-associated maternal illness and anaemia, preterm birth and low birthweight newborns are mostly the result of *P. falciparum* infection and occurs predominantly in Africa. Maternal anaemia, of which malaria remains an important contributor, puts the mother at increased risk of death before and after childbirth. This also leads to preterm births and children of low weight at birth, causing problems with child growth and cognitive development, as well as being major risk factors for perinatal, neonatal and infant mortality (*8, 9*).

In moderate and high transmission settings, where levels of acquired immunity tend to be high, *P. falciparum* infection is usually asymptomatic in pregnancy. Nevertheless, parasites may be present in the placenta and contribute to maternal anaemia even in the absence of documented peripheral parasitaemia. Both maternal anaemia and placental parasitaemia can lead to low birthweight, which is an important contributor to infant mortality (*7, 10, 11*). In these settings, the adverse effects of *P. falciparum* infection in pregnancy are most pronounced for women in their first pregnancy. Infection with *P. vivax* leads to chronic anaemia, reducing the birthweight and increasing the risk of neonatal death. For women in their first pregnancy, the reduction in birthweight due to infection with *P. vivax* is about two thirds of the reduction associated with *P. falciparum* (*12*, *13*).

In addition to a higher risk of low birthweight, infants once again become susceptible to *P. falciparum* malaria when immunity acquired from the mother starts to wane. Infants are at increased risk of rapid disease progression, severe malaria (especially of the severe anaemia form) and death.

To avert the consequences of malaria infections to pregnant women, fetuses, infants and children, WHO recommends – in combination with vector control, and prompt diagnosis and effective treatment of malaria – the use of intermittent preventive treatment in pregnancy (IPTp) with sulfadoxine-pyrimethamine (SP) as part of antenatal care (ANC) (**Section 7.3**); and intermittent preventive treatment in infants (IPTi) with SP in areas of moderate to high transmission in sub-Saharan Africa. In addition, seasonal malaria chemoprevention (SMC) with amodiaquine plus SP in children aged under 5 years is recommended in Africa's Sahel subregion.

In this section, exposure to malaria infection during pregnancy is estimated, then that estimation is used to compute the risk and prevalence of low birthweight. The correlation between malaria in pregnancy and malaria anaemia is presented, as is the prevalence of anaemia in children aged under 5 years, with or without malaria infection, as measured during household surveys. The analysis is restricted to moderate to high transmission countries in sub-Saharan Africa (**Annex 1**), where burden of malaria in pregnancy, infants and children is greatest.

3.1 PREVALENCE OF EXPOSURE TO MALARIA INFECTION DURING PREGNANCY, CORRELATION WITH MATERNAL ANAEMIA AND CONTRIBUTION TO LOW BIRTHWEIGHT

Anaemia is characterized by a decrease in the number of red blood cells in the blood (or a decrease in haemoglobin [Hb] concentration) to a level that impairs the normal physiological capacity of the blood to transport oxygen to cells around the body. WHO defines mild anaemia as a Hb concentration of between 10 g/dL and 10.9 g/dL, moderate anaemia as between 7 g/dL and 9.9 g/dL, and severe anaemia as below 7 g/dL. Deficiency in iron is thought to be the most common cause of anaemia.[1] Maternal anaemia has multiple causes, mainly related to nutrition, infection and genetics (*14*). In malaria endemic countries, malaria is a major cause of anaemia in pregnant women, many of whom also have other conditions, such as HIV and helminths infections and iron deficiency.

Malaria infections cause anaemia through multiple mechanisms; for example, direct destruction of red blood cells, clearance of infected and uninfected red cells by the spleen, and impaired red cell production by bone marrow. Individuals who are anaemic are at a greater risk of mortality, including from malaria. Single or repeated episodes of malaria may result in life-threatening anaemia, metabolic acidosis (*15*) and death. Exposure to malaria infection during pregnancy leads to maternal anaemia, which is associated with higher risk of obstetric haemorrhage and death. WHO estimates of maternal anaemia (Hb concentration of <10.9 g/dL at sea level) by country were obtained for 38 moderate to high malaria transmission countries in sub-Saharan Africa.[2]

Exposure to malaria infection in pregnancy (measured as cumulative prevalence over 40 weeks) was estimated from mathematic models (*16*) that relate estimates of the geographical distribution of *P. falciparum* exposure by age across Africa in 2018 to patterns of infections in placental histology by age and parity (*17*) (**Annex 1**). Fertility rates specific to country, age and gravidity, stratified by urban/rural status, were obtained from demographic health surveys (DHS) and malaria indicator surveys (MIS) where such surveys had been carried out since 2014 and were available from the DHS program website.[3] Countries where surveys were not available were allocated fertility patterns based on survey data from a different country, matched on the basis of total fertility rate (*18*) and geography. The exposure prevalence and the expected number of pregnant women who would have been exposed to infection were computed by country and subregion.

[1] Additional important causes of anaemia include infections, other nutritional deficiencies (e.g. in folate, and vitamins B12, A and C), genetic conditions and haemoglobinopathies (e.g. sickle cell disease and thalassaemia), and chronic kidney disease (*10*). Anaemia is highly prevalent globally and is particularly prevalent in sub-Saharan Africa. According to the WHO guidelines for treatment of malaria (*36*), a Hb concentration of less than 5 g/dL in an individual infected with malaria defines severe malaria.

[2] https://apps.who.int/gho/data/node.main.1?lang=en; Maternal anaemia prevalence estimates are presented to 2016 and were kept the same for the 2018 estimates in this report.

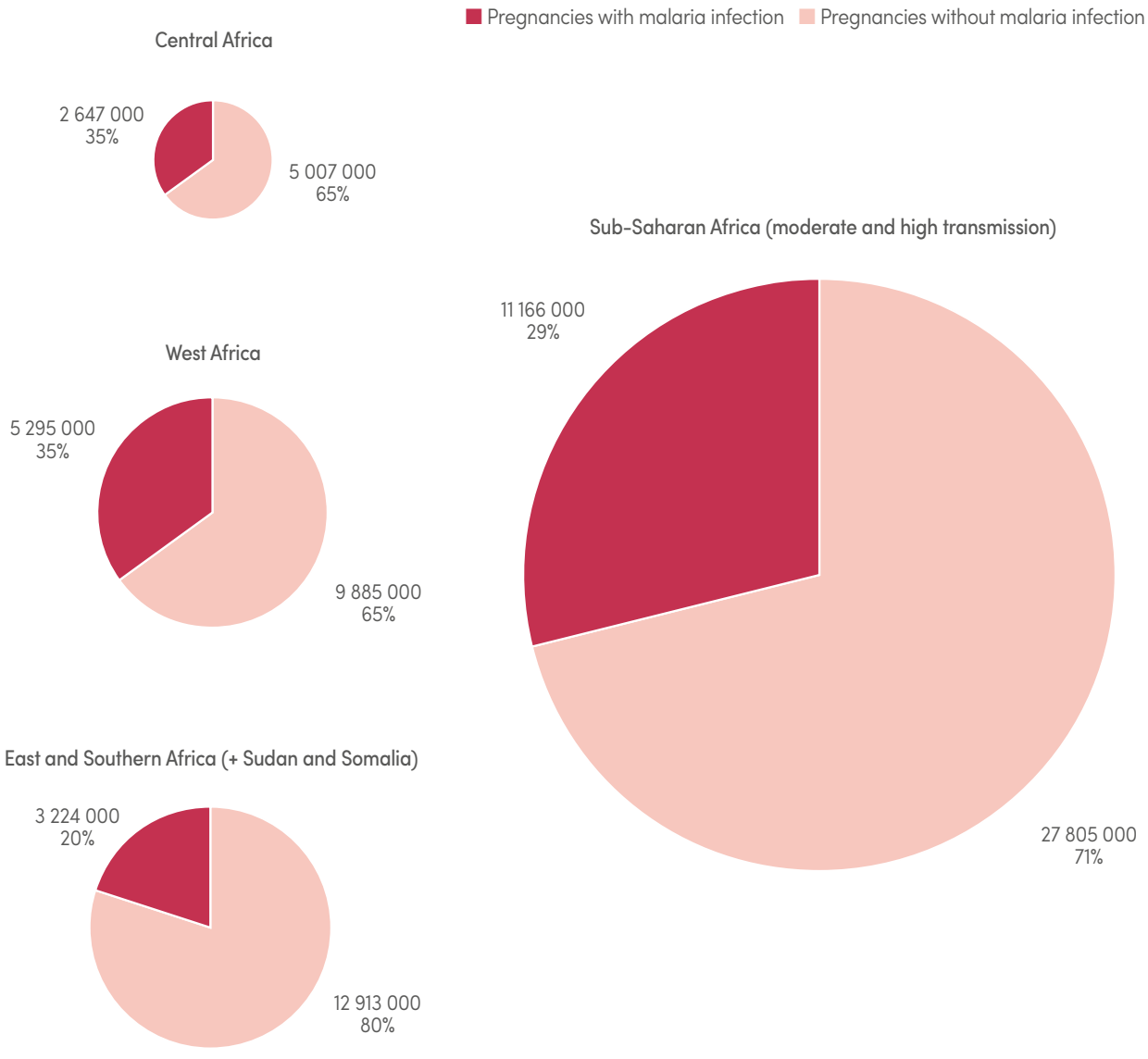
[3] https://dhsprogram.com/

Analysis by subregion showed that the prevalence of exposure to malaria infection in pregnancy was highest in West Africa and Central Africa, each with 35%, followed by East and Southern Africa (20%) (**Fig. 3.1**, **Table 3.1**). Overall prevalence of exposure to malaria infection in pregnancy in moderate to high transmission sub-Saharan Africa was 29%. In total, about 11 million pregnancies would have been exposed to malaria infection in these countries in 2018. About 39% (4.4 million) of these pregnancies were in the Democratic Republic of the Congo and Nigeria.

The analysis shows a positive correlation of maternal anaemia and prevalence of exposure to malaria infection during pregnancy (**Fig. 3.2**). In 20 countries (Benin, Burkina Faso, Burundi, Cameroon, Central

FIG. 3.1.

Estimated prevalence of exposure to malaria infection during pregnancy overall and by subregion in 2018 in moderate to high transmission sub-Saharan Africa *Source: Imperial College, WHO estimates.*



WHO: World Health Organization.

African Republic, Congo, Côte d'Ivoire, the Democratic Republic of the Congo, Equatorial Guinea, Gabon, Ghana, Guinea, Liberia, Malawi, Mozambique, Nigeria, Sierra Leone, South Sudan, Togo and Uganda), prevalence of exposure to malaria infection during pregnancy was 30% or more while maternal anaemia exceeded 40%. Although these countries have some of the highest malaria burden, the results should be interpreted recognizing that in sub-Saharan Africa, iron deficiency, an important cause of maternal anaemia, and malaria infection often coexist, but the relationship between them is complex. Measuring iron status in someone with current or recent past *P. falciparum* malaria infection is complicated by the inflammatory response to malaria infection (*19*).

TABLE 3.1.

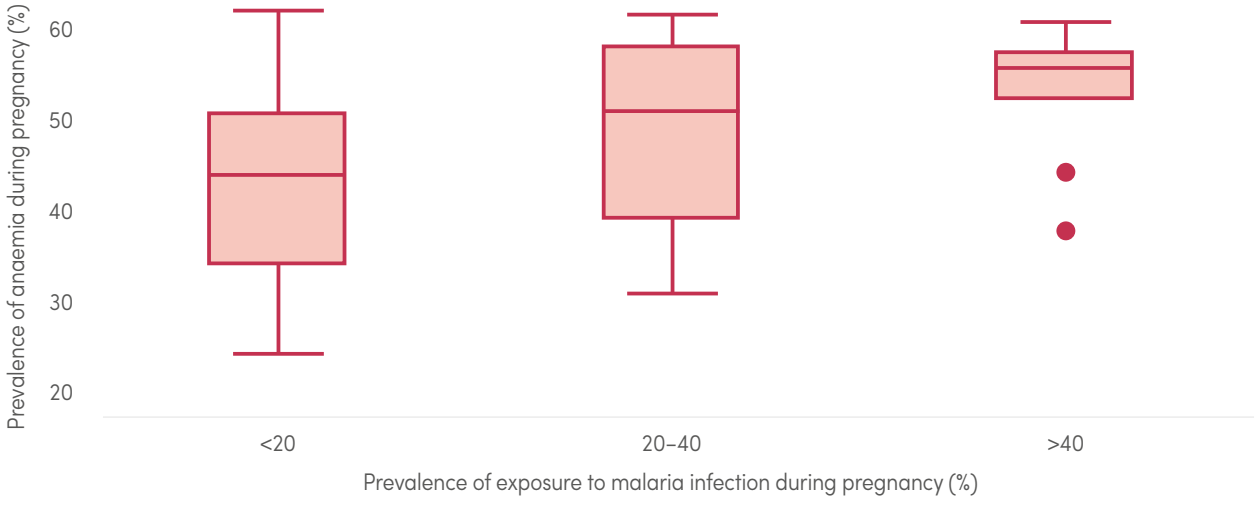
Estimates of pregnancies, livebirths, low birthweights, exposure to malaria infection in pregnancy and malaria-attributable low birthweights in 2018 in moderate to high transmission sub-Saharan Africa *Source: Imperial College, WHO estimates.*

Subregion	Number of pregnancies	Number of children born alive	Number of pregnancies infected during a 40-week gestation period	Number of children born with low birthweight (<2500 g)	Number of children born with low birthweight (<2500 g) due to malaria
Central Africa	7 654 000	7 187 000	2 647 000	934 000	186 000
West Africa	15 180 000	14 253 000	5 295 000	2 321 000	418 000
East and Southern Africa (+ Sudan and Somalia)	16 137 000	15 174 000	3 224 000	2 280 000	268 000
Sub-Saharan Africa: total	**38 971 000**	**36 614 000**	**11 166 000**	**5 535 000**	**872 000**

WHO: World Health Organization.

FIG. 3.2.

Estimated maternal anaemia (*20*)[a] versus exposure to malaria infection in pregnancy in 2018 in moderate to high transmission countries in sub-Saharan Africa *Source: Imperial College, UNICEF-WHO estimates.*



UNICEF: United Nations Children's Fund; WHO: World Health Organization.
[a] Prevalence of all cause low birthweight used in this analysis were those estimated for 2015 as shown in this source.

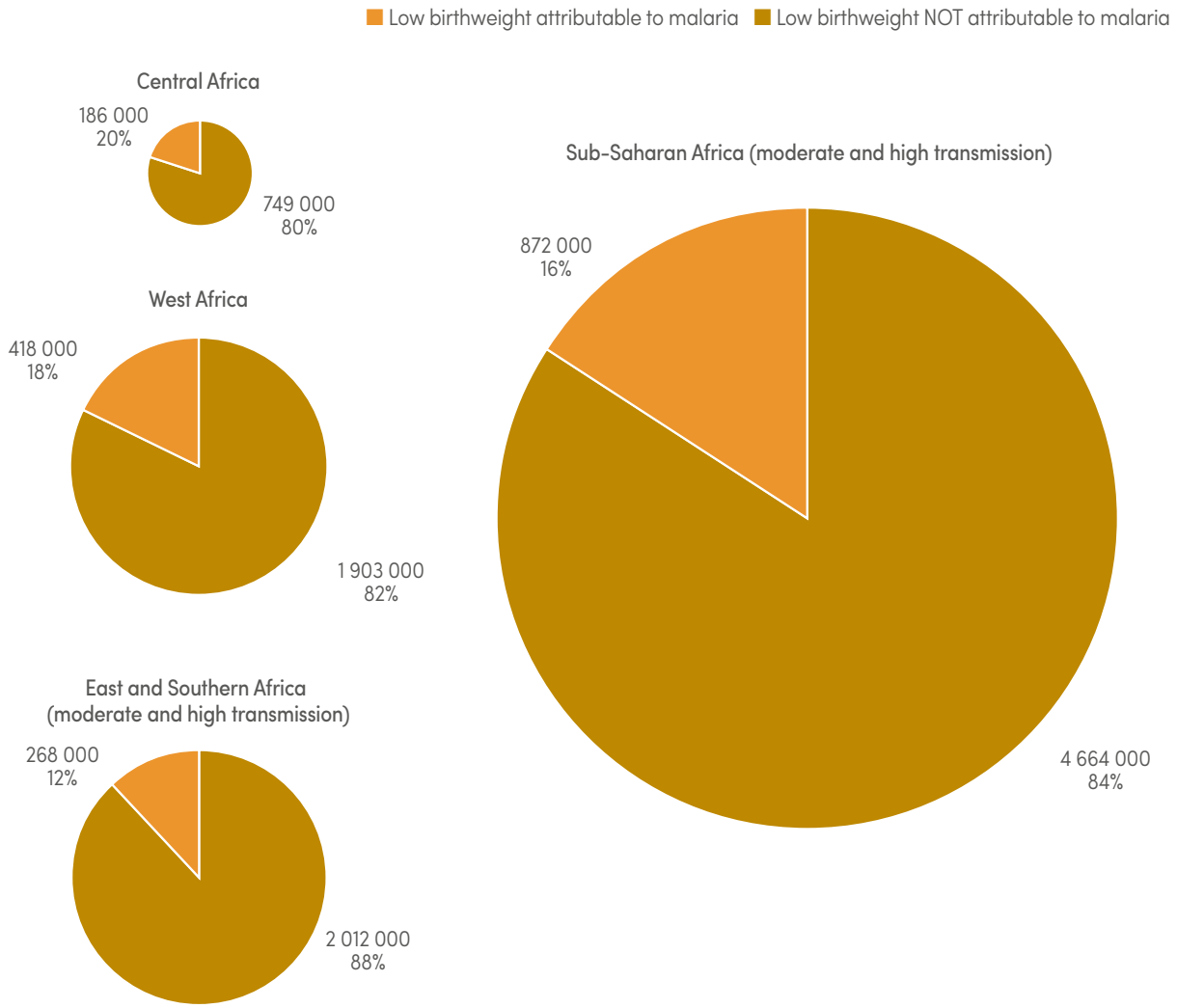
Low birthweight is defined as weight at birth of less than 2500 g, regardless of gestational age (*20*). Premature birth (<37 weeks) and growth faltering in the womb are the main reasons for low birthweight. Several factors contribute to these: maternal malnutrition and anaemia; maternal characteristics such as low or high age, parity and poor birth spacing; health problems such as high blood pressure, diabetes and infections; and other risk factors including smoking and alcohol consumption (*20*). Children with low weight at birth not only have a high risk of stunting and poor cognitive development but also are at higher risk of death.

In moderate to high transmission malaria endemic countries, malaria infection during pregnancy and the consequent placental infection are important contributors to low birthweight (*7, 10, 11*). The incremental risk of low birthweight posed by the different categories of placental infection, and the relation between parity-specific and histology-specific placental infection categories and the risk of low birthweight in the absence of other competing "non-malaria" risk factors were computed with data from different transmission settings (*16*).

In 38 moderate to high transmission countries in sub-Saharan Africa, the estimated 11 million (**Table 3.1**) pregnancies exposed to malaria infection in 2018 resulted in about 872 000 children born with low birthweight (**Fig. 3.3**), representing 16% of all children with low birthweight in these countries (**Fig. 3.3**). By subregion, the percentage of low birthweight children due to malaria was, in line with exposure to malaria infection during pregnancy, highest in West Africa (18% of low birthweight children), followed by Central Africa (20%) and East and Southern Africa (12%) (**Fig. 3.3**).

FIG. 3.3.

Estimated low birthweights due to exposure to malaria infection during pregnancy overall and by subregion in 2018 in moderate to high transmission sub-Saharan Africa *Source: Imperial College, WHO estimates.*



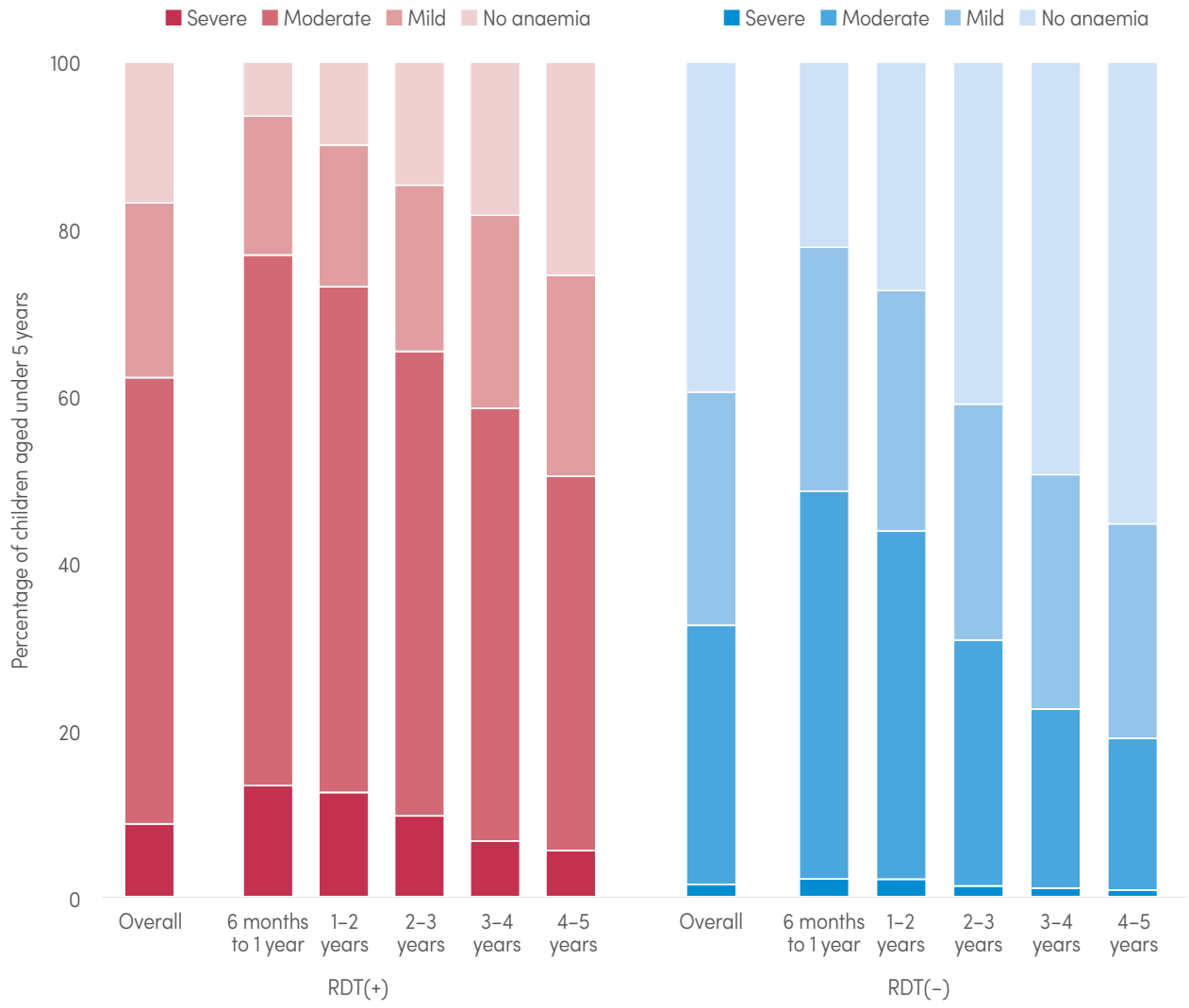
3.2 PREVALENCE AND BURDEN OF MALARIA-RELATED ANAEMIA IN CHILDREN AGED UNDER 5 YEARS

Data from household surveys implemented in 21 moderate to high malaria burden countries between 2015 and 2018 showed that, among children aged under 5 years, the prevalence of any anaemia was 61%, mild anaemia 25%, moderate anaemia 33% and severe anaemia 3%.

When children were categorized by malaria rapid diagnostic test (RDT) results, overall anaemia was higher in children who were positive for malaria than in those who were negative (**Fig. 3.4**). When anaemia prevalence was further classified, of the children who were positive for malaria, 9% had severe anaemia, 54% had moderate anaemia, 21% had mild anaemia and only 17% had no anaemia. In contrast, among those children who had no malaria, 1% had severe anaemia, 31% had moderate anaemia, 28% had mild anaemia and 40% had no anaemia (**Fig. 3.4**).

FIG. 3.4.

Prevalence of severe anaemia (<7 g/dL), moderate anaemia (7–9.9 g/dL) and mild anaemia (10–10.9 g/dL) in children aged under 5 years in sub-Saharan Africa, 2015–2018, by age and malaria infection status
Source: Household surveys.



RDT: rapid diagnostic test.

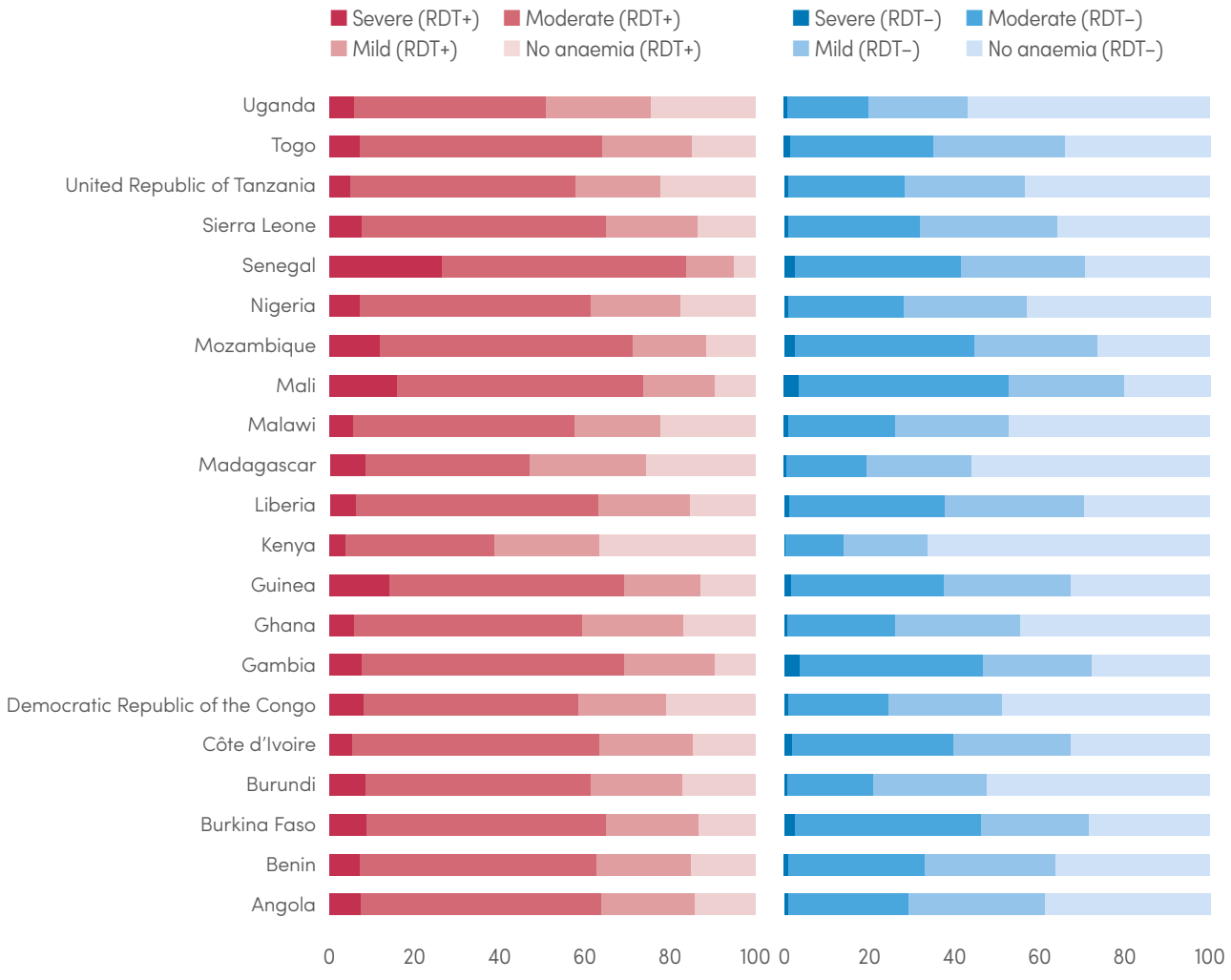
Analysis by country presents a mixed picture, although in general, higher anaemia prevalence was observed among children infected with malaria than among those who were not (**Fig. 3.5**). For most countries, the percentage of severe anaemia among children aged under 5 years who were positive for malaria ranged from 5% to 10%, except in Mozambique (12%), Guinea (14%), Mali (16%) and Senegal (26%).

The number of children who were likely to be infected with *P. falciparum* in moderate to high transmission countries in sub-Saharan Africa was estimated using spatiotemporal methods applied to community parasite prevalence data obtained from household surveys.[1] The anaemia by infection status derived from household surveys (**Fig. 3.4**, **Fig. 3.5**) were then applied to the estimated number of infections among children aged 1–59 months (**Table 3.2**). Overall, about 24 million children were infected with *P. falciparum* in 2018 in sub-Saharan Africa. Of these, 7.2 million were in Central Africa, 6.1 million in East and Southern Africa, and 10.6 million in West Africa. An estimated 1.8 million were likely to have severe anaemia (Hb <7 g/dL), 12 million had moderate anaemia (7–9.9 g/dL), 5.2 million had mild anaemia (10–10.9 g/dL), and only about 4.8 million had no anaemia.

[1] https://apps.who.int/malaria/maps/threats/

FIG. 3.5.

Prevalence of severe anaemia (<7 g/dL), moderate anaemia (7–9.9 g/dL) and mild anaemia (10–10.9 g/dL) in children aged under 5 years in sub-Saharan Africa, 2015–2018, by country *Source: Household surveys.*



RDT: rapid diagnostic test.

3.3 PROTECTING THE MOTHER AND CHILD

The sub-Saharan African countries most affected by malaria-related consequences in pregnancy and early childhood also have some of the highest concentration of other risk factors for unhealthy pregnancies, new-borns and children. Often in these communities, malaria occurs in mothers and children who are already weakened by parasitic, viral and bacterial infections; nutritional deficiencies; and genetic conditions (*21*). Broader determinants, such as socioeconomic status, mother's age, parity and health system factors further threaten the wellbeing of the mother and child, leading to some of the highest levels of maternal, infant and child mortality rates globally (*22*). Addressing these determinants requires a multisectoral approach underpinned by a health system that delivers effective primary health care, both in terms of quality and coverage.

To ensure that mothers and new-borns are protected, long-lasting insecticidal nets (LLINs) are routinely delivered through ANC and expanded programmes for immunization, respectively. About 28 million nets were distributed through these channels in sub-Saharan Africa in 2018. In the same year, about 61% of pregnant women and children slept under a treated mosquito net (**Section 7**). IPTp is now part of the WHO recommended

TABLE 3.2.

Estimated number of children aged 1–59 months infected with *P. falciparum* parasites in 2018 by subregion and overall in sub-Saharan Africa, *Source: WHO estimates.*

	Total number of children aged 1–59 months infected in 2018	Number by anaemia level among children aged 1–59 months who were infected in 2018			
		Severe (<7 g/dL)	Moderate (7–9.9 g/dL)	Mild (10–10.9 g/dL)	Not anaemic
Central Africa	7 130 000	630 000	3 800 000	1 5000 000	1 200 000
East and Southern Africa (+ Sudan and Somalia)	6 080 000	480 000	3 200 000	1 300 000	1 100 000
West Africa	10 610 000	14 253 000	5 000 000	2 400 000	2 500 000
Sub-Saharan Africa: total	**23 810 000**	**1 800 000**	**12 000 000**	**5 200 000**	**4 800 000**

P. falciparum: *Plasmodium falciparum*; WHO: World Health Organization.

ANC package, with an estimated 31% of pregnant women receiving at least three doses of IPTp (**Section 7**). IPTi has been scaled up nationally only in Sierra Leone, despite a WHO recommendation since 2010, following evidence of a significant impact on clinical incidence and severe anaemia in infants. It is recommended for delivery on a schedule that corresponds to that of diphteria, pertussis and tetanus (DPT) and measles vaccines. Management of fever remains inadequate, with nearly 40% of febrile children in sub-Saharan Africa not accessing treatment (**Section 8**). Although integrated community case management (iCCM) is considered an effective strategy in bridging the gap in clinical care for common childhood illnesses, its roll-out in most sub-Saharan African countries remains poor, mainly due to health-financing bottlenecks.

To highlight some of the potential health system quality and coverage issues related to malaria interventions, an analysis of the prevalence of exposure to malaria infection during pregnancy, coverage of four or more ANC visits (ANC4) (*22*) and use of three or more doses of IPTp during pregnancy (IPTp3) were implemented (**Fig. 3.6**). Countries appear to fall into several categories: those where access to ANC services is a major impediment to increasing coverage of IPTp3 (e.g. Central African Republic, Chad, Niger, Somalia and South Sudan); those where ANC4 coverage is relatively high but quality of care is an issue and few women receive IPTp during ANC visits (e.g. Angola, Cameroon, Congo, Equatorial Guinea, Gabon, Guinea-Bissau, Liberia, Mauritania and Zimbabwe); and those where coverage of both ANC4 and IPTp3 are moderate and the main opportunities are in increasing access (Burkina Faso, Burundi, the Democratic Republic of the Congo, Gambia, Ghana, Mali, Mozambique, Sierra Leone, the United Republic of Tanzania and Zambia).

FIG. 3.6.

Country comparison of coverage of ANC4 and IPTp3 in moderate and high transmission sub-Saharan Africa, 2018 Countries in red typeface are those where prevalence of exposure to malaria infection during pregnancy was >20% in 2018. *Source: WHO estimates.*

Coverage of 4 or more ANC visits \ IPTp3 coverage	<20%			>60%
<20%	Somalia South Sudan			
		Central African Republic Chad Niger		
	Eritrea Rwanda Sudan Uganda	Benin Côte d'Ivoire Kenya Madagascar Malawi Nigeria Senegal Togo	Burkina Faso Burundi Democratic Republic of the Congo Mali Mozambique United Republic of Tanzania Zambia	
>60%	Angola Congo Equatorial Guinea Liberia Mauritania Zimbabwe	Cameroon Gabon Guinea-Bissau	Gambia Ghana Sierra Leone	

ANC4: 4 or more antenatal care visits; IPTp3: third dose of intermittent preventive treatment in pregnancy; WHO: World Health Organization.

4 High burden to high impact approach

In November 2018, WHO and the RBM Partnership to End Malaria launched the *high burden to high impact* (HBHI) country-led approach (*23*) as a mechanism to bring the 11 highest burden countries back on track to achieve the 2025 GTS milestones (*1*). This followed the results of the world malaria reports of 2017 (*24*) and 2018 (*25*), which showed that, globally, progress has stalled in high-burden countries and that the GTS 2020 milestones are, therefore, unlikely to be achieved. These 11 countries (Burkina Faso, Cameroon, the Democratic Republic of the Congo, Ghana, India, Mali, Mozambique, Niger, Nigeria, Uganda and the United Republic of Tanzania) account for 70% of the global estimated case burden and 71% of global estimated deaths.

Many factors contribute to the rising malaria burden in these, and other, high-burden countries, including the underlying intensity of malaria transmission, sociodemographic and epidemiologic risk factors, poor access to care and suboptimal malaria intervention coverage, and funding constraints. Consequently, the approach includes the four key response elements shown in **Fig. 4.1**, which have the aim of supporting countries to address their core country challenges so that they can get back on track towards the GTS milestones.

4.1 HBHI INITIATION ACTIVITIES

By November 2019, the HBHI approach had been initiated in Burkina Faso, Cameroon, Democratic Republic of Congo, Ghana, India, Mozambique, Niger, Nigeria and Uganda. The process involved national consultation meetings with in-country stakeholders, key international malaria partners and WHO. Countries implemented self-assessments on various aspects of the four response elements, which formed the basis of HBHI country discussions. Following the HBHI initiation meetings, countries developed detailed activity plans to address challenges revealed during assessments. Mali and the United Republic of Tanzania are expected to have held their national consultation meeting by the end of the first quarter of 2020. The key HBHI response highlights in most countries in 2019 include launch or strengthening of social mobilization and advocacy movements through the launching of the campaign "Zero Malaria Starts With Me" (*26*) with support from the RBM Partnership; initiation of the process of developing national malaria data repositories and stratification for intervention mix analysis with support from WHO, in-country and international partners; and increased political accountability through work with parliamentarians and high level, multisectoral bodies.

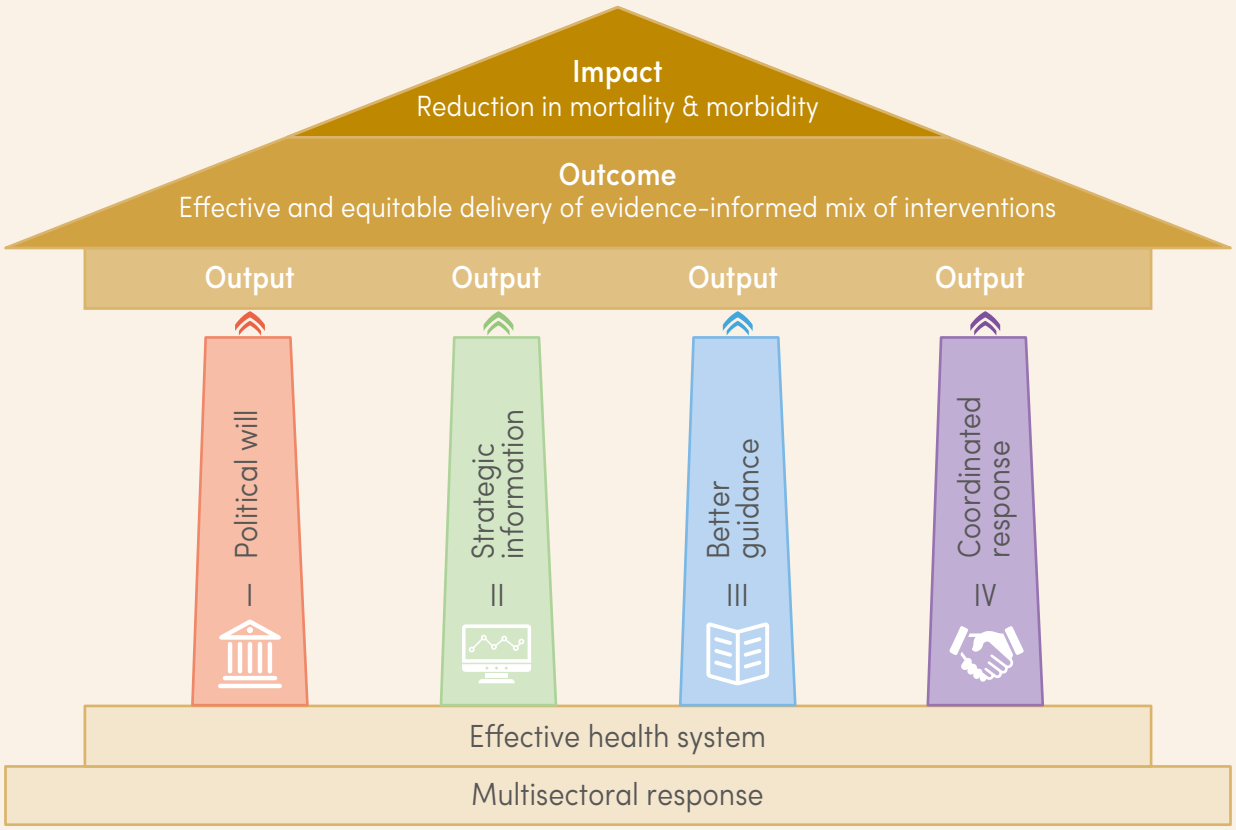
In addition, to ensure greater flexibility in adoption and adaptation of WHO recommendations by countries, the GMP convened an informal consultation in

September 2019 to reconsider the formulation of malaria policy guidance. The outcome of this consultation was submitted to the Malaria Policy Advisory Committee (MPAC) during its meeting in October 2019 (*27*). The MPAC agreed with the conclusion of the informal consultation that intervention prioritization should not be driven solely by sequentially optimizing single interventions for maximal coverage; instead, intervention prioritization should be based on local evidence and aligned to the specific needs of different epidemiological strata or settings, as defined in the country's national strategic plan. The MPAC appreciated the concept of "universal coverage" in striving to save lives, reduce disease and ultimately eradicate malaria. The MPAC encouraged work towards universal coverage of the right mix of interventions, recognizing that the coverage of individual interventions will vary by setting.

This section summarizes the progress made in malaria burden, prevention, diagnosis and treatment for all HBHI countries. It ends with a discussion of trends in external and domestic direct funding (excluding estimated costs of patient care) in the HBHI countries.

FIG. 4.1.

HBHI: a targeted malaria response to get countries back on target for the 2025 GTS milestones *Source: WHO GMP and RBM Partnership.*



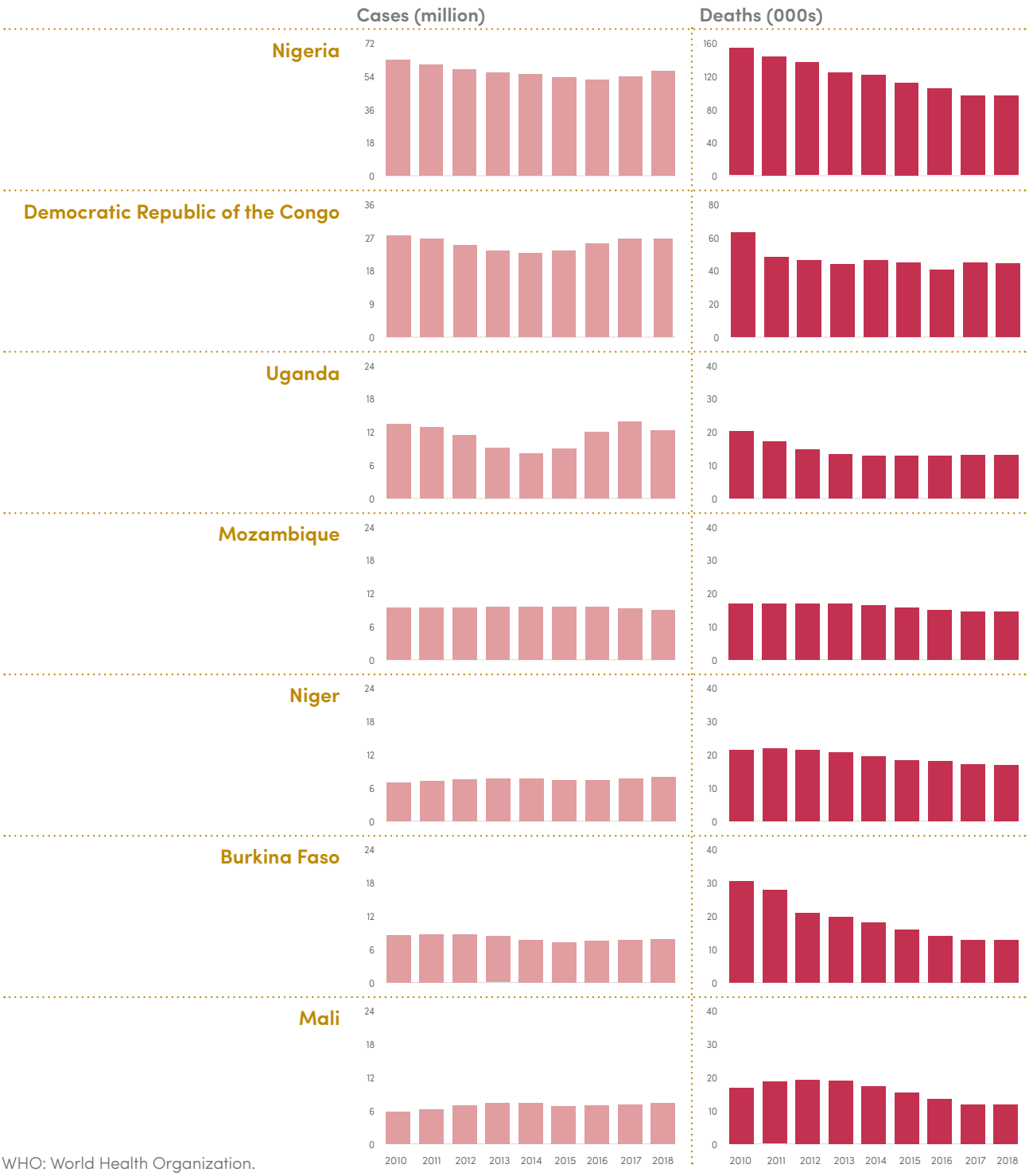
GMP: Global Malaria Programme; GTS: *Global technical strategy for malaria 2016–2030*; HBHI: high burden to high impact; RBM: Roll Back Malaria; WHO: World Health Organization.

4.2 BURDEN OF MALARIA CASES AND DEATHS

There were about 155 million estimated malaria cases in the 11 HBHI countries in 2018, compared with 177 million in 2010. The Democratic Republic of the Congo and Nigeria accounted for 84 million (54%) of total cases (**Fig. 4.2a**). Malaria deaths reduced from about 400 000 in 2010 to about 260 000 in 2018 (**Fig. 4.2a**).

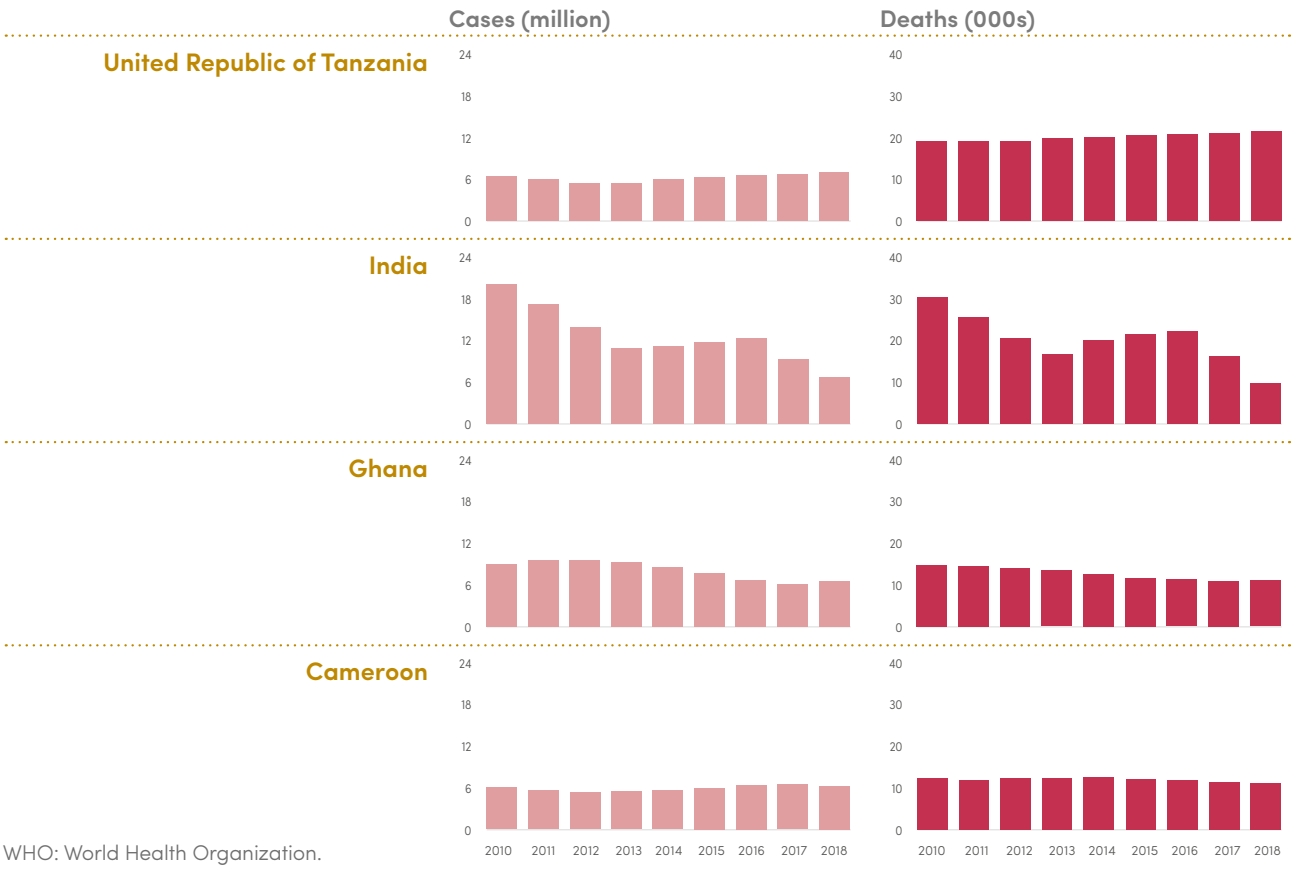
FIG. 4.2a.

Estimated malaria cases and deaths, 2010–2018 Countries are presented from highest to lowest number of estimated malaria cases in 2018. The estimated number of deaths for each country is shown in the right-hand column. *Source: WHO estimates.*



WHO: World Health Organization.

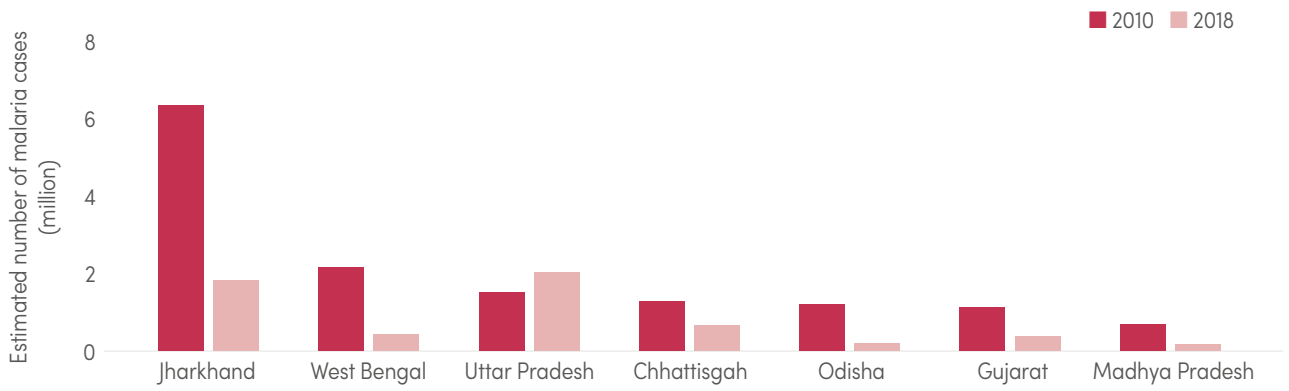
In India, only seven out of 36 states accounted for 90% of the estimated cases in 2018. In these seven states, there were large reductions in malaria cases in 2018 compared with 2010, from a total of 14.3 million cases to 5.7 million cases (**Fig. 4.2b**). For most other countries, however, the rates of reductions were generally slower in the past 3 years than in preceding years.



WHO: World Health Organization.

FIG. 4.2b.

Estimated malaria cases in India, showing seven states that contributed a combined 90% of cases, 2010 versus 2018 *Source: WHO estimates.*



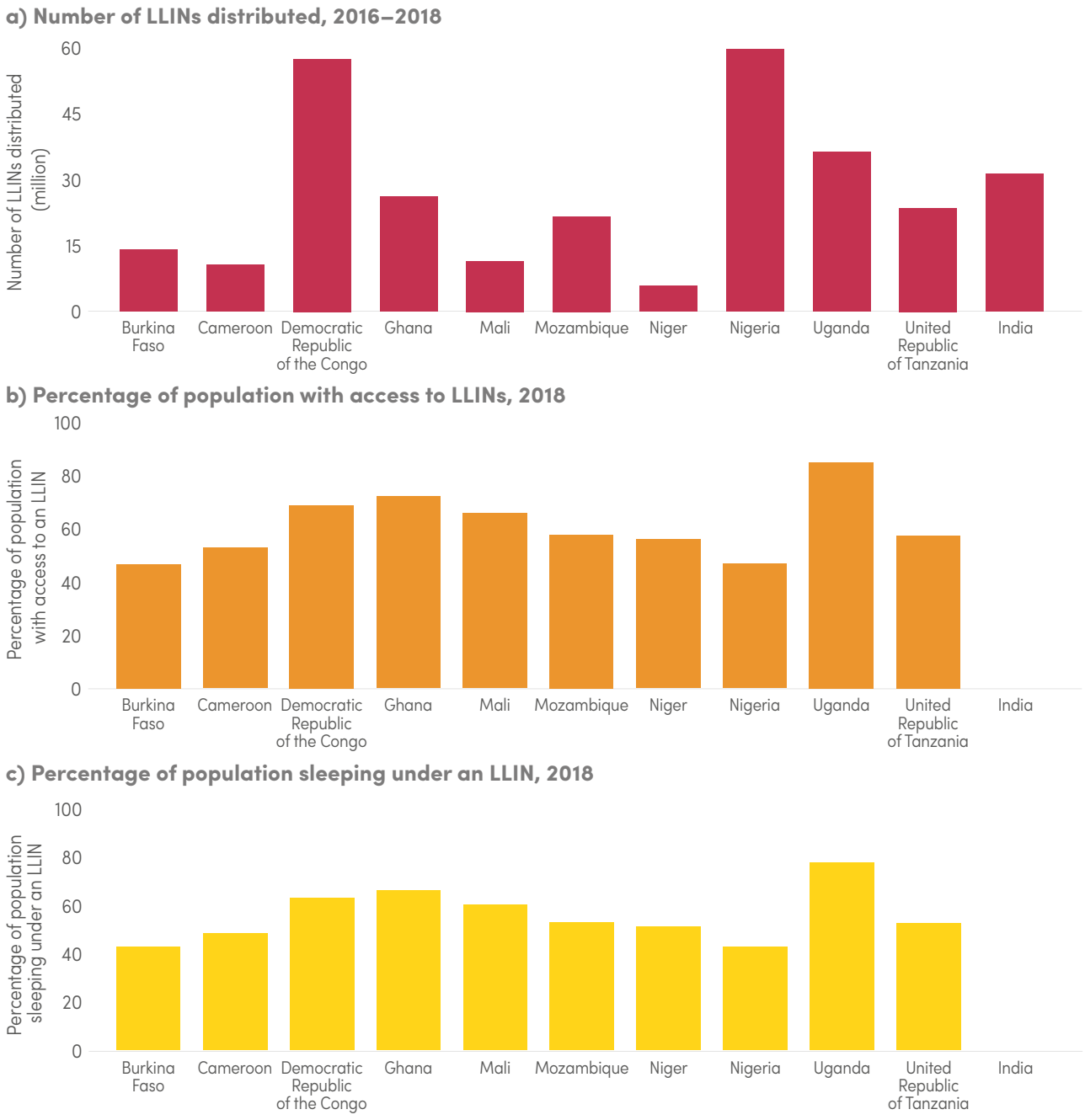
WHO: World Health Organization.

4.3 MALARIA PREVENTION

In the period 2016–2018, about 295 million long-lasting insecticidal nets (LLINs) were distributed in 11 HBHI countries, of which 116 million (39%) were distributed to communities in the Democratic Republic of the Congo and Nigeria (**Fig. 4.3a**). By 2018, access to LLINs was between 40% and 60% in Burkina Faso, Cameroon, Mozambique, Niger, Nigeria and the United Republic of Tanzania; between 60% and 70% in Mali; and between 70% and 80% in the Democratic Republic of the Congo, Ghana and Uganda (**Fig. 4.3b**). The percentage of the population sleeping under LLINs was highest in Uganda and lowest in Nigeria (**Fig. 4.3c**). The percentage of children sleeping under LLINs was about 50% in Burkina Faso and Nigeria, but above 70% in the

FIG. 4.3.

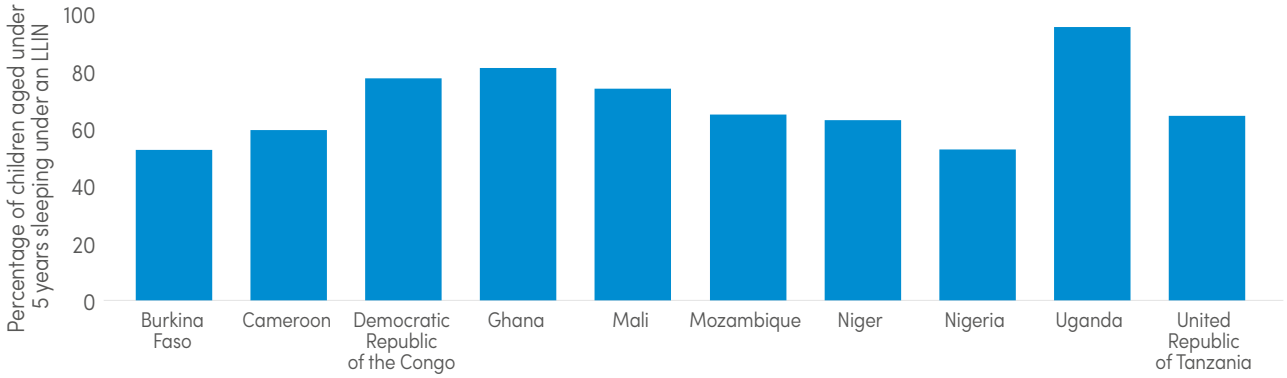
Distribution and coverage of preventive interventions *Source: NMP reports and WHO estimates.*



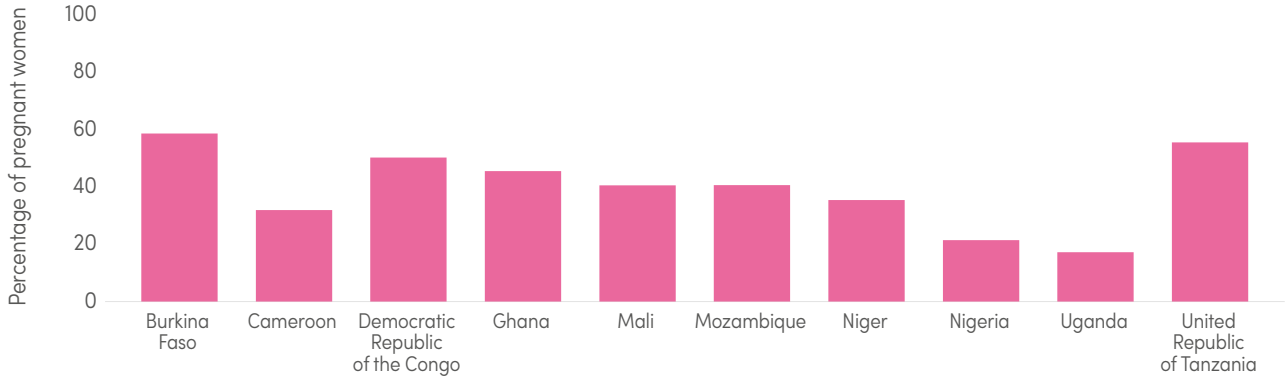
LLIN: long-lasting insecticidal net; NMP: national malaria programme; WHO: World Health Organization

Democratic Republic of Congo, Ghana and Uganda (**Fig. 4.4d**). LLIN use by pregnant women was almost exactly the same as that of children aged under 5 years. Coverage of the recommended three doses of SP for IPTp (IPTp3) was low to moderate, with only Burkina Faso and the United Republic of Tanzania estimated as having more than half of pregnant women receiving IPTp3 in 2018. In Cameroon, Nigeria and Uganda, the estimated coverage was about 30% or less (**Fig. 4.3e**). Of the 10 HBHI countries in Africa, six countries within the sub-Sahelian ecological zone implemented SMC; by 2018, a mean total of 17 million children, out of the 26 million targeted, were treated per SMC cycle. The gap in treatment was greatest in Ghana and Nigeria (**Fig. 4.3f**).

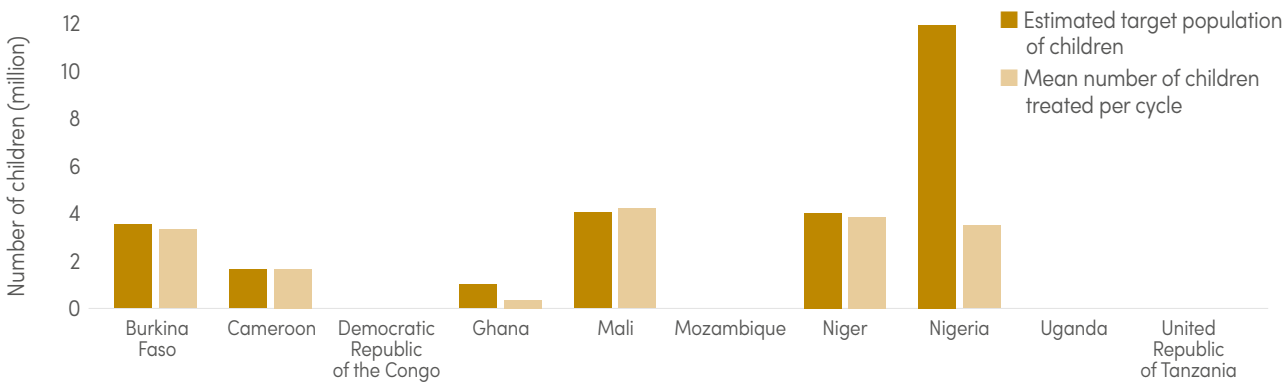
d) Percentage of children sleeping under an LLIN, 2018



e) Percentage of pregnant women who received IPTp3, 2018



f) SMC targeted children and mean treatments per cycle, 2018



HBHI: high burden to high impact; IPTp3: third dose of intermittent preventive treatment in pregnancy; LLIN: long-lasting insecticidal net; SMC: seasonal malaria chemoprevention.

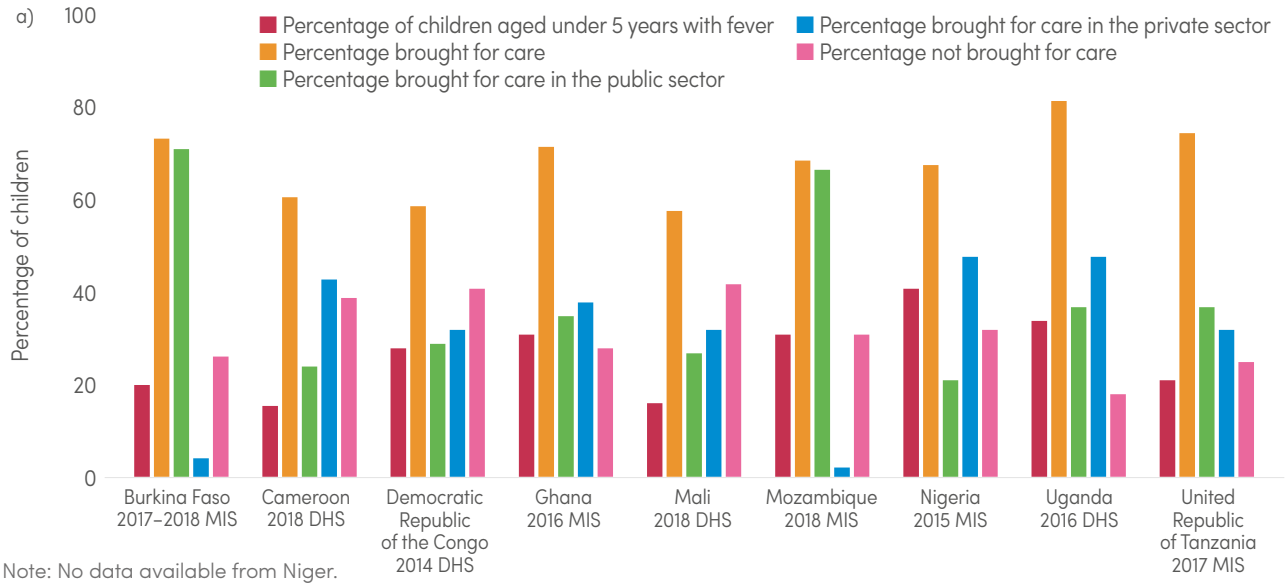
Note: population level coverage of malaria interventions not shown for India due to lack of household surveys. Out of 11 HBHI countries, only Burkina Faso, Cameroon, Ghana, Mali, Niger and Nigeria have areas eligible for SMC.

4.4 MALARIA DIAGNOSIS AND TREATMENT

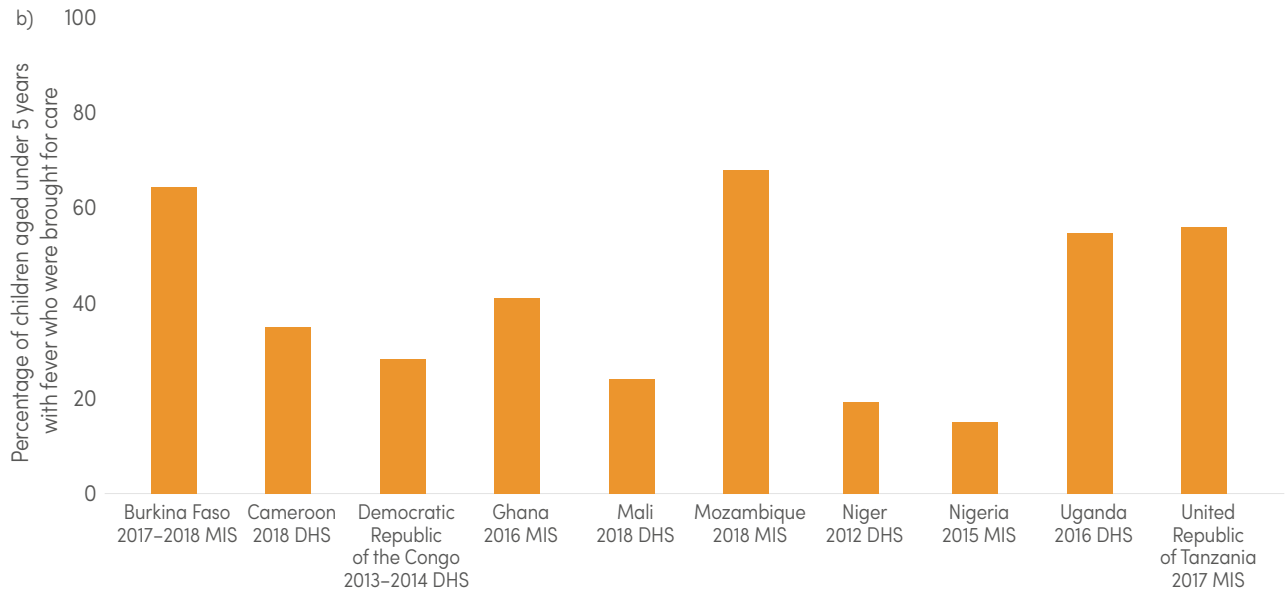
The percentage of children aged under 5 years with fever (in the 2 weeks preceding the survey) varied by country, from 16% in Cameroon to 41% in Nigeria (**Fig. 4.4a**). Among these children, the proportion seeking treatment ranged from 58% in Mali to 82% in Uganda. Only in Burkina Faso and Mozambique were more than 50% of these children treated in the public health sector; in other countries, 37% or less of these children were treated in this sector. The use of the private sector was highest in Nigeria and Uganda (48%), and lowest in Burkina Faso and Mozambique (<4%) (**Fig. 4.4a**). Worryingly, a considerable number of children were not brought for care, and in the Democratic Republic of the Congo and Mali, this figure was more than 40%. Among children who were brought for care, the percentage who were tested for malaria was about 30% or less in Cameroon, the Democratic Republic of the Congo, Mali, Niger and Nigeria; and about 50% or more in Burkina Faso, Ghana, Mozambique, Uganda and the United Republic of Tanzania (**Fig. 4.4b**).

FIG. 4.4.

Diagnosis and treatment of febrile children in HBHI African countries, (a) Treatment seeking for fevers in children aged under 5 years, and source of treatment by health sector, (b) Percentage of children aged under 5 years with fever who sought treatment and were diagnosed using a parasitological test *Source: Household surveys.*



Note: No data available from Niger.



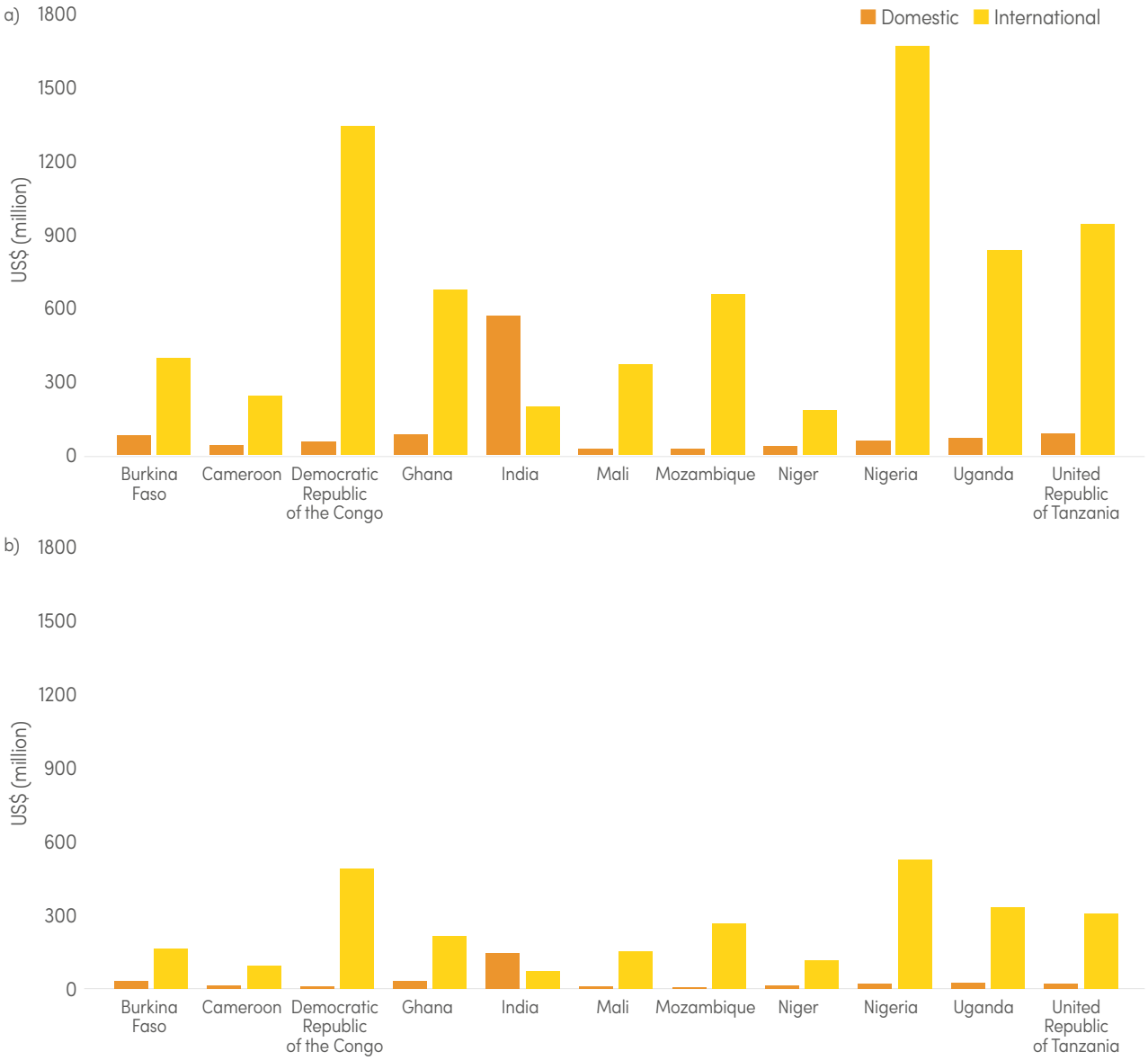
DHS: demographic and health surveys; HBHI: high burden to high impact; MIS: malaria indicator surveys.
Note: Data not available for the Democratic Republic of the Congo and Niger.

4.5 MALARIA FUNDING

An estimated US$ 9.4 billion in funding was directed at the 11 HBHI countries in the period 2010–2018. Of this, US$ 7.7 billion (82%) came from international sources. This funding represents direct budgetary investment in malaria control, but excludes the cost of health workers' time spent on treating patients. Over the 2010–2018 period, the Democratic Republic of the Congo and Nigeria received the largest amount of international funding (**Fig. 4.5a** and **Fig. 4.5b**). In the past 3 years (2016–2018), about US$ 3.5 billion of direct malaria funding was reported in the 11 HBHI countries, with about 31% of this funding being in the Democratic Republic of the Congo and Nigeria (**Fig. 4.5b**). Except for India, direct domestic investment remains very low in the HBHI countries.

FIG. 4.5.

Total international and domestic direct funding for malaria in the 11 HBHI countries, (a) 2010–2018 and (b) 2016–2018 *Sources: ForeignAssistance.gov, United Kingdom Department for International Development, Global Fund, NMP reports, OECD creditor reporting system database, World Bank Data Bank and WHO estimates.*



Global Fund: Global Fund to Fight AIDS, Tuberculosis and Malaria; NMP: national malaria programme; OECD: Organisation for Economic Co-operation and Development; WHO: World Health Organization.

5 Malaria elimination and prevention of re-establishment

An increasing number of countries are progressing towards elimination of malaria. Globally, the number of countries that were malaria endemic in 2000 and that reported fewer than 10 000 malaria cases increased from 40 in 2010 to 49 in 2018; in the same period, the number of countries with fewer than 100 indigenous cases increased from 17 to 27. Between 2017 and 2018, the number of countries with fewer than 10 indigenous cases increased from 19 to 24 (**Fig. 5.1**).

The GTS milestone for 2020 is to eliminate malaria from at least 10 countries that were malaria endemic in 2015 (*1*). Between 2000 and 2018, 19 countries attained zero indigenous cases for 3 years or more (**Table 5.1**); four countries that were malaria endemic in 2015 have since eliminated malaria. In 2018, no malaria endemic country reached zero indigenous malaria cases for the third consecutive year. However, several countries recorded zero indigenous cases for the first time in 2018, or for a second consecutive year (**Section 5.1**).

Certification of elimination by WHO is the official recognition of a country being free from indigenous malaria cases; this is based on an independent evaluation verifying the interruption of transmission and the country's ability to prevent re-establishment of transmission. Paraguay and Uzbekistan were awarded WHO certification of elimination in 2018, with Algeria and Argentina achieving certification in early 2019.

5.1 E-2020 INITIATIVE

In April 2016, WHO published an assessment of the likelihood of countries achieving malaria elimination by 2020. This assessment was based on the countries' trends in the number of indigenous malaria cases, their declared malaria elimination objectives and the informed opinions of WHO experts in the field (*28*). Twenty-one countries, across five WHO regions, were identified as being the most likely to reach zero indigenous cases by 2020. These countries were termed as the "eliminating countries for 2020" (E-2020), and they are the special focus of WHO efforts to accelerate national elimination efforts and monitor progress towards malaria free status (**Fig. 5.2**). An inaugural meeting of the national malaria programmes (NMPs) for the E-2020 countries, referred to as the Global Forum of Malaria-Eliminating Countries (Global Forum), was organized by WHO in March 2017 in Geneva, Switzerland; the Global Forum was held again in June 2018 in San José, Costa Rica, and in June 2019 in Wuxi, China.

In April 2018, WHO established the Malaria Elimination Oversight Committee (MEOC) to help countries to reach their elimination goals. The MEOC attended the 2018 and 2019 Global Forums and, in February 2019, met with a small group of countries on track to reach malaria elimination by 2020, to support those countries in their attempts to achieve malaria elimination. The MEOC has produced a series of recommendations to help countries accelerate towards this goal.

TABLE 5.1.

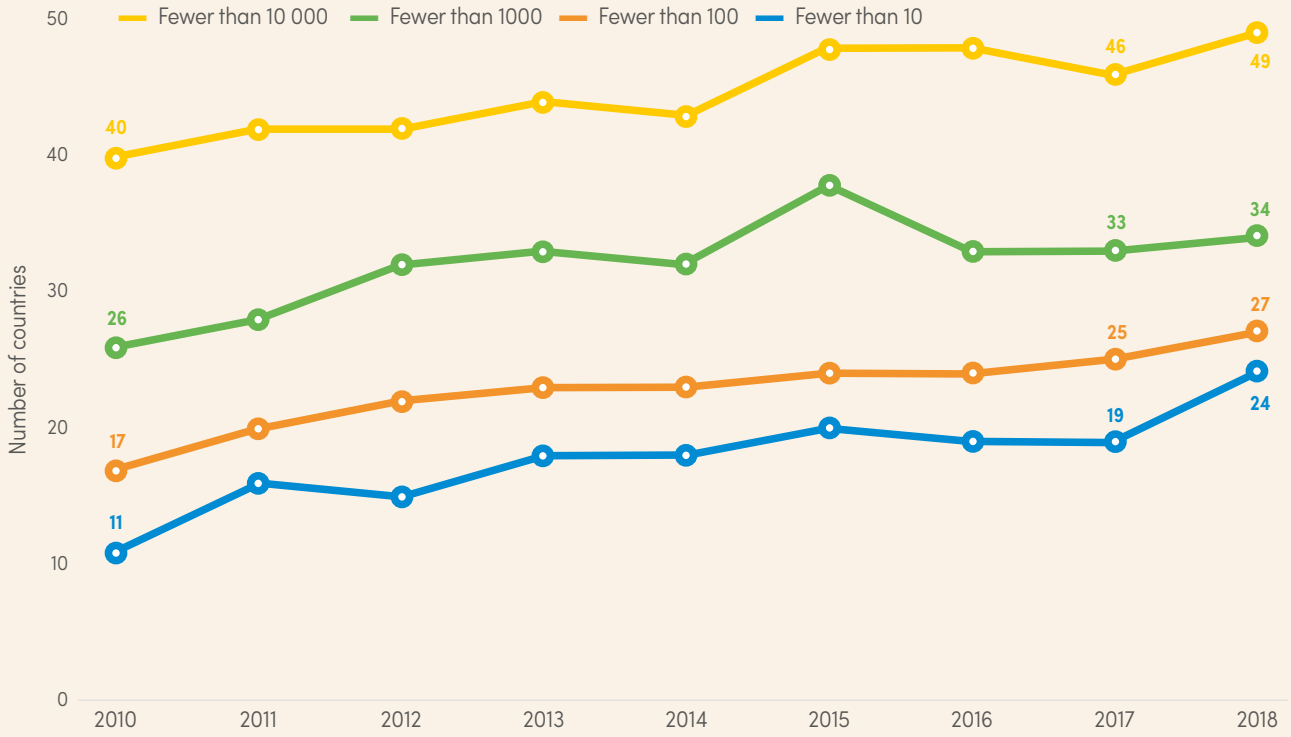
Countries eliminating malaria since 2000 Countries are shown by the year that they attained 3 consecutive years of zero indigenous cases; countries that have been certified as free from malaria are shown in green (with the year of certification in parentheses). *Source: Country reports and WHO.*

2000	Egypt	United Arab Emirates (2007)		
2001				
2002				
2003				
2004	Kazakhstan			
2005				
2006				
2007	Morocco (2010)	Syrian Arab Republic	Turkmenistan (2010)	
2008	Armenia (2011)			
2009				
2010				
2011	Iraq			
2012	Georgia	Turkey		
2013	Argentina (2019)	Kyrgyzstan (2016)	Oman	Uzbekistan (2018)
2014	Paraguay (2018)			
2015	Azerbaijan	Sri Lanka (2016)		
2016	Algeria (2019)			
2017	Tajikistan			
2018				

WHO: World Health Organization.

FIG. 5.1.

Number of countries that were malaria endemic in 2000, with fewer than 10, 100, 1000 and 10 000 indigenous malaria cases between 2010 and 2018 *Sources: NMP reports and WHO estimates.*



NMP: national malaria programme; WHO: World Health Organization.

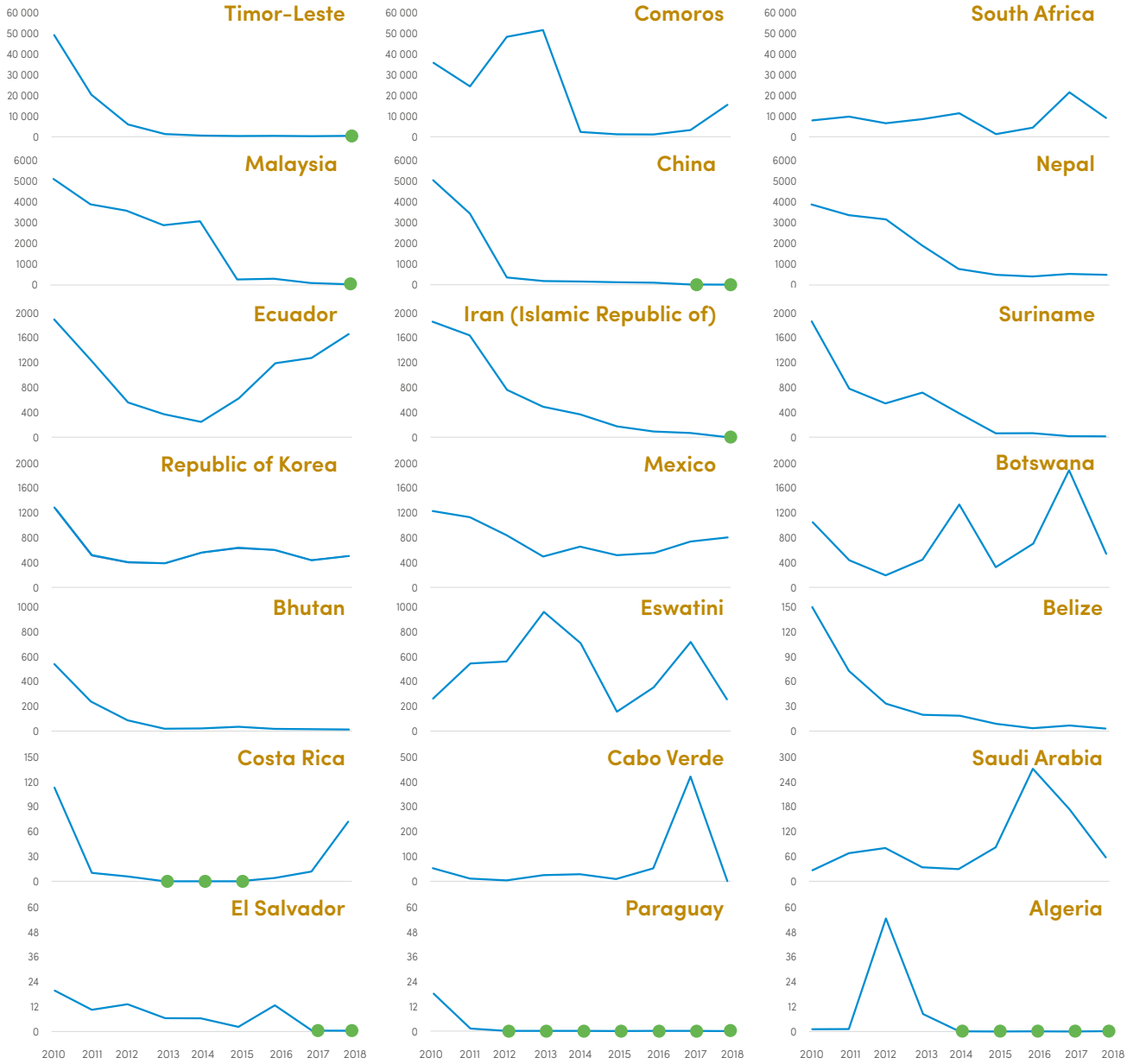
In 2018, several countries reported significant progress towards elimination (**Fig. 5.2**). For the first time, Iran (Islamic Republic of), Malaysia and Timor-Leste reported zero indigenous cases, while China and El Salvador reported their second year of zero indigenous cases. Cabo Verde, Eswatini, Saudi Arabia and South Africa reported large reductions in the number of cases in 2018 compared with 2017. Comoros and Costa Rica, however, reported large increases in the number of cases.

5.2 GREATER MEKONG SUBREGION

The six countries of the Greater Mekong subregion (GMS) – Cambodia, China (Yunnan Province), Lao People's Democratic Republic, Myanmar, Thailand and Viet Nam – continue to make significant gains as

FIG. 5.2.

Trends in indigenous malaria cases in E-2020 countries, 2010–2018 Countries are presented from highest to lowest number of indigenous malaria cases at baseline year, 2010; the graphs show the number of indigenous malaria cases from 2010 to 2018. Years with zero indigenous malaria cases are represented by green dots. *Source: NMP reports.*



E-2020: malaria-eliminating countries for 2020; NMP: national malaria programme.

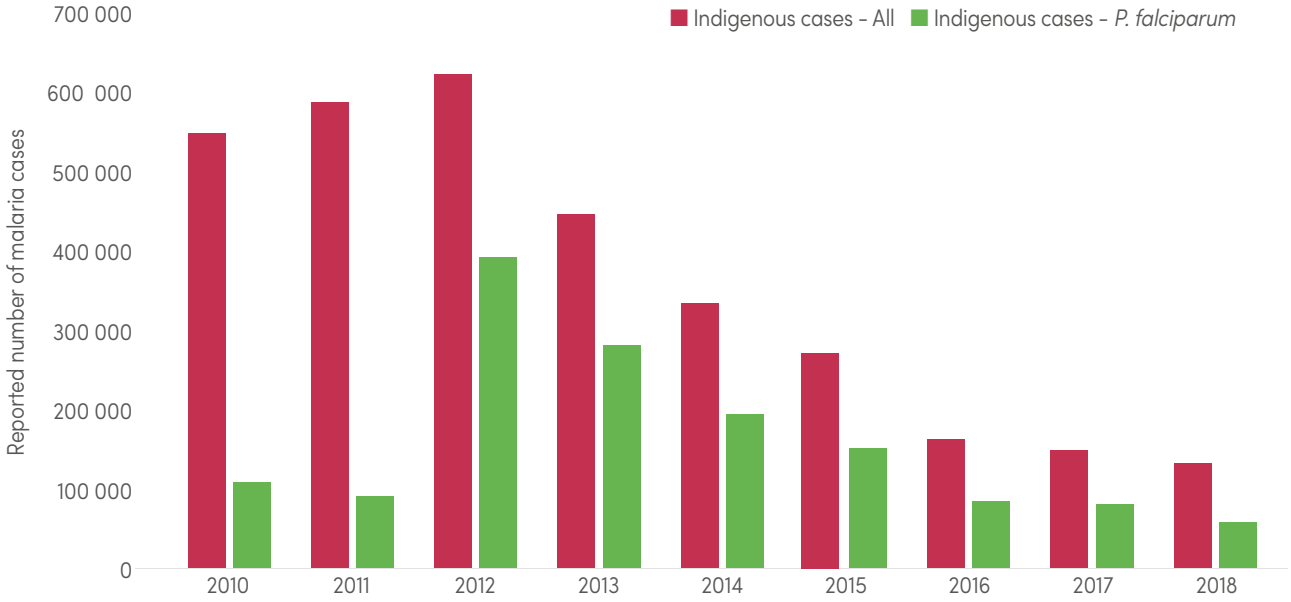
Note: Cases for Botswana, Nepal and Timor-Leste are derived from adjusting reported data for reporting and testing rates, and treatment seeking in different health sectors.

they aim for malaria elimination by 2030. Between 2010 and 2018, the reported number of malaria cases fell by 76% (**Fig. 5.3**); over the same period, malaria deaths fell by 95%. The GMS has reported a steep decline in *P. falciparum* cases: a decrease of 48% since 2010, and an 80% reduction in 2018 from the peak of 390 000 cases in 2012. This accelerated decrease in *P. falciparum* is especially critical because of drug resistance: in the GMS, *P. falciparum* parasites have developed partial resistance to artemisinin – the core compound of the best available antimalarial drugs.

In 2018, Cambodia reported no malaria-related deaths for the first time in the country's history. China also reported its second consecutive year of zero indigenous cases. Meanwhile, Thailand is nearing *P. falciparum* elimination, with a 38% decrease in *P. falciparum* cases between 2017 and 2018.

FIG. 5.3.

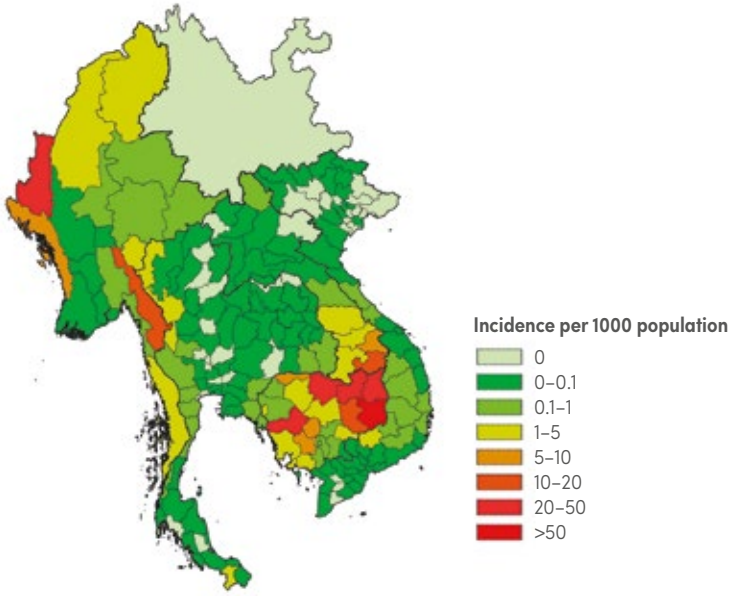
***P. falciparum* cases in the GMS, 2010–2018** *Source: NMP reports.*



GMS: Greater Mekong subregion; NMP: national malaria programme; *P. falciparum*: *Plasmodium falciparum*.

FIG. 5.4.

Regional map of malaria incidence in the GMS by area, 2018 *Source: NMP reports.*



GMS: Greater Mekong subregion; NMP: national malaria programme.

6 Investments in malaria programmes and research

For 2020, the GTS milestones are a global reduction of at least 40% in malaria case incidence and mortality rates compared with 2015, elimination in at least 10 countries and prevention of re-establishment in all malaria free countries (*1*). Estimates of the funding required to achieve these milestones have been set out in the GTS. Total annual resources needed were estimated at US$ 4.1 billion in 2016, rising to US$ 6.8 billion in 2020. An additional US$ 0.72 billion is estimated to be required annually for global malaria research and development (*1*).

This section presents the most up-to-date funding trends for malaria control and elimination, by source and channel of funding for the period 2010–2018, both globally and for major country groupings. It then presents investments in malaria-related research and development (R&D) for the same period.

A large proportion of the investment in malaria is spent on scaling up malaria prevention, diagnosis and treatment. This section presents trends in the sales and in-country distribution of insecticide-treated mosquito nets (ITNs), artemisinin-based combination therapies (ACTs) and RDTs.

6.1 FUNDING FOR MALARIA CONTROL AND ELIMINATION

For the 91 countries analysed in this section, total funding for malaria control and elimination was estimated at US$ 2.7 billion in 2018, compared with US$ 3.2 billion in 2017. The amount invested in 2018 falls short of the US$ 5.0 billion estimated to be required globally to stay on track towards the GTS milestones (*1*). Moreover, the funding gap between the amount invested and the resources needed widened from US$ 1.3 billion in 2017 to US$ 2.3 billion in 2018.

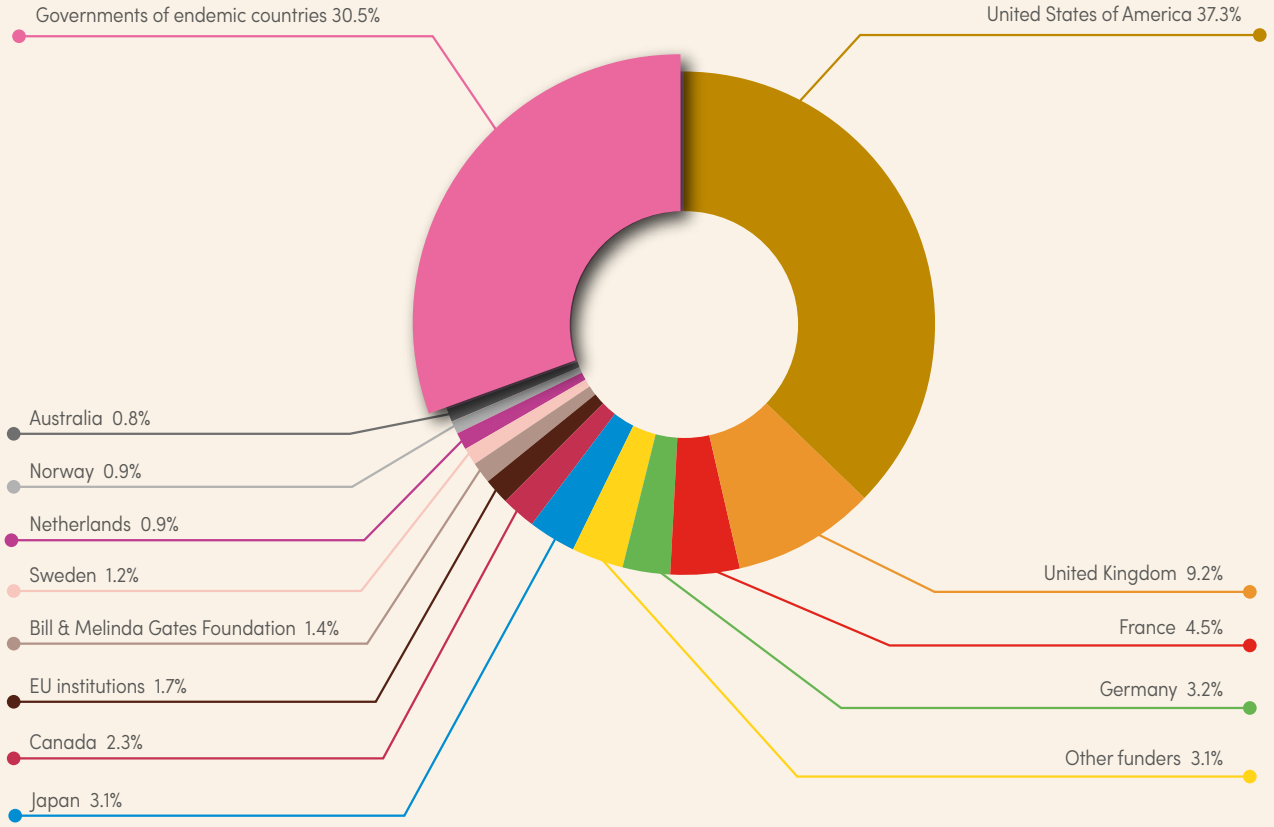
Over the period 2010–2018, nearly 70% of the total funding for malaria control and elimination was provided by international sources (**Fig. 6.1**). However, the aggregated figures hide substantial variations in the relative share of funding from domestic and international sources across country groups, as noted later in this section.

Of the US$ 2.7 billion invested in 2018, US$ 1.8 billion came from international funders. The government of the United States of America (USA) contributed a total of US$ 1.0 billion through planned bilateral funding and contributions to multilateral funding agencies, followed by bilateral and multilateral disbursements from the United Kingdom of Great Britain and Northern Ireland (United Kingdom) of US$ 0.2 billion; France, Japan and Germany with contributions of about US$ 0.1 billion each; and other country members of the Development Assistance Committee and private sector contributors of about US$ 0.3 billion combined (**Fig. 6.2**).

Governments of malaria endemic countries continued to contribute about 30% of the total funding (**Fig. 6.1**), with investments reaching US$ 0.9 billion in 2018 (**Fig. 6.2**). Of this amount, US$ 0.6 billion was invested in malaria control activities, and US$ 0.3 billion was estimated to have been spent on malaria case management in the public sector.

FIG. 6.1.

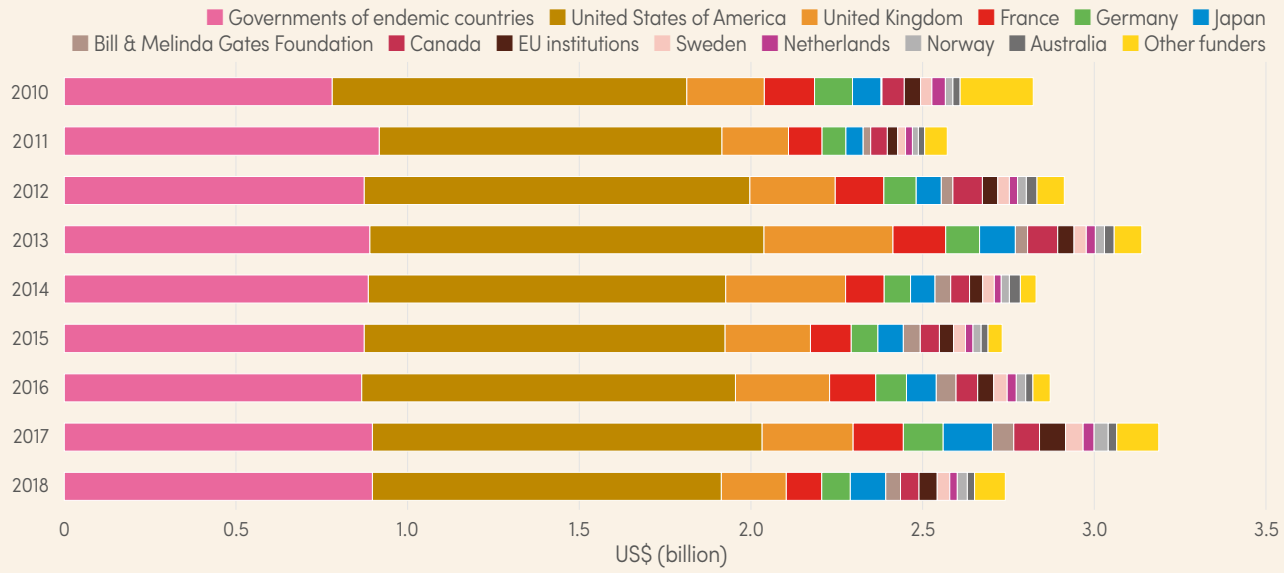
Funding for malaria control and elimination over the period 2010–2018 (% of total funding), by source of funds (constant 2018 US$) *Sources: ForeignAssistance.gov, United Kingdom Department for International Development, Global Fund, NMP reports, OECD creditor reporting system database, the World Bank Data Bank and WHO estimates.*



EU: European Union; Global Fund: Global Fund to Fight AIDS, Tuberculosis and Malaria; NMP: national malaria programme; OECD: Organisation for Economic Co-operation and Development; WHO: World Health Organization.

FIG. 6.2.

Funding for malaria control and elimination 2010–2018, by source of funds (constant 2018 US$) *Sources: ForeignAssistance.gov, United Kingdom Department for International Development, Global Fund, NMP reports, OECD creditor reporting system database, the World Bank Data Bank and WHO estimates.*



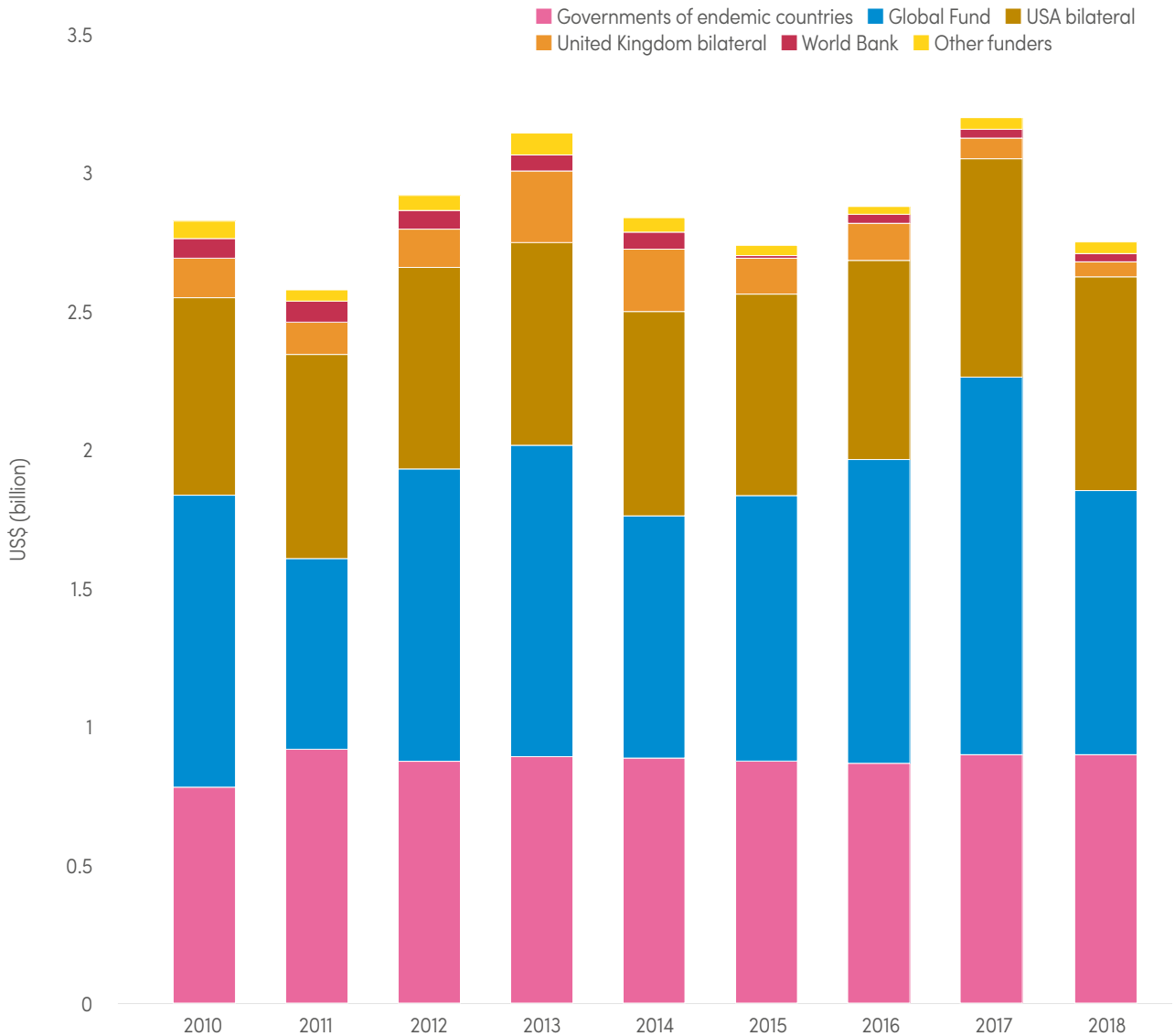
EU: European Union; Global Fund: Global Fund to Fight AIDS, Tuberculosis and Malaria; NMP: national malaria programme; OECD: Organisation for Economic Co-operation and Development; WHO: World Health Organization.

Of the US$ 2.7 billion invested in 2018, nearly US$ 1.0 billion (35%) was channelled through the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) (**Fig. 6.3**). Compared with 2017, the Global Fund's disbursements to malaria endemic countries decreased by about US$ 0.4 billion in 2018. This difference in the disbursement amount in 2018 and 2017 reflects the cyclical distribution of ITNs supported by the Global Fund, and an increase in disbursements in 2017, corresponding to the end of most malaria grants in that year (**Fig. 6.3**).

Planned bilateral funding from the government of the USA amounted to US$ 0.8 billion in 2018, which was slightly lower than in 2017, although above the levels of all other annual planned contributions since 2010 (**Fig. 6.3**). The United Kingdom remains the second-largest bilateral funder, with about US$ 0.1 billion in 2018, followed by contributions from the World Bank and other Development Assistance Committee members (**Fig. 6.3**). With US$ 0.9 billion invested in 2018, the total contribution from governments of malaria endemic countries remained the same as in 2017.

FIG. 6.3.

Funding for malaria control and elimination 2010–2018, by channel (constant 2018 US$) *Sources: ForeignAssistance.gov, United Kingdom Department for International Development, Global Fund, NMP reports, OECD creditor reporting system database, the World Bank Data Bank and WHO estimates.*



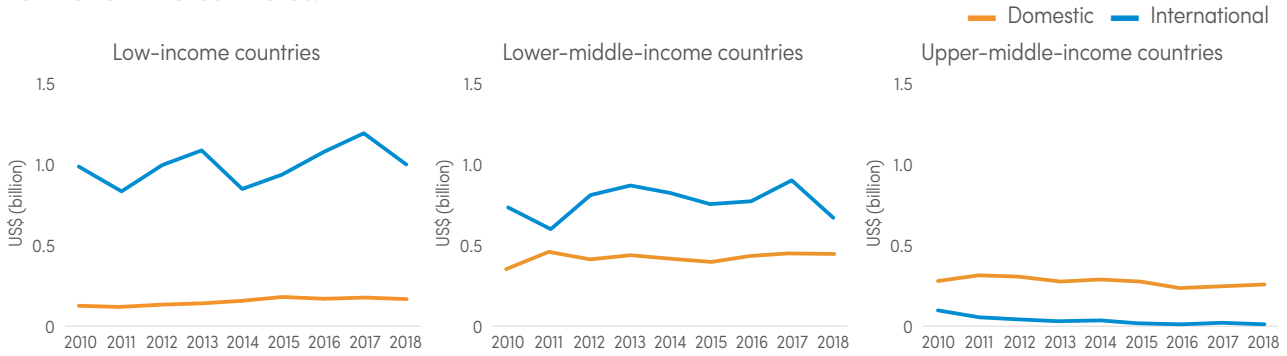
Global Fund: Global Fund to Fight AIDS, Tuberculosis and Malaria; NMP: national malaria programme; OECD: Organisation for Economic Co-operation and Development; USA: United States of America; WHO: World Health Organization.

Fig. 6.4 shows the substantial variation across country income groups in the share of funding from domestic and international sources. The 29 low-income countries accounted for 47% of total funding for malaria in 2018 (and >90% of global malaria cases and deaths, respectively) with 85% of their funding coming from international sources. International funding also dominated in the group of 36 lower-middle-income countries (43% of total funding in 2018), accounting for 61% of the amount invested in these countries. In contrast, in the group of 23 upper-middle-income countries (11% of the total funding in 2018), 5% of their malaria funding came from international sources, and 95% came from domestic public funding.

Of the US$ 2.7 billion invested in 2018, nearly three quarters benefited the WHO African Region, followed by the WHO Region of the Americas (7%), WHO South-East Asia Region (6%), and WHO Eastern Mediterranean Region and WHO Western Pacific Region (5% each) (**Fig. 6.5**). Funding flows for which no geographical information on recipients was available represented 5% of the total funding in 2018 (**Fig. 6.5**).

FIG. 6.4.

Funding for malaria control and elimination 2010–2018, by World Bank 2018 income group and source of funding (constant 2018 US$)[a] *Sources: ForeignAssistance.gov, United Kingdom Department for International Development, Global Fund, NMP reports, OECD creditor reporting system database, the World Bank Data Bank and WHO estimates.*

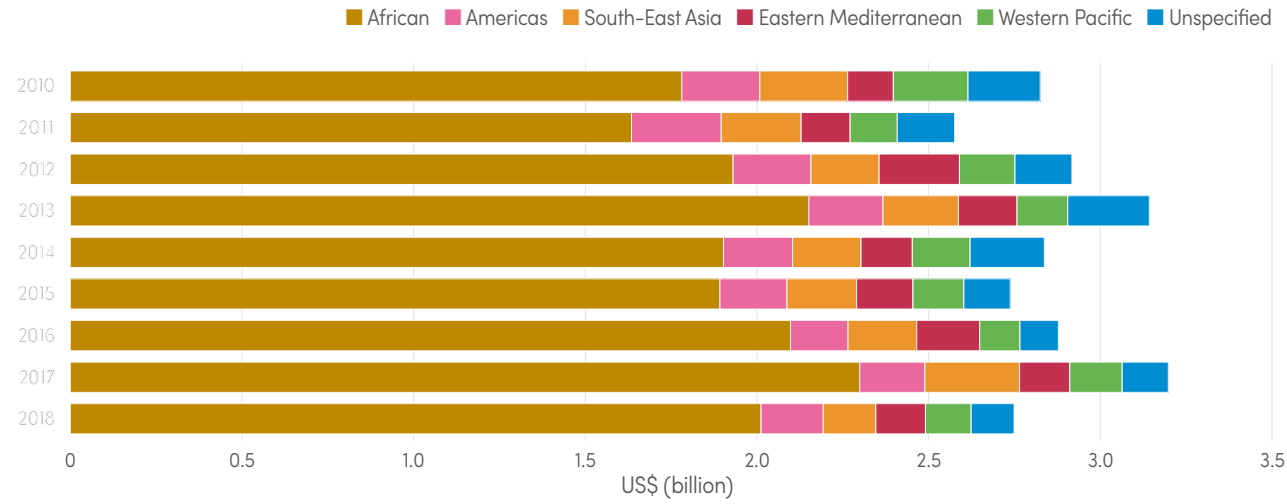


Global Fund: Global Fund to Fight AIDS, Tuberculosis and Malaria; NMP: national malaria programme; OECD: Organisation for Economic Co-operation and Development; WHO: World Health Organization.

[a] Domestic excludes out-of-pocket spending by households.

FIG. 6.5.

Funding for malaria control and elimination 2010–2018, by WHO region (constant 2018 US$)[a] *Sources: ForeignAssistance.gov, United Kingdom Department for International Development, Global Fund, NMP reports, OECD creditor reporting system database, World Bank Data Bank and WHO estimates.*



Global Fund: Global Fund to Fight AIDS, Tuberculosis and Malaria; NMP: national malaria programme; OECD: Organisation for Economic Co-operation and Development; WHO: World Health Organization.

[a] "Unspecified" category refers to funding flows, with no information on the geographical localization of their recipients.

6.2 INVESTMENTS IN MALARIA R&D

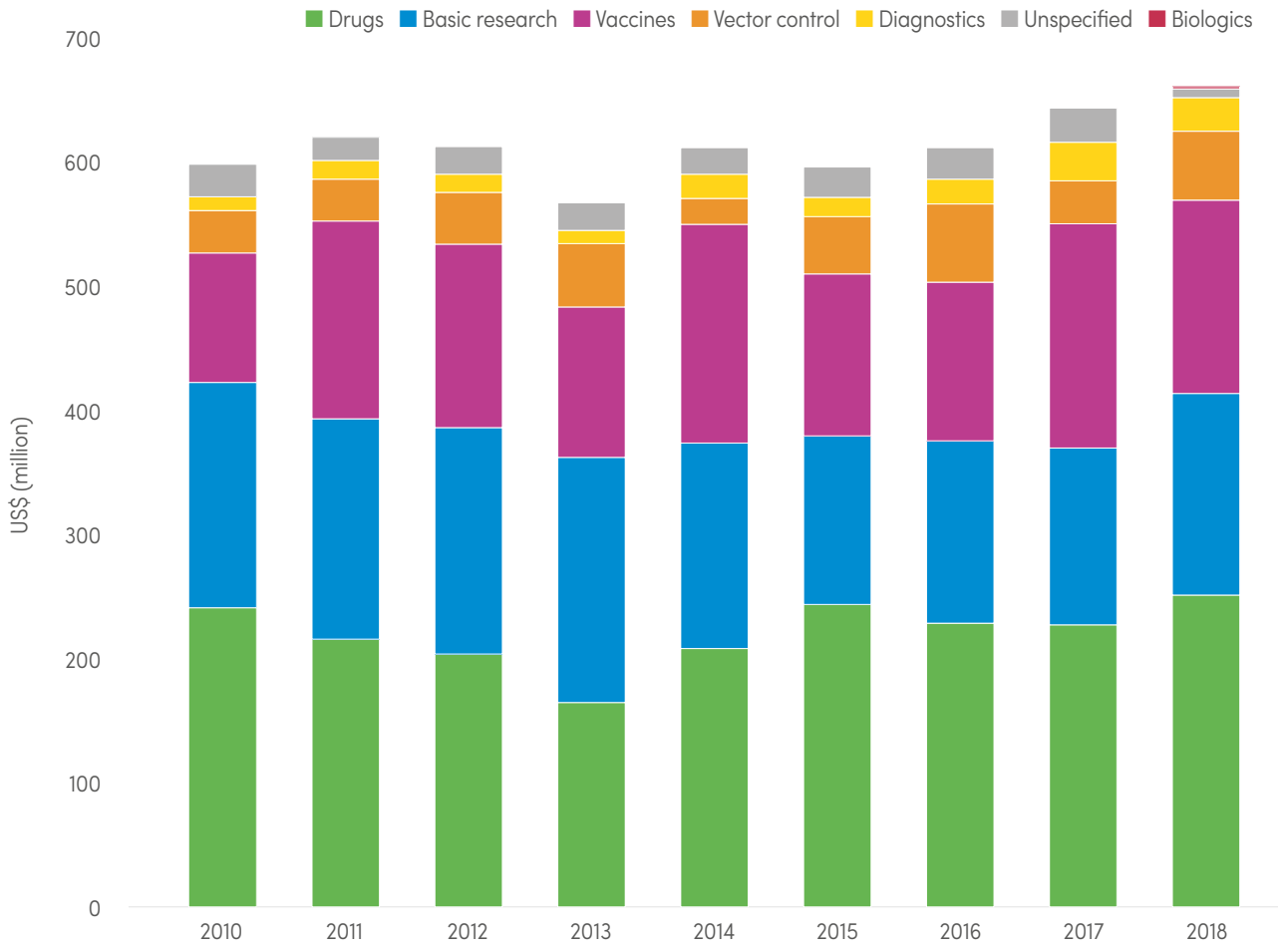
Globally, a total funding of US$ 663 million was invested in basic research and product development for malaria in 2018. This was a modest increase from the previous year (an increase of US$ 18 million, or 2.8%), but marked the third consecutive year of increased funding, and the largest annual investment in malaria R&D since its peak of US$ 676 million in 2009.

Funding for drug R&D increased to the highest level ever recorded (from US$ 228 million in 2017 to US$ 252 million in 2018) (**Fig. 6.6**), driven by increased private sector industry investment in several Phase II trials of new chemical entities with the potential for single-exposure radical cure. Funding for basic research also increased (from US$ 143 million in 2017 to US$ 163 million in 2018) (**Fig. 6.6**), as did funding for vector control product R&D (from US$ 35 million in 2017 to US$ 56 million in 2018) (**Fig. 6.6**), although this latter change was due largely to the cyclical funding patterns of the Bill & Melinda Gates Foundation.

Funding for vaccine R&D decreased (from US$ 181 million in 2017 to US$ 156 million in 2018)

FIG. 6.6.

Funding for malaria-related R&D 2010–2018, by product type (constant 2018 US$) *Sources: Policy Cures Research - G-FINDER 2019 report (in preparation).*



R&D: research and development.

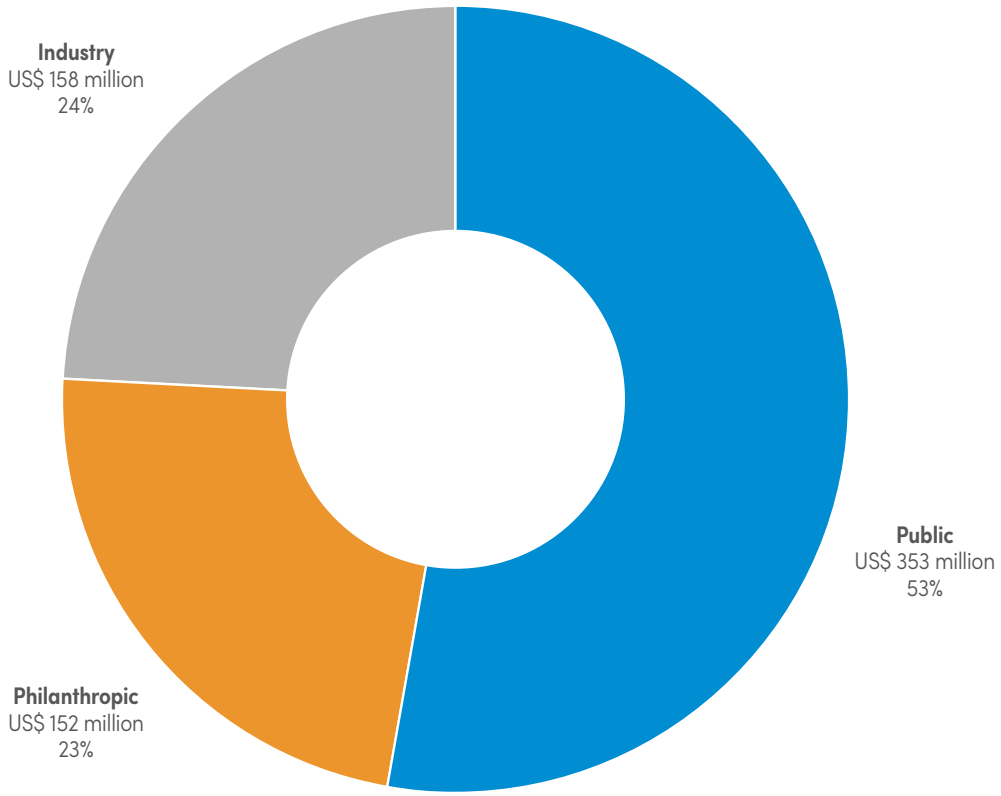
(**Fig. 6.6**), owing to lower investment from private sector industry, which in turn reflects a pipeline that saw no new candidates advance from or enter into late-stage clinical trials, and pilot implementation studies for the vaccine RTS,S not commencing until 2019. Diagnostic R&D was the only other product area to receive lower funding in 2018, falling from US$ 31 million in 2017 to US$ 27 million in 2018 (**Fig. 6.6**).

Just over half (US$ 352 million, or 53%) of all malaria R&D funding in 2018 was for basic and early stage research; a further 27% (US$ 176 million) went to clinical development and post-registration studies. The remaining funding was not allocated to specific products or R&D stages, but mostly consisted of core funding to product development partnerships.

The public sector provided just over half (US$ 353 million, or 53%) of all malaria R&D funding in 2018 (**Fig. 6.7**), which was the same as in each of the previous 8 years. The remaining funding was split evenly between private sector industry (US$ 158 million, or 24%) and the philanthropic sector (US$ 152 million, or 23%) (**Fig. 6.7**). This was a record high investment by private sector industry, and marked the fourth consecutive year that its contribution equalled that of the philanthropic sector.

FIG. 6.7.

Malaria R&D funding in 2018, by sector (constant 2018 US$) *Sources: Policy Cures Research - G-FINDER 2019 report (in preparation).*



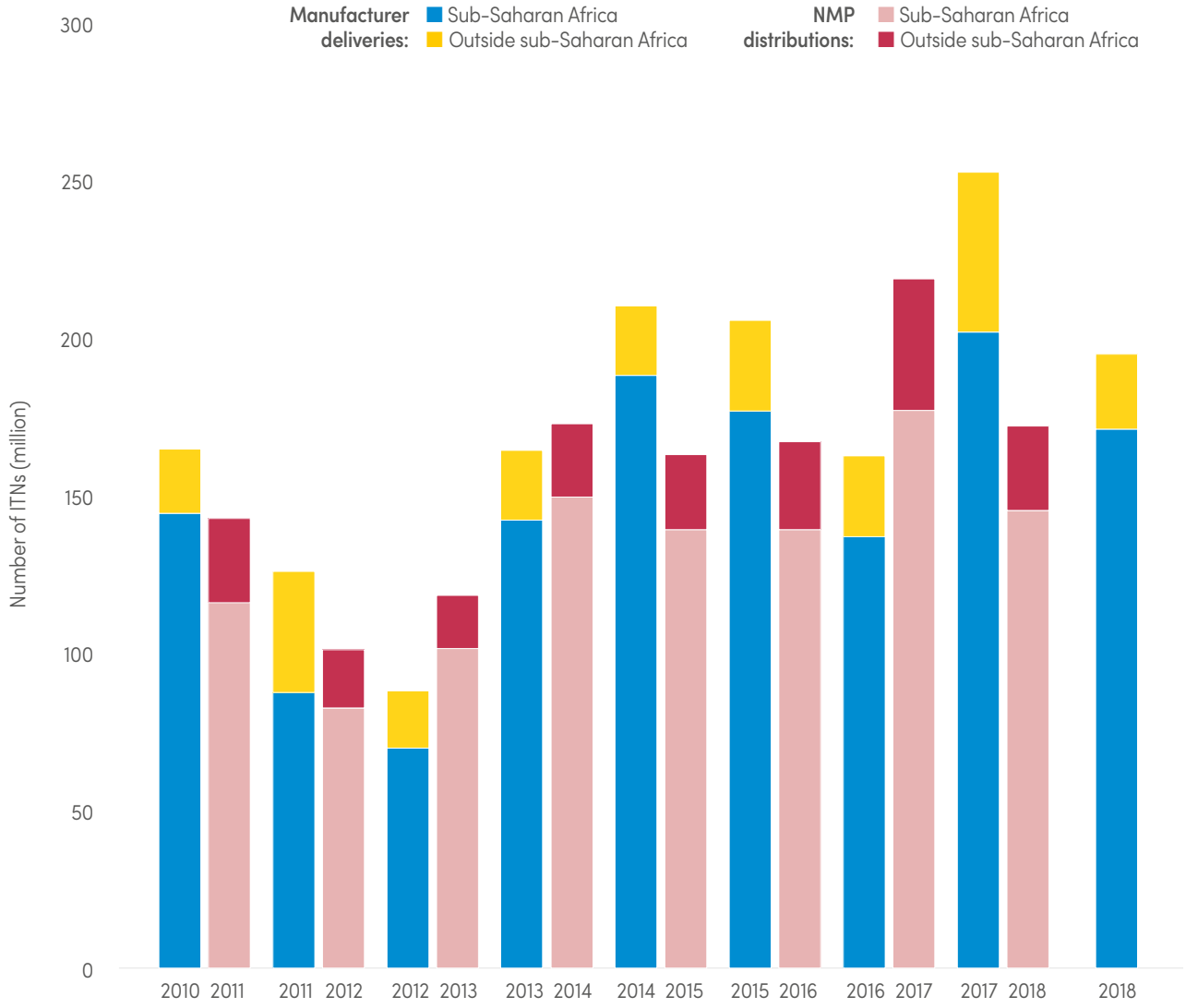
R&D: research and development.

6.3 PROCUREMENT AND DISTRIBUTIONS OF ITNs

The peak year for manufacturer deliveries of ITNs was 2017, when 251 million nets were reported as having been delivered globally. In 2018, about 197 million ITNs were delivered by manufacturers, of which more than 87% were delivered to countries in sub-Saharan Africa. This is fewer than in 2017, when 224 million nets were delivered worldwide (**Fig. 6.8**). Globally, the main channel of delivery was mass campaigns, while routine

FIG. 6.8.

Number of ITNs delivered by manufacturers[a] and distributed[b] by NMPs, 2010–2018 *Sources: Milliner Global Associates and NMP reports.*



ITN: insecticide-treated mosquito net; NMP: national malaria programme.

[a] Deliveries by manufacturers in a given year are often not reflected in distributions by NMPs in that year; a lag of up to 1 year may occur.

[b] Distributions of ITNs reported by NMPs do not always reflect all the nets that have been distributed to communities, depending on completeness of recording.

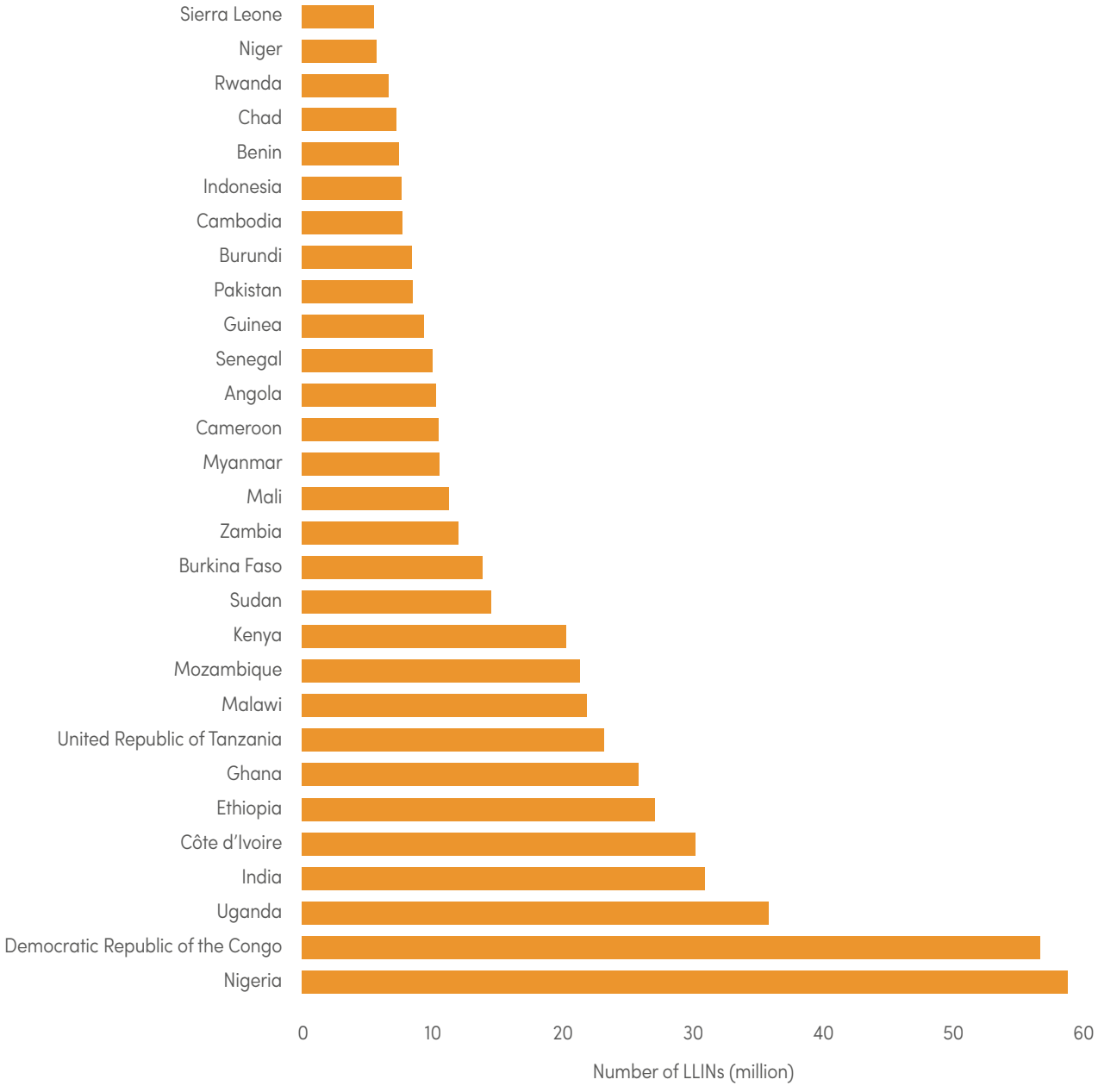
Note: A lag between manufacturer deliveries to countries and NMP distributions of about 6–12 months is expected, which should be considered when interpreting the relationship between manufacturer deliveries, NMP distributions and likely population coverage. Additional considerations include nets that are in storage in country but have not yet been distributed by NMPs, and those sold through the private sector that are not reported by the programmes.

distributions through immunization programmes in ANC facilities continue to play an important role.

During the 3-year period 2016–2018, 578 million ITNs – most of which were LLINs – were distributed globally by NMPs in malaria endemic countries. Of these, about 90% were delivered to 29 countries (**Fig. 6.9**), with 50% going to Côte d'Ivoire, the Democratic Republic of the Congo, Ethiopia, Ghana, India, Nigeria, Uganda and the United Republic of Tanzania.

FIG. 6.9.

Total LLINs distributed to communities by country in the period 2016–2018, in countries accounting for about 90% of global distributions by NMPs *Source: NMP reports.*



LLIN: long-lasting insecticidal net; NMP: national malaria programme.

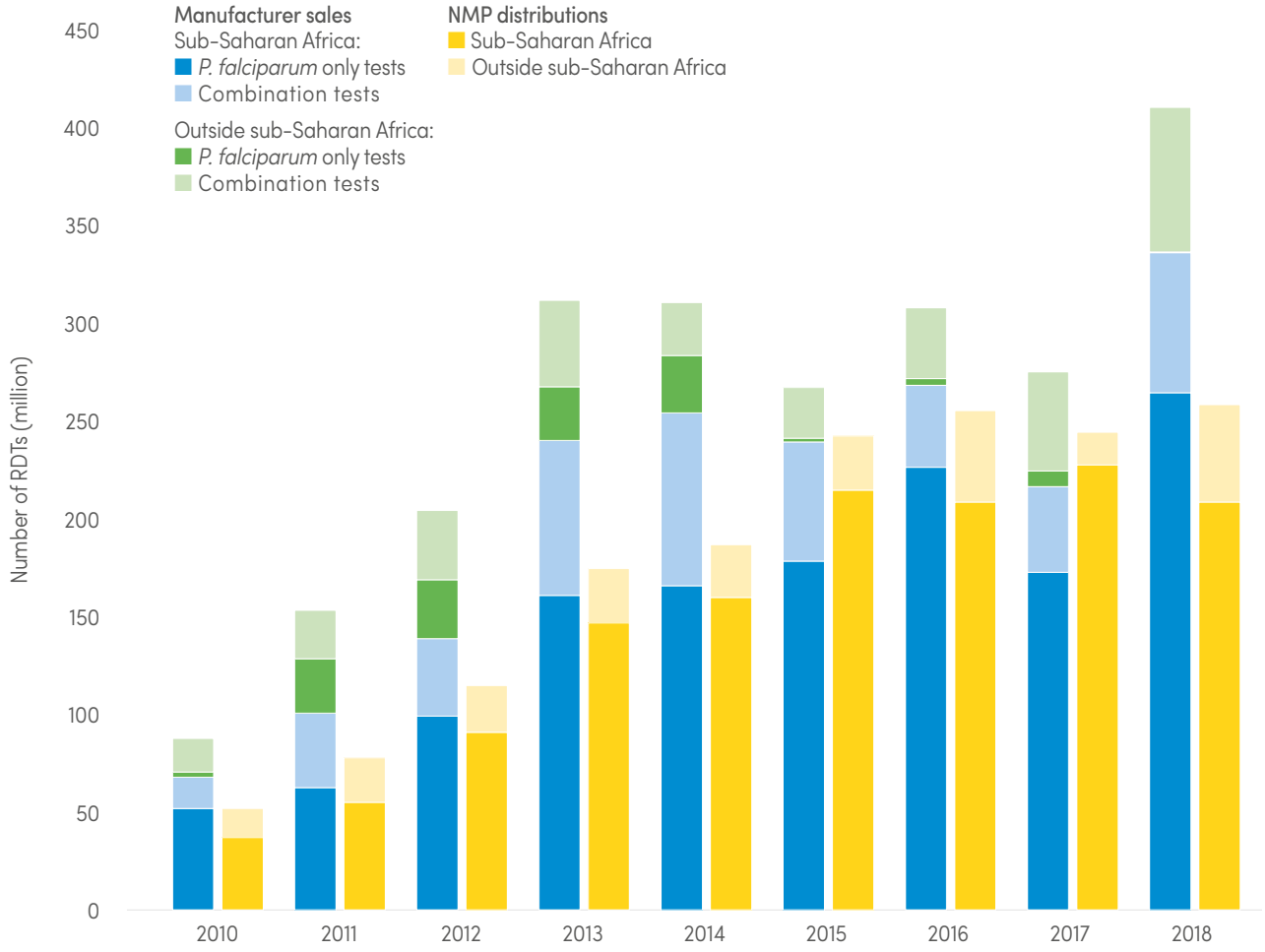
6.4 DELIVERIES OF RDTs

Globally, 2.3 billion RDTs for malaria were sold by manufacturers in the period 2010–2018, with nearly 80% of these sales to countries in sub-Saharan Africa. These were sales by manufacturers that were eligible for procurement according to the Malaria RDT Product Testing Programme and WHO Prequalification and NMP distributions of RDTs. In the same time period NMPs distributed 1.6 billion RDTs.

In 2018, 412 million RDTs were sold by manufacturers, compared with 276 million in 2017 (**Fig. 6.10**). However, NMPs distributed 259 million RDTs in 2018, compared with 245 million in 2017, with 80% of distributions also occurring in sub-Saharan Africa. Usually, differences between sales and distributions of RDTs can be attributed to one or more of the following causes: manufacturer data include both public and private health sector sales, whereas NMP-distributed RDTs represent tests in the public sector only; an initial high distribution may be followed by a lower one, as countries use commodities procured in the previous year; misreporting may occur, where RDTs in ministry of health central stores are not included in NMP distributions; and reporting systems may be weak or manufacturer data may represent recent orders that are yet to arrive in the country. Most of the RDTs sold globally (266 million), particularly in sub-Saharan Africa, were tests that detected only *P. falciparum*.

FIG. 6.10.

Number of RDTs sold by manufacturers and distributed by NMPs for use in testing suspected malaria cases,[a] 2010–2018 *Sources: NMP reports and sales data from manufacturers eligible for WHO's Malaria RDT Product Testing Programme.*



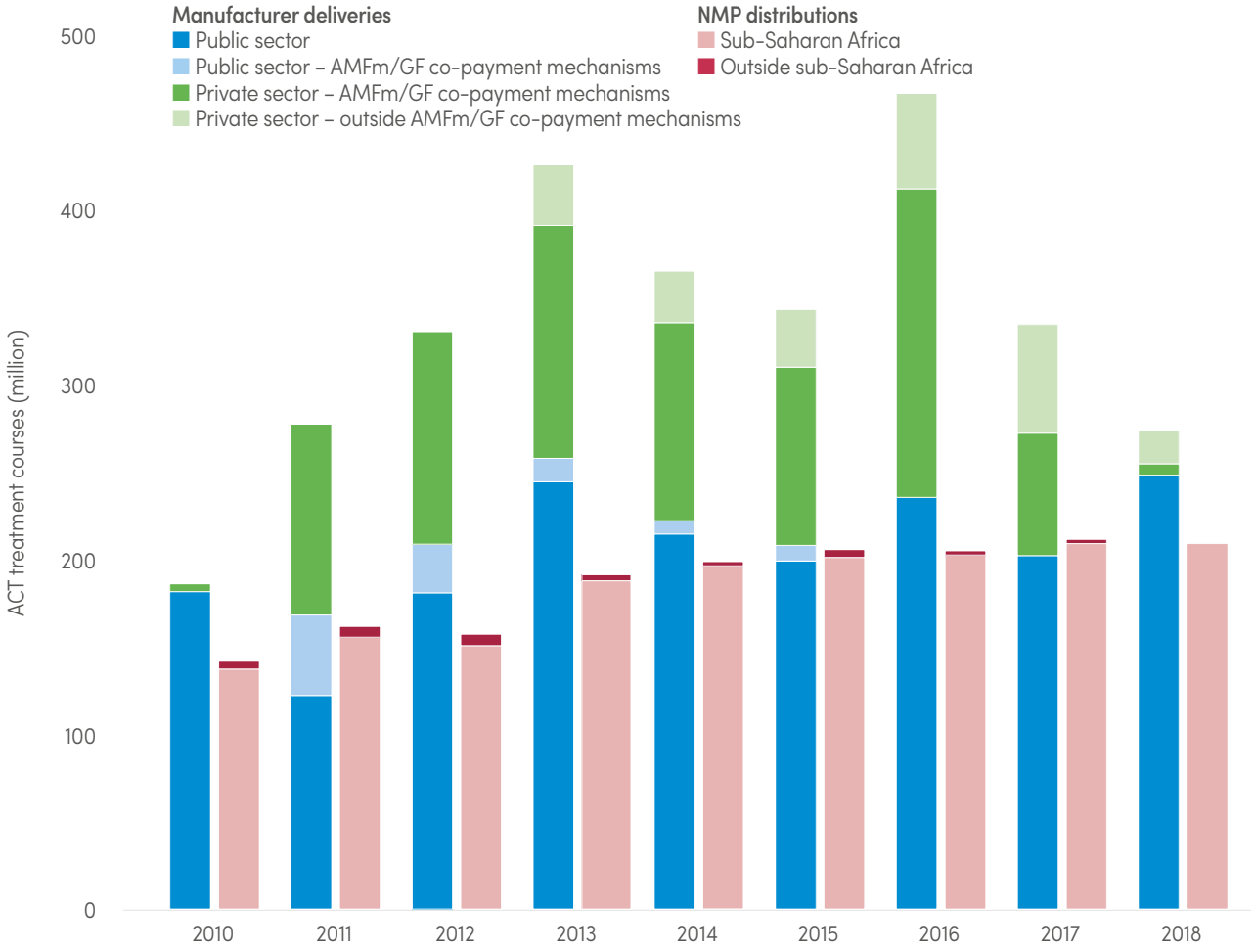
NMP: national malaria programme; *P. falciparum*: *Plasmodium falciparum*; RDT: rapid diagnostic test; WHO: World Health Organization.
[a] NMP distributions do not reflect those RDTs still in storage that have yet to be delivered to health facilities and community health workers.

6.5 DELIVERIES OF ACTs

More than 3 billion treatment courses of ACT were sold globally by manufacturers in the period 2010–2018 (**Fig. 6.11**). About 1.9 billion of these sales were to the public sector in malaria endemic countries, and the rest were sold through either public or private sector co-payments (or both), or sold exclusively through the private retail sector. National data reported by NMPs show that, in the same period, 1.7 billion ACTs were delivered to health facilities to treat malaria patients in the public health sector. The discrepancy between global sales and national distributions is, in part, due to the lack of reports from the private sector for most countries. However, with declines in co-payments from the Global Fund, the number of ACTs procured for the private sector has decreased substantially since 2016. In 2018, some 249 million ACTs were sold by manufacturers to the public health sector, and in the same year 214 million ACTs were distributed to this sector by NMPs, of which 98% were in sub-Saharan Africa.

FIG. 6.11.

Number of ACT treatment courses delivered by manufacturers and distributed by NMPs to patients, 2010–2018[a,b] *Sources: Companies eligible for procurement by WHO/UNICEF and NMP reports.*



ACT: artemisinin-based combination therapy; AMFm: Affordable Medicines Facility–malaria; GF: Global Fund to Fight AIDS, Tuberculosis and Malaria; NMP: national malaria programme; UNICEF: United Nations Children's Fund; WHO: World Health Organization.

[a] NMP deliveries to patients reflect consumption reported in the public health sector.

[b] AMFm/GF indicates that the AMFm operated from 2010 to 2013, with the GF co-payment mechanism operating from 2014.

7 Preventing malaria

For the prevention of malaria, WHO recommends vector control (i.e. reducing the chances of mosquitoes biting human beings) or chemoprevention (i.e. providing drugs that suppress infections) in specific population subgroups (i.e. pregnant women, children and other high-risk groups) or in specific contexts (e.g. complex emergencies and elimination). The core interventions recommended by WHO to prevent mosquito bites are sleeping under an ITN and indoor residual spraying (IRS). In a few specific settings and circumstances, ITNs and IRS can be supplemented by larval source management or other environmental modifications (*29*).

With regard to chemoprevention, WHO recommends a number of context-specific interventions. In sub-Saharan Africa, IPTp with SP has been shown to reduce maternal anaemia, low birthweight and perinatal mortality (*30*). IPTi with SP provides protection against clinical malaria and anaemia (*31*). SMC with amodiaquine (AQ) plus SP (AQ+SP) for children aged 3–59 months reduces the incidence of clinical attacks and severe malaria by about 75%, and could avert millions of cases and thousands of deaths among children living in areas of highly seasonal malaria transmission (*32*). Since March 2012, WHO has recommended SMC for children aged 3–59 months living in areas of highly seasonal malaria transmission in the Sahel subregion of Africa. Mass drug administration is defined as the time-limited administration of antimalarial treatment to all age groups of a defined population or to every person living in a defined geographical area (except those for whom the medicine is contraindicated) at about the same time and at specific repeated intervals. It is recommended for malaria elimination settings in combination with high coverage of core interventions and as a means of rapidly reducing the malaria burden in epidemics and complex emergencies, as part of the rapid initial response (*33*).

This section discusses the population-level coverage of ITNs, IRS, IPTp and SMC. Analysis of coverage indicators for ITNs is limited to sub-Saharan Africa, where there are sufficient household survey data to measure progress. IPTp and SMC are also reported only for sub-Saharan Africa, where these interventions are applicable. The coverage of IPTi is not reported because, as for 2018, no country has adopted it. In 2019, Sierra Leone began national scale-up of IPTi.

7.1 POPULATION AT RISK COVERED WITH ITNs

Indicators of population-level coverage of ITNs were estimated for countries in sub-Saharan Africa in which ITNs are the main method of vector control. Household surveys were used, together with manufacturer deliveries and NMP distributions, to estimate the following main indicators (*34, 35*):

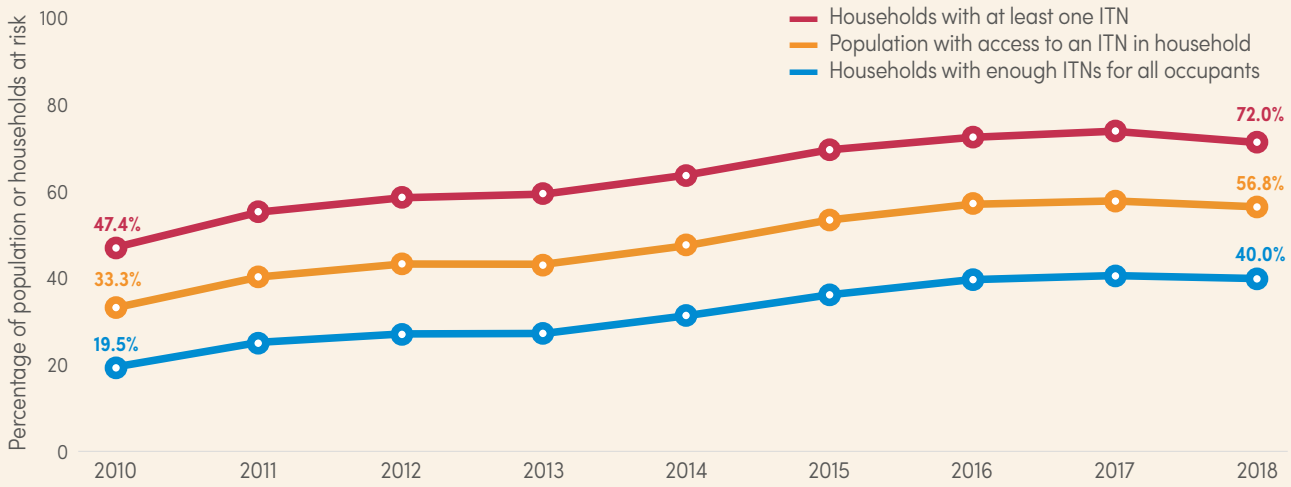
- net use (i.e. the percentage of a given population group that slept under an ITN the night before the survey);
- ITN ownership (i.e. the percentage of households that owned at least one ITN);
- percentage of households with at least one ITN for every two people;
- percentage of the population with access to an ITN within their household (i.e. the percentage of the population that could be protected by an ITN, assuming that each ITN in a household can be used by two people); and
- household ITN ownership gap, measured as the percentage of households with at least one ITN for every two people among households owning any ITN.

By 2018, 72% of households in sub-Saharan Africa had at least one ITN and about 57% of the population had access to an ITN, while 40% of the population lived in households with enough ITNs for all occupants. These indicators represented impressive progress from 2010, but no significant change since 2016 (**Fig. 7.1**).

Use of ITNs by household members, measured as the percentage of people who slept under an ITN the night before the survey, was 61% in 2018 compared with 36% in 2010 for both pregnant women and children aged under 5 years, and was 50% in 2018 compared with 29% in 2010 for the overall population (**Fig. 7.2**).

FIG. 7.1.

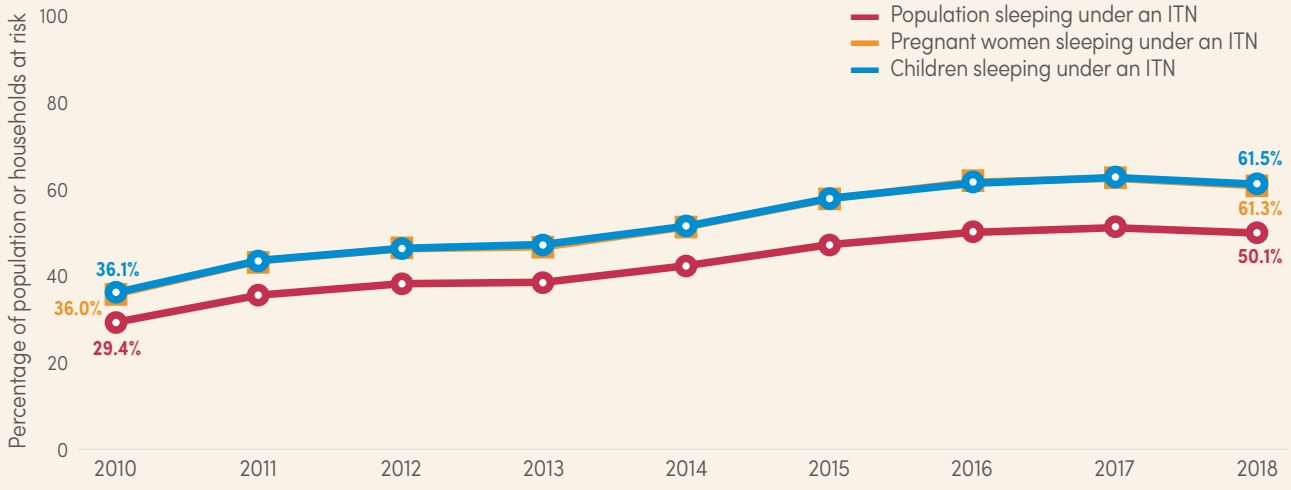
Percentage of population at risk with access to an ITN, and percentage of households with at least one ITN and enough ITNs for all occupants, sub-Saharan Africa, 2010–2018 *Source: ITN coverage model from MAP.*[a]



ITN: insecticide-treated mosquito net; MAP: Malaria Atlas Project.
[a] https://map.ox.ac.uk/

FIG. 7.2.

Percentage of population at risk, pregnant women and children aged under 5 years[a] sleeping under an ITN, sub-Saharan Africa, 2010–2018 *Source: ITN coverage model from MAP.*[b]



ITN: insecticide-treated mosquito net; MAP: Malaria Atlas Project.
[a] Estimates for children aged under 5 years and pregnant women highly overlap and show the same values in the trend since 2010.
[b] https://map.ox.ac.uk/

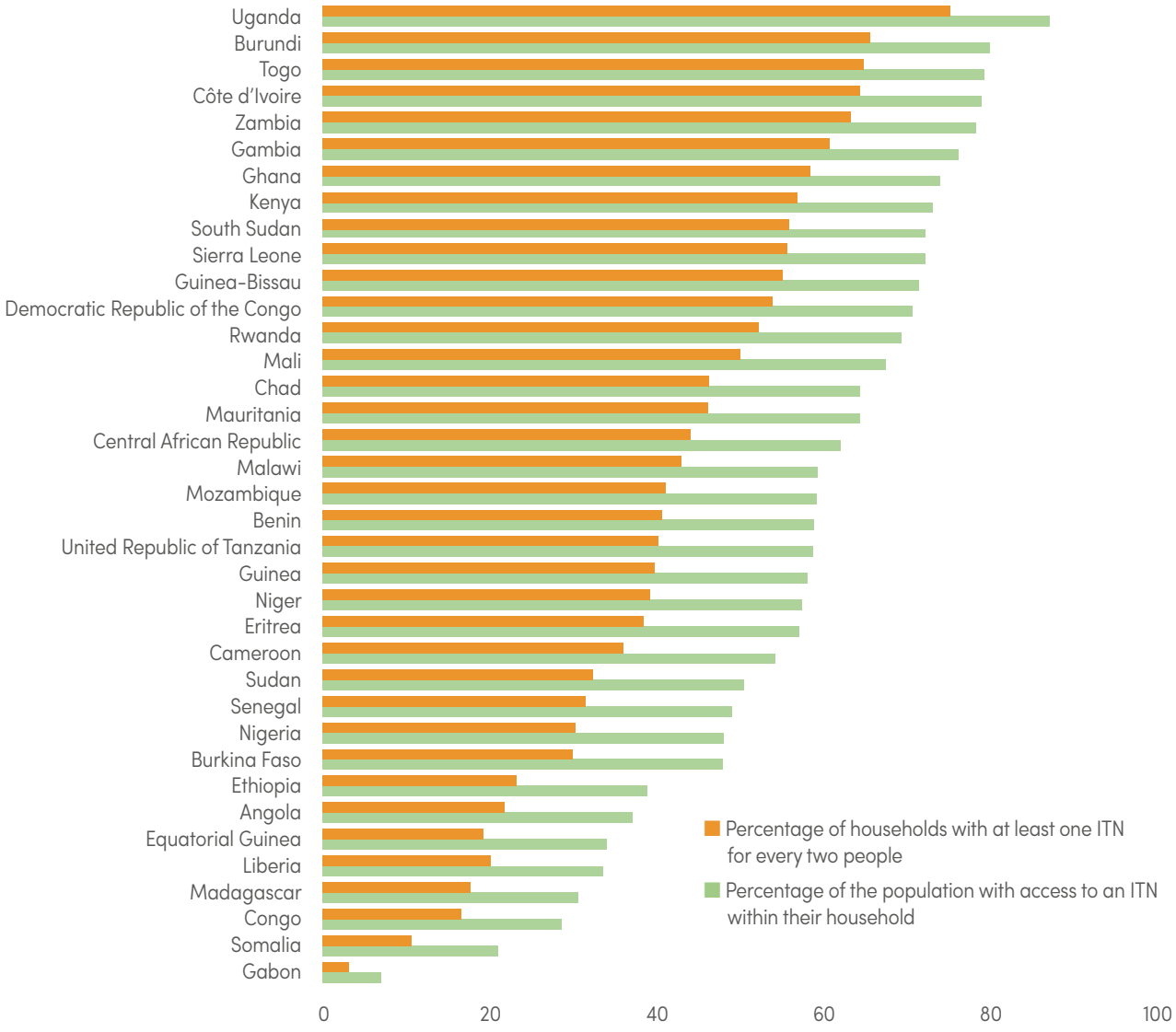
Results by country in sub-Saharan Africa on percentage of population with access to ITNs and proportion of households with enough ITNs for all occupants are shown in **Fig. 7.3**. These are countries where ITNs are the main vector control intervention. The analysis showed high levels of access (>70%) in 13 of 37 countries, moderate levels of access (50–70%) in an additional 13 countries, and access levels below 50% in 11 countries, including Burkina Faso and Nigeria, two very high burden countries. The percentage of households with at least one ITN for each two people was, as expected, highly correlated with, but consistently lower than, the percentage with access to ITN.

7.2 POPULATION AT RISK PROTECTED BY IRS

In most countries, IRS is targeted at a few focal areas, which may vary over time. Operational coverage of IRS is likely to be very high among the targeted populations. However, when interpreting the trends in IRS coverage presented here, the denominator of "population at risk" used is that of all populations

FIG. 7.3.

Percentage of population at risk with access to an ITN, and percentage of households with enough ITNs for all occupants, sub-Saharan Africa, 2010–2018 *Source: ITN coverage model from MAP.*[a]



ITN: insecticide-treated mosquito net; MAP: Malaria Atlas Project.

[a] https://map.ox.ac.uk/

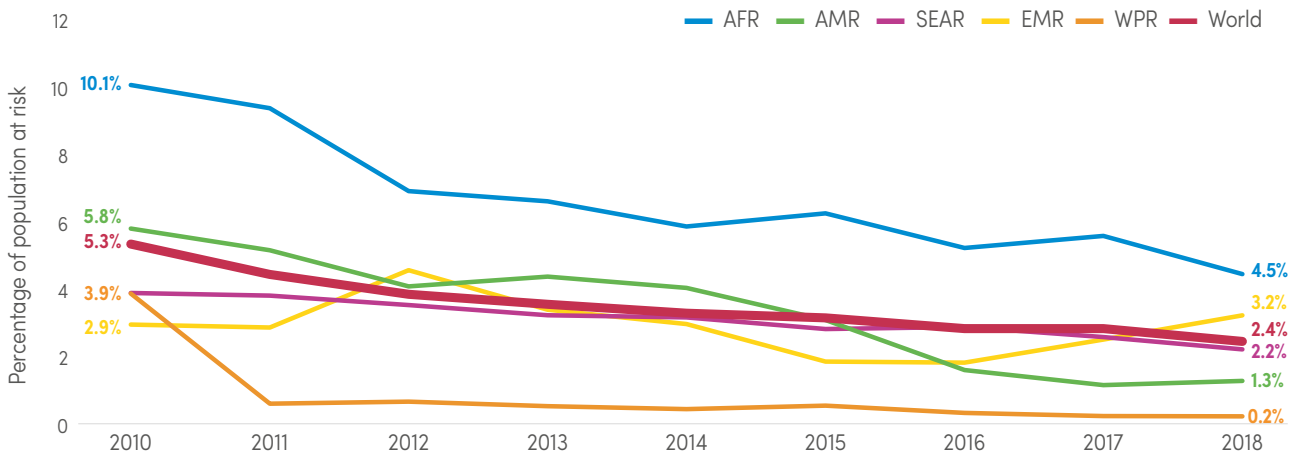
living in areas where there is ongoing malaria transmission, to allow for consistency in trend.

Globally, the percentage of the populations at risk protected by IRS declined from 5% in 2010 to 2% in 2018, with increases seen in 2018 compared with 2017 in the regions for which data were analysed: the WHO Region of the Americas and WHO Eastern Mediterranean Region (**Fig. 7.4**). The number of people protected in 2010 was 180 million globally, but by 2018 this number had reduced to about 93 million, with a decrease of 13 million compared with 2017.

Reasons for the declining global IRS coverage may include the switch from pyrethroids to more expensive insecticides in response to increasing pyrethroid resistance, or changes in operational strategies (e.g. decreasing at-risk populations in countries aiming for elimination of malaria). **Fig. 7.5** shows the main chemical class used for IRS across countries that have reported the implementation of this intervention. Most countries still rely on pyrethroids, although in 2018 about half of countries reported using other insecticides, mainly organophosphates (**Section 10.3**).

FIG. 7.4.

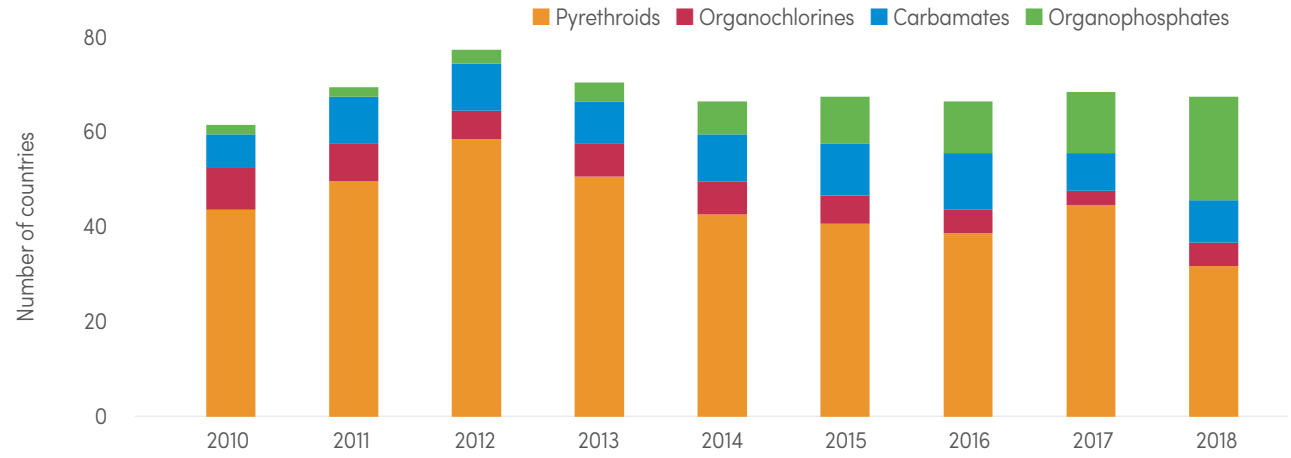
Percentage of the population at risk protected by IRS, by WHO region, 2010–2018 *Source: NMP reports and IVCC data.*



AFR: WHO African Region; AMR: WHO Region of the Americas; EMR: WHO Eastern Mediterranean Region; IRS: indoor residual spraying; IVCC: Innovative Vector Control Consortium; NMP: national malaria programme; SEAR: WHO South-East Asia Region; WHO: World Health Organization; WPR: WHO Western Pacific Region.

FIG. 7.5.

Main chemical classes used for IRS by national programmes globally, 2010–2018 *Source: NMP reports.*



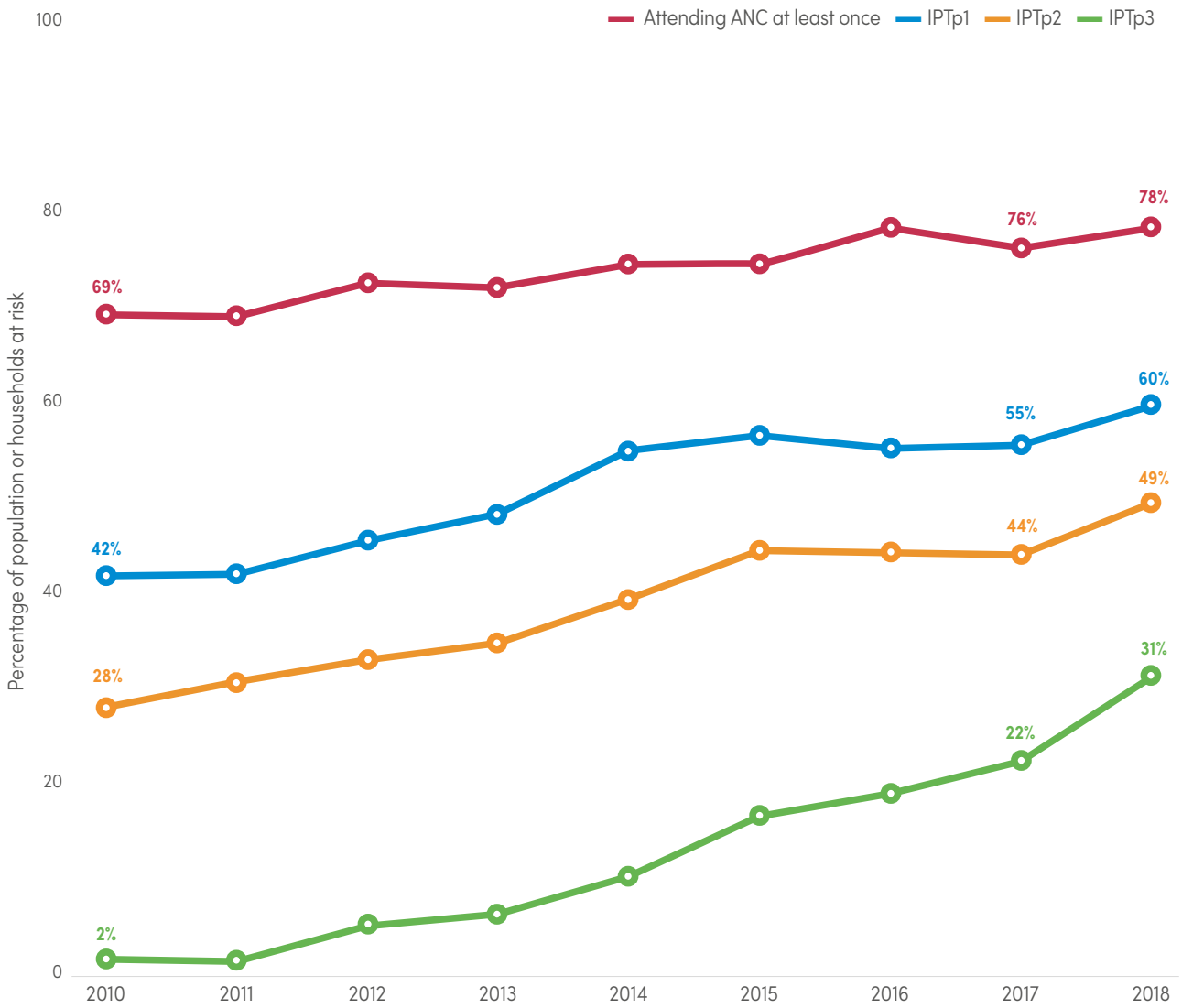
IRS: indoor residual spraying; NMP: national malaria programme.

7.3 PREGNANT WOMEN RECEIVING THREE OR MORE DOSES OF IPTp

WHO recommends that IPTp be given to all pregnant women at each ANC visit, starting as early as possible in the second trimester (i.e. not during the first trimester). Each SP dose should be given at least 1 month apart, with women receiving at least three SP doses (IPTp3) during each pregnancy (*30*). To date, 36 African countries have adopted this policy. These countries reported routine health facility data from the public sector on the number of women receiving the first, second, third and fourth doses of IPTp (i.e. IPTp1, IPTp2, IPTp3 and IPTp4). Using annual expected pregnancies, discounted for fetal loss and stillbirths, as the denominator, the percentage IPTp use by dose was computed. As of 2018, coverage rates of IPTp1, IPTp2 and IPTp3 were 60%, 49% and 31%, respectively (**Fig. 7.6**). The 2018 estimate of IPTp3 coverage, relative to the 22% in 2017, represents the highest single annual increase in this indicator, indicating

FIG. 7.6.

Percentage of pregnant women attending ANC at least once and receiving IPTp, by dose, sub-Saharan Africa, 2010–2018 *Source: NMP reports, WHO and US Centers for Disease Control and Prevention estimates.*



ANC: antenatal care; IPTp: intermittent preventive treatment in pregnancy; IPTp1: first dose of IPTp; IPTp2: second dose of IPTp; IPTp3: third dose of IPTp; NMP: national malaria programme; US: United States; WHO: World Health Organization.

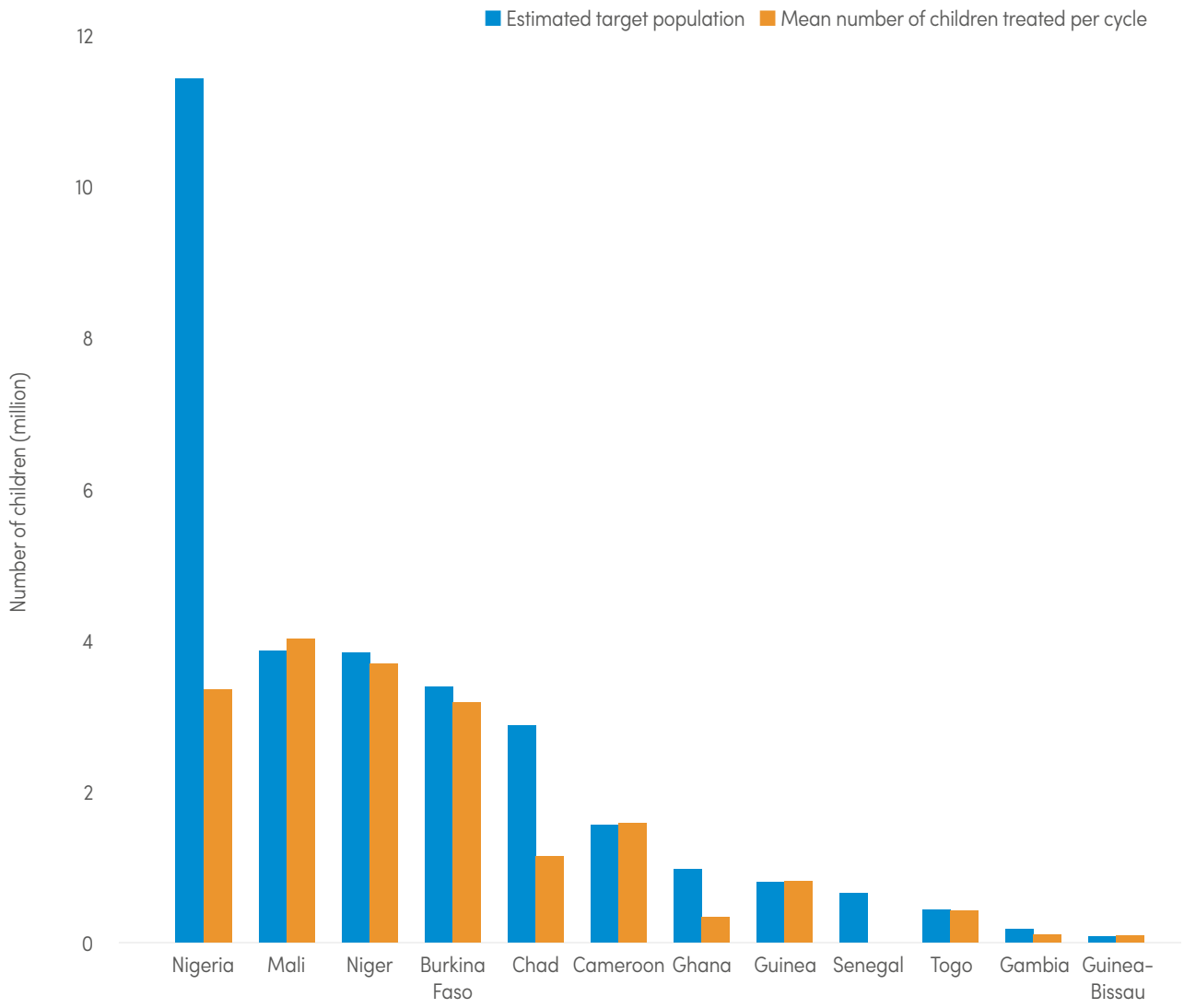
considerable improvements in country uptake. The analysis suggests, however, that about 18% of women who use ANC services at least once do not receive any IPTp, representing a missed opportunity that, if harnessed, could considerably and rapidly improve IPTp coverage.

7.4 SEASONAL MALARIA CHEMOPREVENTION

In the 12 countries in the Sahel subregion that have scaled up SMC, 31 million children aged under 5 years were in SMC-eligible areas; of these, 19 million children (62%) were treated. The main gaps in treatment were in Nigeria (70%, 8.4 million), Chad (67%, 1.8 million), Ghana (66%, 0.7 million), Senegal (100%, 0.7 million) and Gambia (47%, 0.1 million). All targeted children received treatment in Cameroon, Guinea, Guinea-Bissau and Mali (**Fig. 7.7**).

FIG. 7.7.

Number of SMC treatments administered in scale-up countries in 2018 *Source: London School of Hygiene & Tropical Medicine.*



SMC: seasonal malaria chemoprevention.

8 Diagnostic testing and treatment

Diagnostic testing and treatment is a key component of malaria control and elimination strategies. In addition to the treatment of uncomplicated malaria illness, prompt and effective case management helps to prevent severe disease and probable death; it may also reduce the pool of individuals who contribute to malaria transmission. Diagnosing patients rather than treating them presumptively may help health service providers to further investigate other potential causes of febrile illnesses that have a negative parasitological result, reduce the unnecessary use of antimalarial drugs and associated side-effects, and contribute to reducing the spread of drug resistance (*36*).

The ability of health systems to provide quality malaria case management at high coverage is influenced by three indicators: the extent to which patients with suspected malaria seek treatment, receive a diagnostic test after seeking care, and (if that test is positive for malaria) receive appropriate treatment. These indicators are usually measured through household surveys, such as MIS and DHS. For reasons of data availability, the analysis in this section is largely confined to sub-Saharan Africa, the region that carries the highest share of the global malaria burden; it covers 4-year periods because most countries conduct household surveys once every 3–5 years. **Annex 1** discusses the countries included, the calculation methods, and the limitations of the use of DHS and MIS data.

The signs and symptoms of malaria are similar to those of many other febrile illnesses. In non-immune individuals, malaria typically presents with fever, sometimes accompanied by chills, sweats, headache or other symptoms that may resemble signs or symptoms of other febrile illnesses. Consequently, fever is the main basis for suspecting malaria and triggering diagnostic testing of the patient in most malaria endemic settings. A history of fever in children aged under 5 years and subsequent steps taken to seek treatment have been the basis of measuring access to malaria case management. However, some important limitations of these data are as follows: what constitutes a "fever" varies by cultural context, which means that making comparisons across cultural groups can be problematic; the percentage of fevers that are due to malaria varies according to the underlying transmission intensity and level of control; there is no conclusive evidence that the household-level and individual-level processes for making the decision to seek treatment for malaria fevers are the same as those for other fevers or across different ages; and a percentage of respondents may not recall the medication they received, resulting in misclassification of the drugs that were prescribed.

8.1 PREVALENCE OF FEVER IN CHILDREN AGED UNDER 5 YEARS

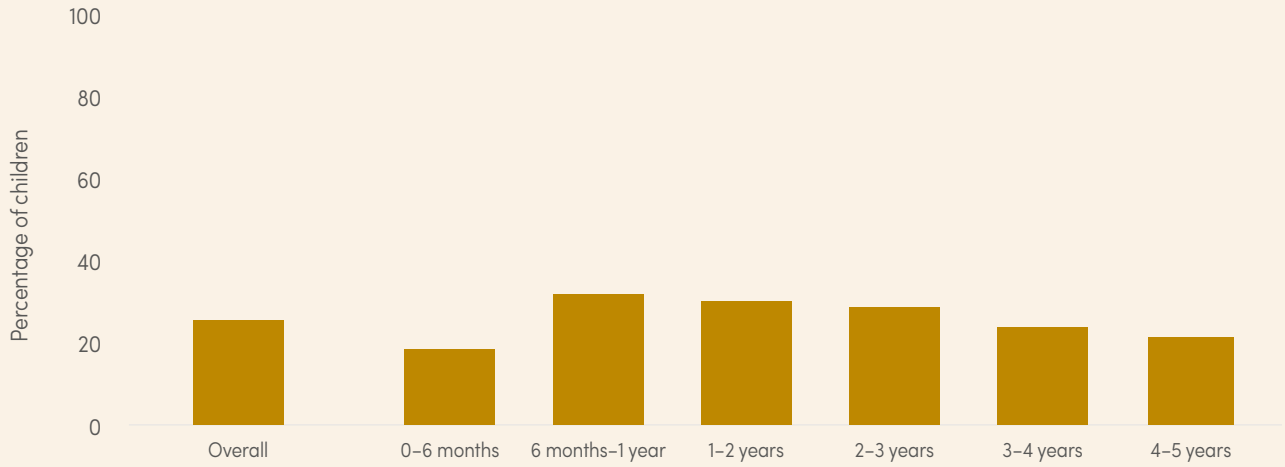
Based on 20 household surveys conducted in sub-Saharan Africa between 2015 and 2018, a median of 26% of children (interquartile range [IQR]: 19–35%) had a fever in the 2 weeks preceding the survey. Children aged 6 months to 3 years had a higher prevalence (around 30%) of fever than children aged under 6 months or over 3 years (**Fig. 8.1**). Prevalence of fever ranged from more than 40% in Malawi and Nigeria to less than 20% in Angola, Ethiopia, Madagascar, Mali and Zimbabwe (**Annex 3-Eb**). However, the data should be interpreted with caution because of potential bias in the season in which surveys are conducted.

8.2 NUMBERS OF CHILDREN WITH FEVER BROUGHT FOR CARE

Based on 20 nationally representative household surveys in sub-Saharan Africa conducted between 2015 and 2018, a median of 42% (IQR: 34–49%) of febrile children aged under 5 years were brought for care in the public sector compared with 10% (IQR: 8–22%) in the formal private sector and 3% (IQR: 2–7%) in the informal private sector (i.e. shops, markets, kiosks, itinerant drug sellers, traditional healers, friends and relatives, and other nonmedical health facilities). A considerable percentage of febrile children were not brought for care (median: 36%, IQR: 28–45%). When looking more closely at the subcategories of health sectors, visits to public health facilities and community health workers (CHWs) accounted for 37% (IQR: 31–48%) and 3% (IQR: 1–4%), respectively. Visits to the formal private sector were to the formal medical private sector, excluding pharmacies (median: 8%, IQR: 4–11%), and to pharmacies or accredited drug stores (median: 5%, IQR: 1–10%). Overall, a median of 58% (IQR: 47–70%) of febrile children brought for care were taken to a trained provider (i.e. to public sector health facilities, CHWs, formal private health facilities or pharmacies) (**Fig. 8.2**).

FIG. 8.1.

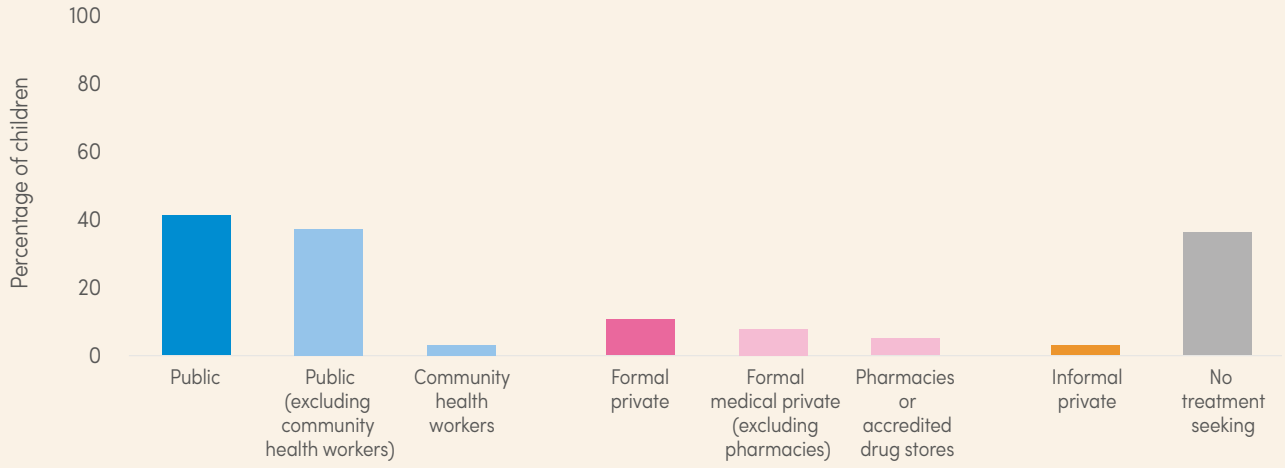
Median percentage of children who had a fever in the 2 weeks preceding the survey, overall and by age group, sub-Saharan Africa, 2015–2018 (latest survey) *Sources: Nationally representative household survey data from DHS and MIS.*



DHS: demographic and health surveys; MIS: malaria indicator surveys.

FIG. 8.2.

Median percentage of febrile children brought for care, by health sector, sub-Saharan Africa, 2015–2018 (latest survey) *Sources: Nationally representative household survey data from DHS and MIS.*



DHS: demographic and health surveys; MIS: malaria indicator surveys.

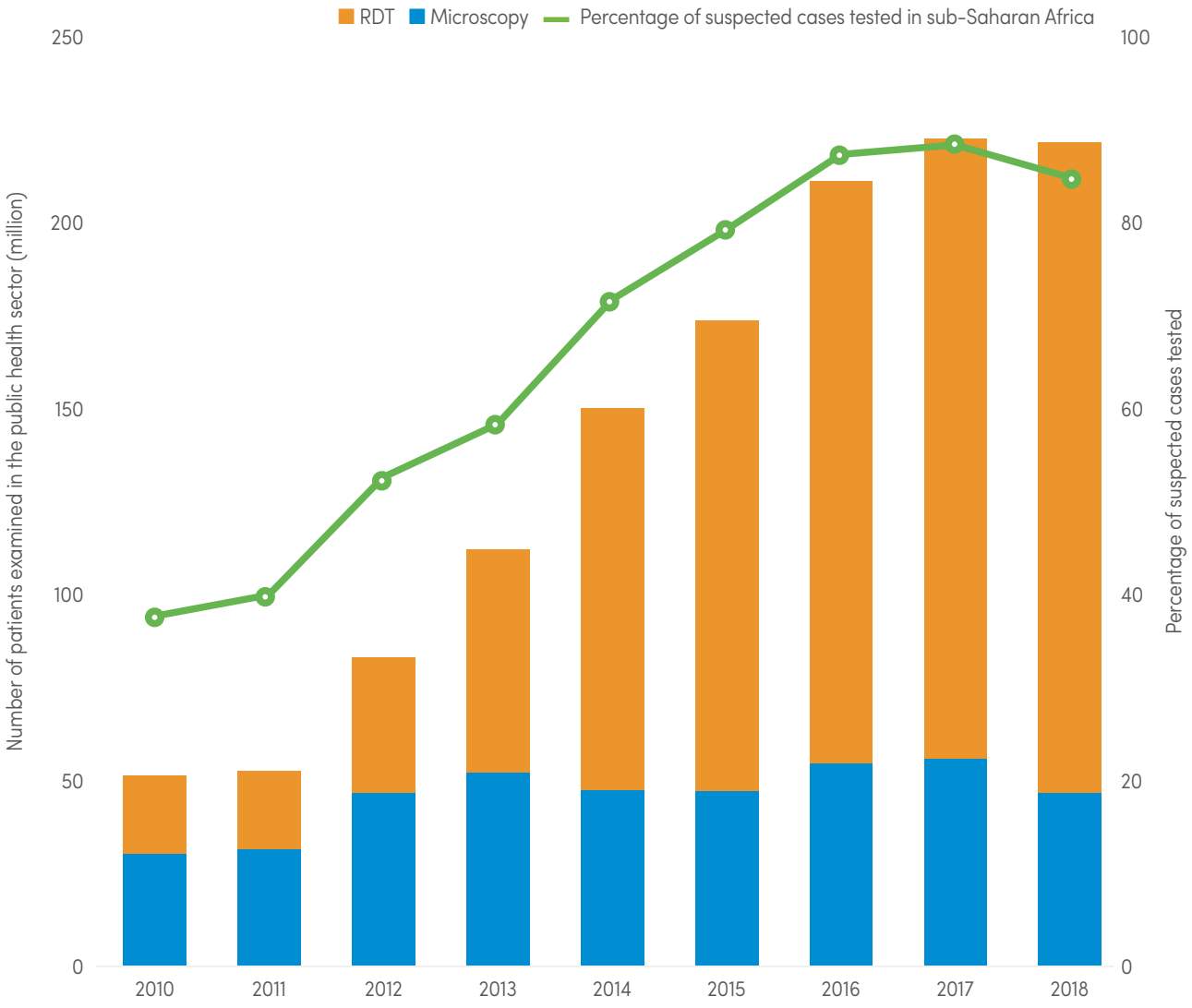
Variation in care-seeking behaviour was substantial across countries. In Burkina Faso, Mozambique and Sierra Leone, most febrile children (>60%) were brought for care in the public sector, whereas in Nigeria and Uganda they were mainly taken to the private sector. In Benin, Ghana, Mali and Togo, more than 10% of febrile children attended the informal private sector. Also, in Benin, Ethiopia, Malawi, Mali, Senegal, Togo and Zimbabwe, most febrile children were not brought for care (**Annex 3-Eb**).

8.3 PARASITOLOGICAL TESTING OF FEBRILE CHILDREN

Data from NMP country reports show that, because of the increasing scale-up of diagnostics, the percentage of patients suspected of having malaria who are seen in public health facilities and tested with either an RDT

FIG. 8.3.

Malaria patients examined using RDT and microscopy, and percentage of suspected cases tested in public health facilities, sub-Saharan Africa, 2010–2018 *Source: NMP reports.*



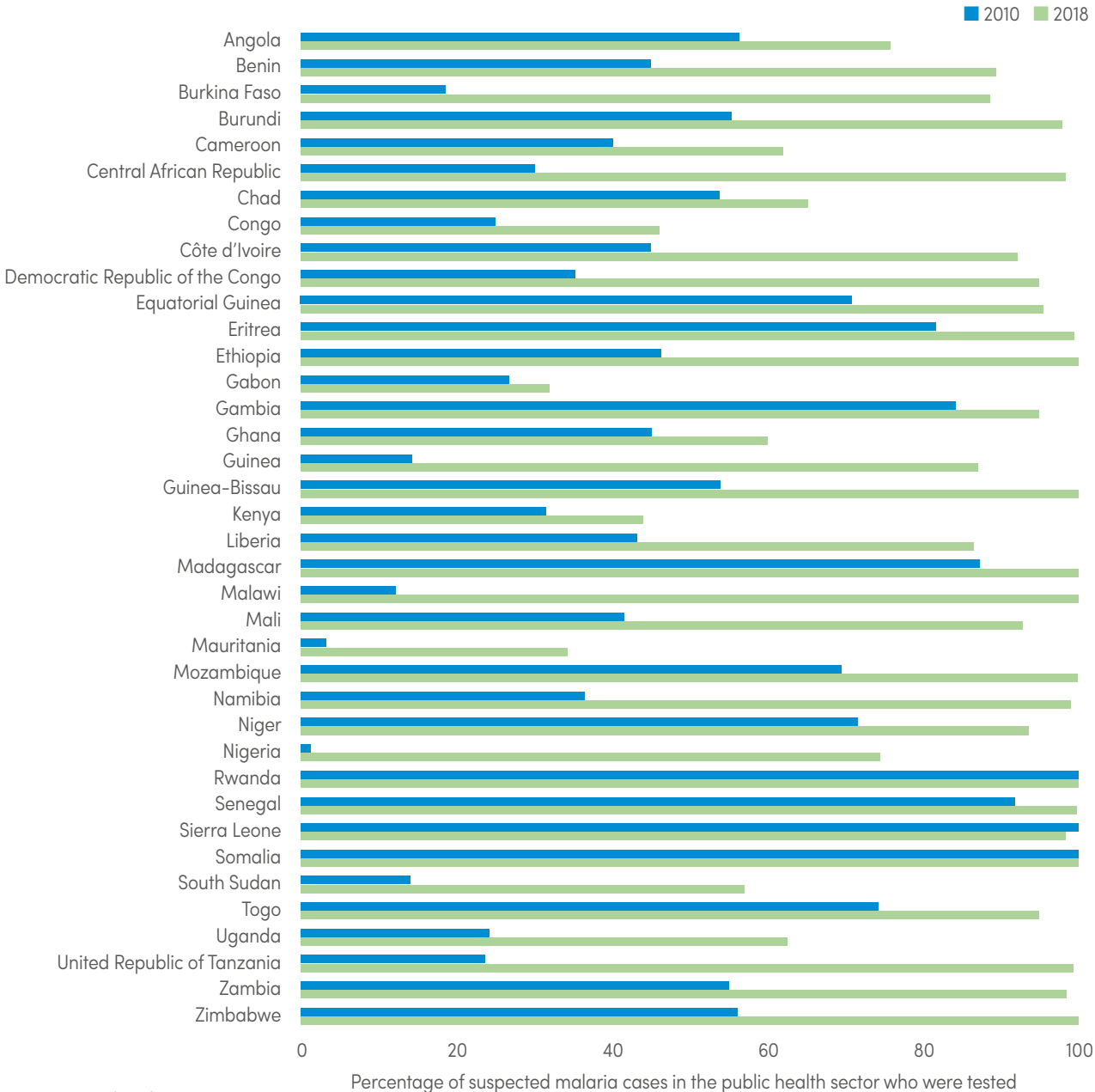
NMP: national malaria programme; RDT: rapid diagnostic test.

or microscopy, has risen from 38% in 2010 to 85% in 2018 (**Fig. 8.3**).

Data reported by NMPs from 38 moderate to high transmission countries in sub-Saharan Africa show a considerable increase between 2010 and 2018 in the number of suspected malaria cases tested with a parasitological test (**Fig. 8.4**). In 27 of these countries, the percentage of suspected cases tested was greater than 80% in 2018; however, in Congo, Gabon, Kenya and Mauritania, less than 50% of suspected cases in the public health sector were tested for malaria.

FIG. 8.4.

Percentage of suspected cases tested in public health facilities, sub-Saharan Africa, 2010–2018 *Source: NMP reports.*

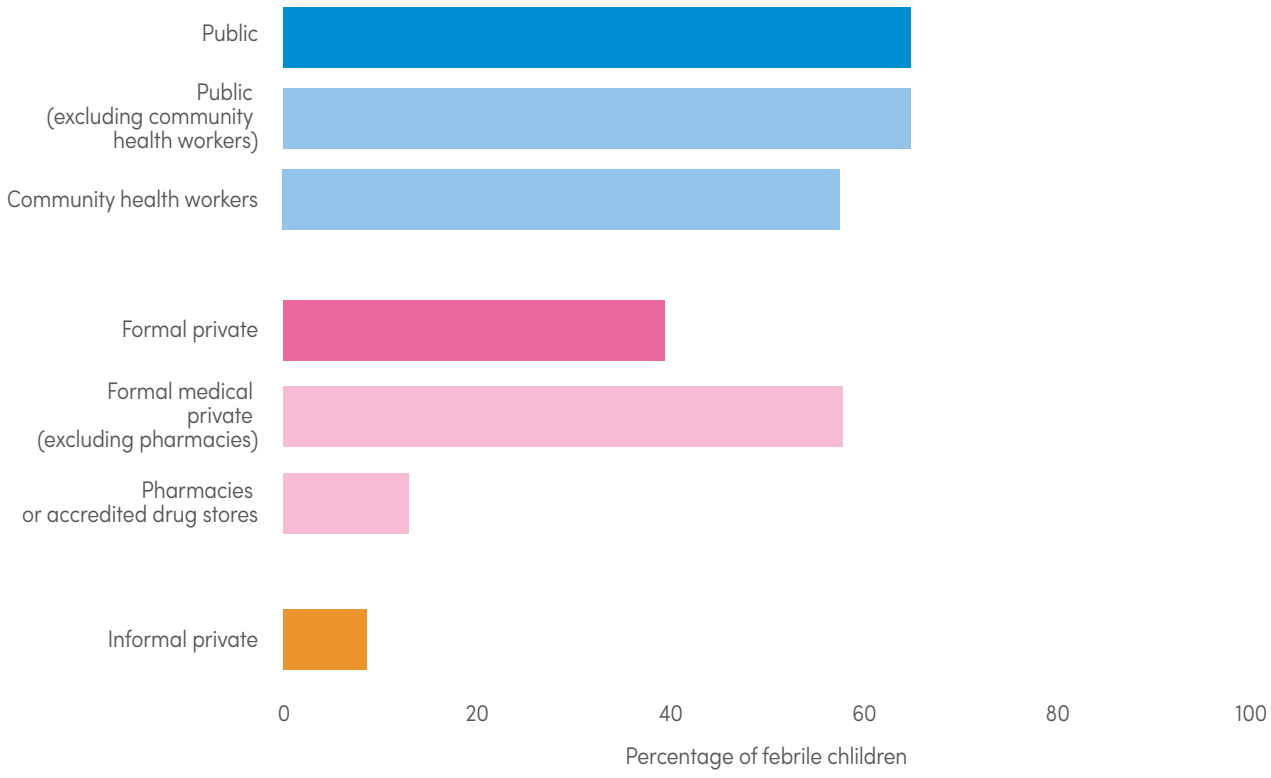


NMP: national malaria programme.

At community level, based on 19 nationally representative household surveys conducted between 2015 and 2018 in sub-Saharan Africa, the median percentage of febrile children brought for care who received a finger or heel stick (suggesting that a malaria diagnostic test may have been performed) was greater in the public sector (median: 66%, IQR: 49–75%) than in the formal private sector (median: 40%, IQR: 16–46%) or the informal private sector (median: 9%, IQR: 5–22%). In the public sector, 66% of febrile children received a diagnostic test in public health facilities (IQR: 49–75%) and 58% when visiting a CHW (IQR: 39–75%). In the formal private sector, the percentage of those brought for care who had a blood test was 58% in the formal medical private sector, excluding pharmacies (IQR: 30–76%), compared with 13% in pharmacies (IQR: 9–22%). Overall, 57% of children brought to a trained provider for care received a diagnostic test (IQR: 36–68%) (**Fig. 8.5**). This percentage ranged from more than 70% in Burundi,

FIG. 8.5.

Median percentage of febrile children who received a blood test, by health sector, sub-Saharan Africa, 2015–2018 (latest survey) *Sources: Nationally representative household survey data from DHS and MIS.*



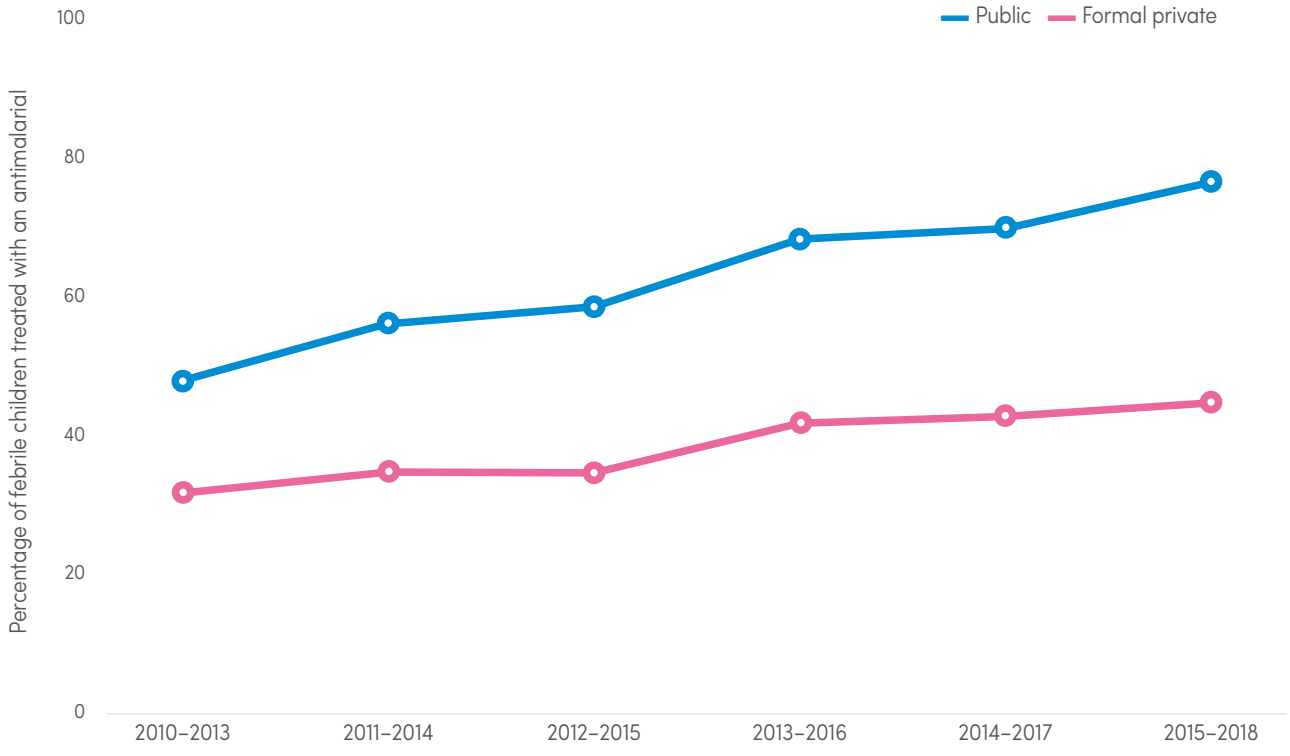
DHS: demographic and health surveys; MIS: malaria indicator surveys.

Malawi and Sierra Leone, to less than 20% in Nigeria (**Annex 3-Eb**).

Based on 61 surveys conducted in 29 sub-Saharan African countries between 2010 and 2018, the percentage of febrile children attending public health facilities who had a blood test before treatment increased from a median of 48% (IQR: 30–62%) in 2010–2013 to a median of 76% (IQR: 60–86%) in 2015–2018. In the formal private sector, this median percentage also increased, from 32% (IQR: 16–49%) in 2010–2013 to 45% (IQR: 34–62%) in 2015–2017 (**Fig. 8.6**). Although median percentages are relatively high, antimalarial treatment continues to be prescribed based on fever without laboratory confirmation. The availability of high-quality, inexpensive RDTs in the public sector has significantly improved and expanded, but RDTs are often unavailable in the formal private sector.

FIG. 8.6.

Trend in the median percentage of febrile children who received a blood test among those treated with an antimalarial drug, by health sector, sub-Saharan Africa, 2010–2018 (all surveys) *Sources: Nationally representative household survey data from DHS and MIS.*



DHS: demographic and health surveys; MIS: malaria indicator surveys.

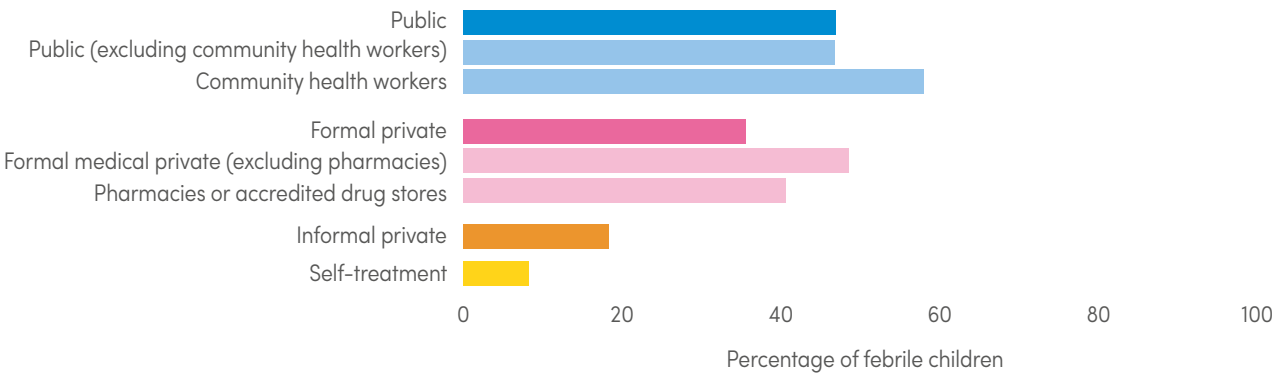
8.4 TREATMENT OF FEBRILE CHILDREN WITH ANTIMALARIAL DRUGS

Based on 20 household surveys conducted in sub-Saharan Africa in 2015–2018, the median percentage of febrile children who were treated with any antimalarial drug was higher in the public sector (median: 48%, IQR: 30–69%) than in the formal private sector (median: 40%, IQR: 21–51%) or the informal private sector (median: 18%, IQR: 10–29%) (**Fig. 8.7**). This pattern was consistent across countries except in Angola, Ethiopia, Kenya, Nigeria and the United Republic of Tanzania, where febrile children mainly received antimalarial drugs through the formal private sector. In some countries (e.g. Ghana, Liberia and Uganda), antimalarial treatment coverage was high in the informal private sector, where there is a risk that non-recommended treatments and poor-quality products may be used (**Annex 3-Eb**). When analysed by subcategory of source of care, the median percentage of children receiving antimalarial drugs was 47% (IQR: 29–69%) among those attending public health facilities, and 59% (IQR: 53–84%) among those visiting a CHW. In the private sector, this percentage was 49% (IQR: 19–55%) among those attending the formal medical private sector (excluding pharmacies), and 41% among those visiting pharmacies (IQR: 23–56%). Overall, 48% (IQR: 31–66%) of febrile children received an antimalarial drug among those visiting a trained provider. Among febrile children not brought for care, 8% (IQR: 5–19%) received an antimalarial drug as part of self-treatment at home.

Although there is considerable variation among countries, the median percentage of febrile children

FIG. 8.7.

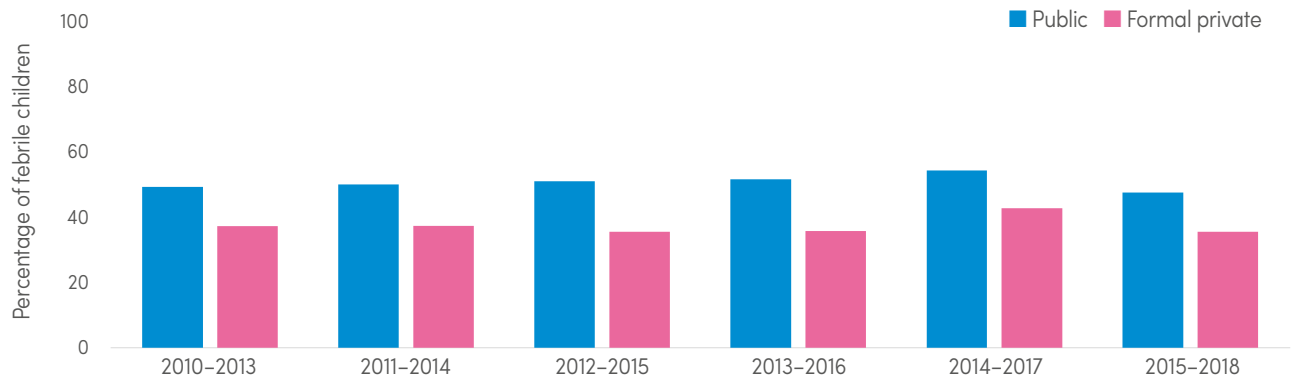
Median percentage of febrile children who were treated with an antimalarial drug, by health sector, sub-Saharan Africa, 2015–2018 (latest survey) *Sources: Nationally representative household survey data from DHS and MIS.*



DHS: demographic and health surveys; MIS: malaria indicator surveys.

FIG. 8.8.

Trend in the median percentage of febrile children who were treated with an antimalarial drug, by health sector, sub-Saharan Africa, 2010–2018 (all surveys) *Sources: Nationally representative household survey data from DHS and MIS.*



DHS: demographic and health surveys; MIS: malaria indicator surveys.

receiving antimalarial drugs has remained stable, both in the public sector (around 50%) and in the formal private sector (close to 40%) (**Fig. 8.8**). Interpretation of levels and trends in malaria treatment coverage among all febrile children is limited because fevers are not always the result of malaria infection. Even if a country achieves a reasonably high level of treatment of fevers with an antimalarial drug, this measure can be misleading because it includes inappropriate treatment of non-malarial fevers.

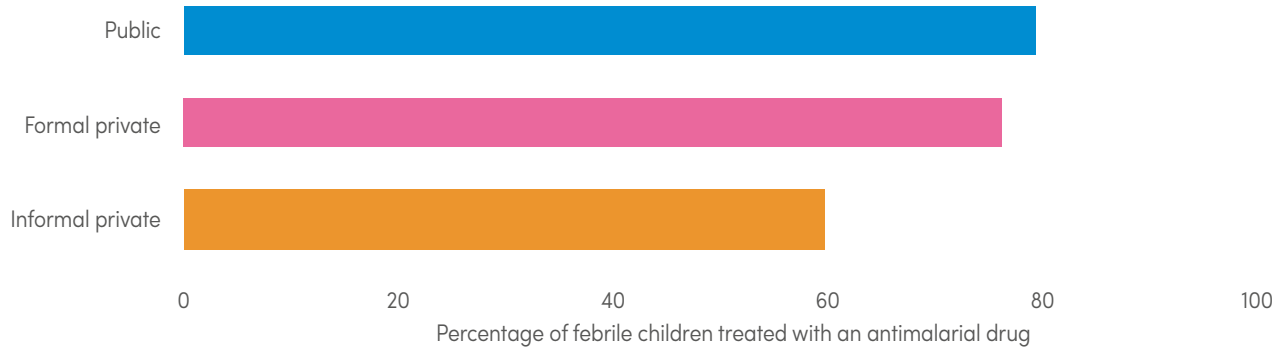
8.5 USE OF ACT FOR THE TREATMENT OF FEBRILE CHILDREN

Based on 19 surveys, ACT was the most commonly used drug-based therapy among febrile children who received antimalarial medicine (median: 80%, IQR: 45–94%). Antimalarial treatments were slightly more likely to be ACT if treatment was sought in the public sector (median: 80%, IQR: 45–94%) than in the formal private sector (median: 77%, IQR: 43–87%) or the informal private sector (median: 60%, IQR: 40–84%) (**Fig. 8.9**). However, those relatively high percentages do not guarantee that each ACT was a quality-assured ACT, especially in the private sector.

Based on 69 nationally representative household surveys conducted in 32 sub-Saharan African countries between 2010 and 2018, the percentage of febrile children receiving an ACT among those treated with antimalarial medicine in public health facilities increased from a median of 45% (IQR: 29–77%) in 2010–2013 to 82% (IQR: 44–95%) in 2015–2018 (**Fig. 8.10**).

FIG. 8.9.

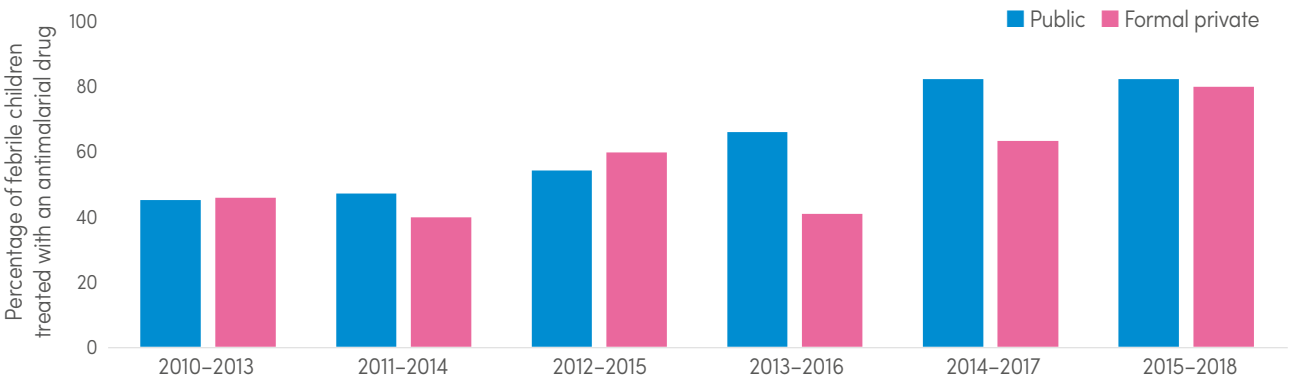
Median percentage of febrile children who received an ACT among those treated with an antimalarial drug, by health sector, sub-Saharan Africa, 2015–2018 (latest survey) *Sources: Nationally representative household survey data from DHS and MIS.*



ACT: artemisinin-based combination therapy; DHS: demographic and health surveys; MIS: malaria indicator surveys.

FIG. 8.10.

Trend in the median percentage of febrile children who received an ACT among those treated with an antimalarial drug, by health sector, sub-Saharan Africa, 2010–2018 (all surveys) *Sources: Nationally representative household survey data from DHS and MIS.*



ACT: artemisinin-based combination therapy; DHS: demographic and health surveys; MIS: malaria indicator surveys.

8.6 INTEGRATED COMMUNITY CASE MANAGEMENT

Nearly 40% of children with fever do not access care (**Fig. 8.2**). Integrated community case management (iCCM) is a proven strategy to deliver effective and simple life-saving interventions for major killers of children (i.e. malaria, pneumonia and diarrhoea) to hard-to-reach and under-served communities. iCCM involves using trained CHWs who may or may not be paid, to deliver health services to these communities. Thirty countries now implement iCCM at different levels, with only a few implementing nationally.

The Global Fund financed a thematic review report on iCCM across 18 countries through desk reviews and field visits with support from WHO and the United Nations Children's Fund (UNICEF). Released in September 2018, this report found that from 2014 to 2017 major donors and development partners increased their funding and technical support for iCCM implementation in all 18 countries. The report also found that many factors that contributed to iCCM success included establishment of national iCCM policies, strong leadership and partnership, and the presence of an existing competent pool of CHWs partnership support.[1]

In 2012, the Government of Canada awarded a grant to the WHO's GMP to support the scale-up of iCCM of pneumonia, diarrhoea and malaria among children aged under 5 in sub-Saharan Africa under the Rapid Access Expansion Programme (RAcE). The two main objectives of the programme were to contribute to the reduction of child mortality, and to document best practices to catalyse scale-up of iCCM. In 2019, WHO and implementing partners published the results of the implementation research on the impact of the RAcE programme, as well the best practices to improving coverage of iCCM in routine health systems (*37*).

To build on the lessons from these studies and experiences from country programmes that are implementing iCCM, in July 2019 UNICEF and WHO co-hosted in Addis Ababa, Ethiopia, a meeting on institutionalizing iCCM to end preventable child deaths. The technical consultation brought together technical experts and country teams to refine guiding principles and develop recommendations for iCCM, and priorities for national strategic plans to strengthen country programming and to identify needs and gaps for resource mobilization. Several challenges and possible solutions for achieving and maintaining an acceptable level of quality of care and coverage were identified during this meeting (**Box 8.1**).

[1] Desk review in the following 18 countries: Burundi, Ethiopia, Kenya, Rwanda, South Sudan and Uganda (East Africa); Malawi and Zambia (Southern Africa); and Benin, Burkina Faso, Cameroon, the Democratic Republic of the Congo, Ghana, Mali, Niger, Nigeria, Senegal and Sierra Leone (West and Central Africa). Field visits were conducted in Burkina Faso, Cameroon, Malawi, Nigeria, South Sudan and Zambia.

BOX. 8.1.

Challenges to and proposed solutions for the scale-up of iCCM

Source: WHO-UNICEF

Challenges

- Weaknesses in sustainable financing and integration of iCCM into national health system
- In some countries it is not clear which institution is in charge of activities
- Only a few countries have institutionalized CHWs as part of the system. Most countries rely on unpaid or volunteer CHWs
- Poor supervision due to shortage of staff at health facilities, weak links between CHWs and health facilities
- Non-integrated supply chain, poor data on iCCM commodity consumption
- Inadequate funding for pneumonia and diarrhoea commodities in some countries limit scale-up of malaria interventions through iCCM
- Multiple parallel community information systems supported, lack of complete information on performance of CHWs

Proposed solutions

- Planning for iCCM should take place under the umbrella of primary health care and overall health sector development
- National community health policies and strategies should be in place, containing clear, official guidelines for recruitment, job description and motivation of CHWs, as well as clear criteria for implementing iCCM with a focus on hardest to reach populations
- Domestic and external funding should be targeted at system strengthening, with an inclusive focus on malaria, pneumonia and diarrhoea as well as community and facility based provision of care
- iCCM should be included in the national costing exercise and the annual health sector budgeting processes, with specific budget lines
- To promote institutionalization and sustainability, donors should coordinate iCCM funding with the ministry of health and support the ministry's iCCM implementation plan, instead of funding disease-specific or site-specific projects
- iCCM commodities should be an integral part of health facility and district level quantification
- Supportive supervision of CHWs as part of the primary health care system is core to quality iCCM, and needs to be budgeted and included in district implementation plans
- iCCM requires continuum of care from community to first level health facility to referral facility, having the capacity to fully manage referred children
- Community engagement is key to institutionalization of iCCM: local communities are central for effective planning, implementation and uptake of quality ICCM services
- The training of CHWs should not be considered complete until demonstration of defined competencies, with post training follow-up (time to be fixed as per area context) as part of training programme

9 Malaria surveillance

Pillar 3 of the GTS (*1*) is to transform malaria surveillance into a core intervention. This requires surveillance systems that can accurately and reliably track the burden of malaria, the interventions to reduce it, and the impact achieved geographically and temporally. To understand whether malaria surveillance systems are fit for purpose, WHO recommends the regular monitoring and evaluation of surveillance systems (*38*). This involves assessment of the structure, core and support functions, and the quality of the data, across both passive and active case-detection systems. Such information is critical to the continuous improvement of surveillance systems.

This section provides a summary of WHO initiatives to work with NMPs and partners in developing surveillance standards and tools to support the strengthening of national systems. It also presents an example of a country surveillance system assessment, to demonstrate the type of information such assessments provide and their potential role in improving surveillance systems (**Box 9.1**).

9.1 STRENGTHENING NATIONAL SURVEILLANCE SYSTEMS

Over the past 3 years, GMP has embarked on an intensified process of improving national surveillance systems and the use of data for programmatic decision-making. This includes the development of the following information products and tools:

- the *WHO Malaria surveillance, monitoring and evaluation: a reference manual* (*38*), released in March 2018, which outlines the global standards and core features of malaria surveillance across the transmission continuum;
- malaria surveillance modules that are based on the above WHO surveillance reference manual and are built into the District Health Information Software 2 (DHIS2),[1] for burden reduction (aggregate data) and elimination (case-based data) settings, entomological surveillance and vector-control interventions;
- national malaria data repositories that consolidate routine surveillance and non-routine data sources as part of the support provided to the HBHI countries; and
- surveillance system assessments to evaluate the ability of the surveillance system to collect complete, timely and accurate data that can be used to inform decisions, stratification of transmission and deployment of interventions.

9.2 MALARIA MODULES

The DHIS2 malaria modules were developed, in collaboration with partners, as part of the Health Data Collaborative, which is coordinated by the WHO Integrated Services Department and includes

[1] https://www.dhis2.org/inaction

surveillance support activities across WHO departments dealing with health information systems; immunization; maternal, newborn and child health; tuberculosis; and HIV/AIDS. The modules comprise a standard set of data elements and indicators, validation rules and dashboards for visualization of core epidemiological and data quality indicators, as charts, tables and maps. Routine reports and data exports can be easily generated for rapid dissemination of information to decision-makers. The modules, which are configurable and can be used either separately or in conjunction with one another, are accompanied by a guidance document and a curriculum for facility-level data analysis,[1] to help programmes to understand the content and how the data can be used in practice.

9.2.1 Aggregate malaria module

In settings in which transmission remains relatively high and where the main aim of NMPs is to reduce the burden of morbidity and mortality, data are aggregated to provide an overall picture of where and when malaria occurs and who is most affected.[2] Surveillance data in high-transmission settings is used to monitor trends in the number of cases and deaths, over time and by geography; the characteristics of people infected or dying from malaria; and the seasonality of transmission. In high-transmission settings, surveillance data can also be used to stratify geographical units by their malaria prevalence or annual parasite incidence, to better target interventions and optimize resource allocation.

As of October 2019, 23 countries have installed the WHO aggregate malaria module and another six installations are planned over the next year (**Fig. 9.1**). Five countries have already developed and integrated their own malaria module into DHIS2.

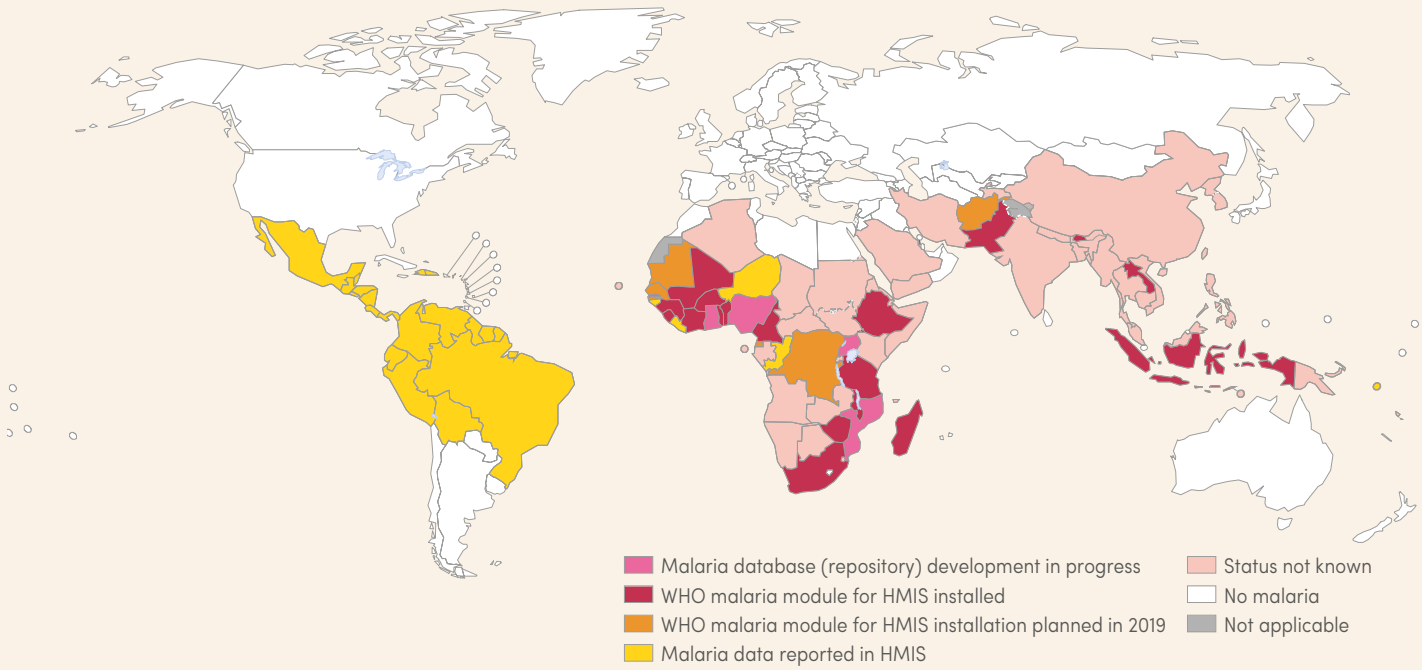
9.2.2 Case-based malaria module

The case-based malaria module, due to be released soon, will support case investigations in elimination settings by allowing the collection of line-listed data for

[1] https://www.who.int/healthinfo/tools_data_analysis_routine_facility/en/
[2] https://www.who.int/malaria/areas/surveillance/support-tools/en/

FIG. 9.1.

Status of malaria surveillance modules implemented in DHIS2, October 2019 *Source: NMPs and the African Leaders Malaria Alliance.*



DHIS2: District Health Information Software 2; HMIS: health management information system; NMP: national malaria programme; WHO: World Health Organization.

suspected cases (optional); diagnosis and treatment; treatment follow-up (optional); case investigation; and foci investigation, response and follow-up. Data will be aggregated and displayed on elimination dashboards for analysis and reporting. This work is being developed in partnership with the Clinton Health Access Initiative and the University of Oslo.

9.2.3 Entomology and vector control modules

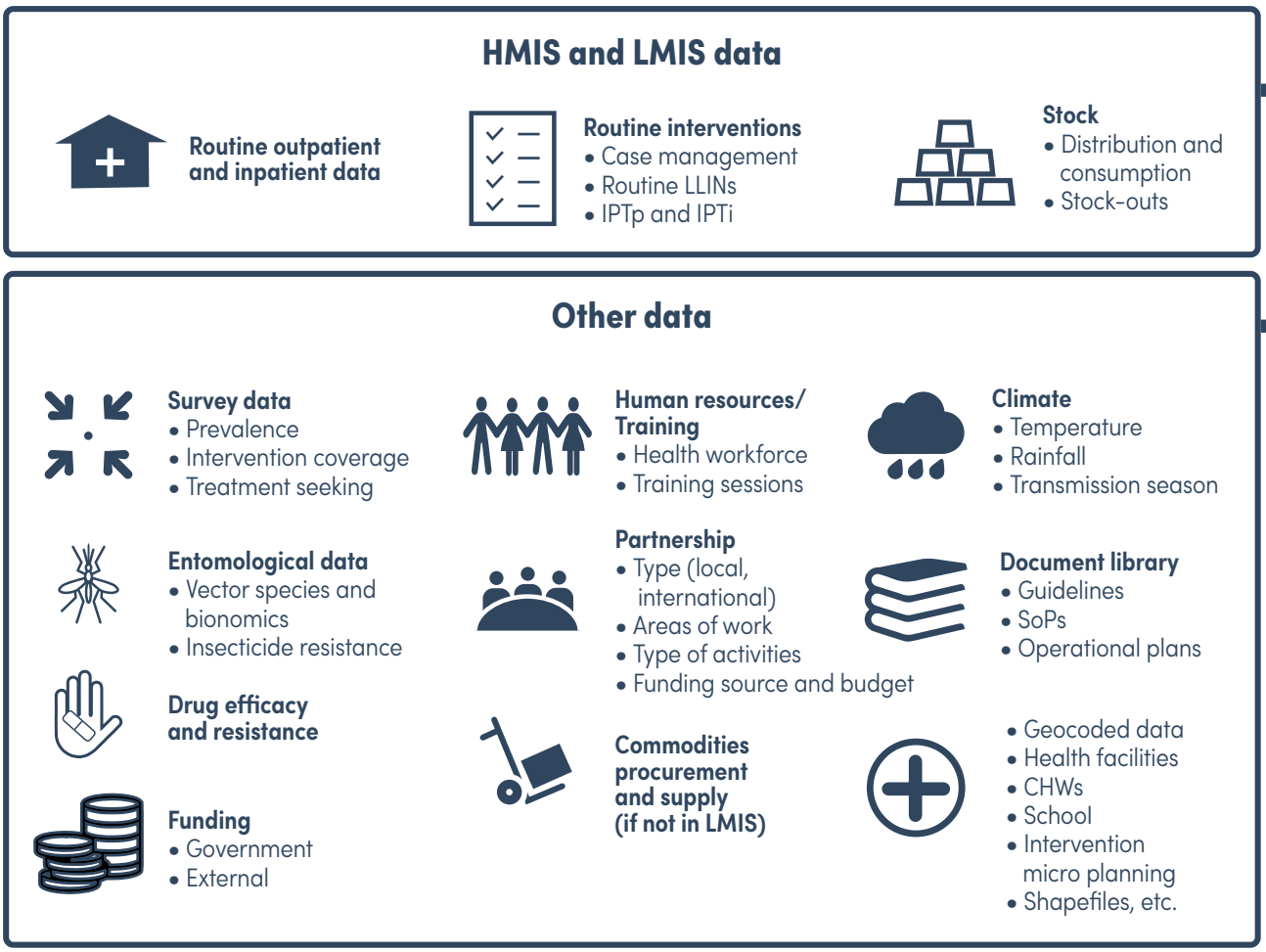
These modules have been developed to facilitate the collection and use of entomology and vector-control data to inform decision-making at country level. The modules consist of electronic data collection forms, standard indicators and automatically generated dashboards that cover the following interventions areas: ITN mass campaign distribution, ITN bioefficacy monitoring, IRS campaigns, IRS residual efficacy monitoring, insecticide resistance monitoring, adult mosquito surveillance and identification, and monitoring of mosquito larval habitats. All modules have been designed based on WHO-recommended data collection protocols and standard indicators. As of November 2019, one country was already using the modules and implementation had started in another two countries. In the course of 2020, significant geographical scale-up across Africa is planned and a module for ITN durability monitoring will be developed.

9.2.4 National malaria data repositories

WHO has been working in coordination with national health management information systems (HMIS) departments of ministries of health, in particular the HBHI countries, to establish structured dynamic databases (**Fig. 9.2**) that support NMPs subnationally

FIG. 9.2.

Proposed structure and examples of thematic areas for national malaria data repositories *Source: WHO-GMP.*



CHW: community health worker; GMP: Global Malaria Programme; HMIS: health management information system; IPTi: intermittent preventive treatment in infants; IPTp: intermittent preventive treatment in pregnancy; LLIN: long-lasting insecticidal net; LMIS: logistics management and information system; SoP: standard operating procedure; WHO: World Health Organization.

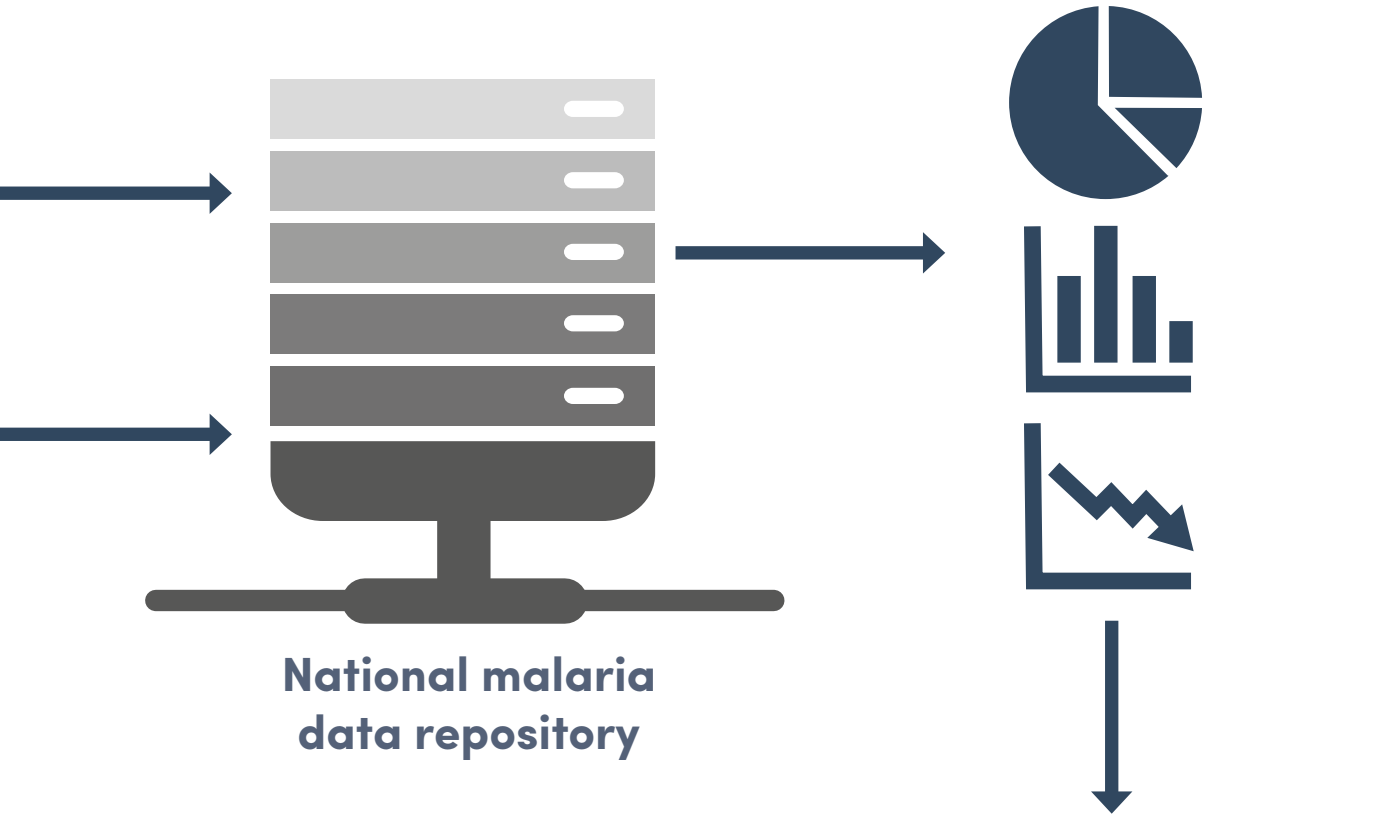
to implement targeted malaria activities informed by clear stratification, to monitor disease trends, to effectively respond to epidemics, to evaluate programme performance and to develop national strategic plans.

These national data repositories are developed either as part of WHO-supported national health observatories or as a direct service provided by the HMIS to disease programmes. GMP has developed an easily adaptable repository structure in DHIS2 with guidance on relevant data elements and indicators, their definitions and computation to cover key thematic areas (**Fig. 9.2**). So far, work to develop these databases has started in Gambia, Ghana, Mozambique, Nigeria, Uganda and the United Republic of Tanzania.

9.3 ASSESSMENT OF NATIONAL SURVEILLANCE SYSTEMS

Surveillance systems need to be assessed regularly to enable understanding of the quality of the data generated by the system, the use of the data to inform decision-making and the bottlenecks that impede the efficiency and effectiveness of the system. WHO recommends surveillance system assessments that monitor the following: structure, core functions, support functions and quality of surveillance (*38*).

A Mozambique case study is presented (**Box 9.1**) to illustrate the process of a surveillance assessment, the core findings and their contribution to strengthening the surveillance system.



BOX. 9.1.

Assessing and strengthening malaria surveillance: an example from Mozambique

Background: In July 2017, Mozambique's national malaria programme (NMP) and partners developed a National Malaria Surveillance Roadmap that outlines the core component of a surveillance system required to support malaria elimination (**Fig. B.9.1**). To determine whether the current surveillance system was able to provide good-quality epidemiological and intervention data for timely stratification of transmission and subsequent deployment of targeted interventions, a comprehensive malaria surveillance system assessment was carried out in July 2018. The main objective of this assessment was to assess performance and to identify bottlenecks that may hinder the collection, transmission, analysis and use of data. The NMP implemented the assessment with Malaria Consortium as the lead partner. WHO provided technical support and the Bill & Melinda Gates Foundation provided funding.

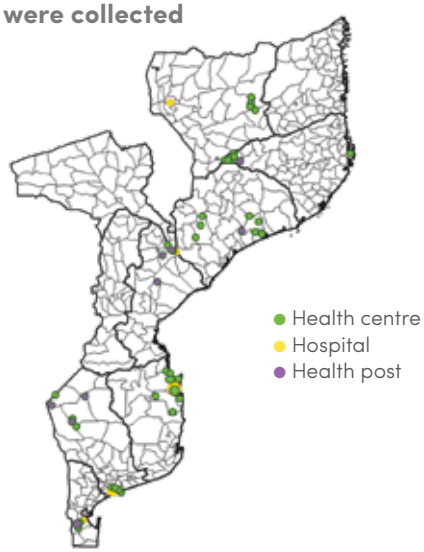
Fig. B.9.1. Surveillance components for evaluation during field assessment

HIS performance	HIS processes	Technical factors	Organizational factors	Behavioural factors
Data quality completeness	Data collection	Complexity of forms	Staff training	Self efficacy
Data quality timeliness	Data transmission	Availability of forms	Discussion on use of information	Promotion of a culture of information
Data quality completeness	Data processing /analysis	Software complexity	Promotion and use of information	Personal motivation
Report production			Supervision	
Display of information			Organizational factors	

Methods: Adapted Performance Review Information System Management (PRISM) (*39*) tools were used to collect data from a sample of 80 health facilities and 58 CHW sites, in 15 randomly sampled districts across eight provinces (**Fig. B.9.2**). Technical, organizational and behavioural factors that influence key surveillance system processes and data quality were evaluated to assess the overall performance of MIS. The assessment focused on the public health sector.

Results: Reporting completeness was more than 90% across all administrative levels, and completeness of key data fields was more than 80% (**Fig. B.9.3**). There were challenges, however, with receiving timely reports from CHWs, and accuracy of data was poor at both health facility and CHW levels. Also, a significant number of patients who were tested with RDTs and confirmed cases treated with ACTs were not reported, which can result in stock-outs, poor commodity quantification and resource allocation. The main reason for inaccurate data was the lack of recording tools (e.g. registers and consultation books) (**Fig. B.9.4**).

Fig. B.9.2. Map showing location of health facilities and community health worker sites from which data were collected



With regard to data analysis and use, although the capacity to perform basic analysis and interpretation was greater than was self-perceived at both health facility (70% versus 56%) and district levels (89% versus 63%), there was a lack of regular production of analytical reports and bulletins, and the analysis carried out was limited, particularly at the health facility level. This was partly from lack of training and problems with computer and internet access. As a consequence, the district was found to be overburdened with data management responsibilities, resulting in low motivation.

Conclusions: Inaccurate and incomplete data have a direct impact on key epidemiological indicators that inform decision-making, strategic planning, and programmatic action at all levels. This assessment allowed the NMP of Mozambique to investigate and identify the reasons behind the suboptimal performance of MIS, and to define the activities and investments required to strengthen malaria surveillance. The key recommendations were to prioritize enforcement of data quality checks; nurture the use of information; and provide and enforce simple and clear technical guidelines for data management.

Following these recommendations, Mozambique's NMP and partners' support have initiated the following activities aimed at strengthening surveillance: capacity-building and training on quality of data to data management staff at all levels of government; initiation of integrated supportive supervision of CHWs, health facility and district malaria focal points; development of iMISS technical requirements; piloting of automated data visualization dashboards at different levels; development of standard operating procedures for routine data management activities and actions that should be undertaken in response to findings; and initiation of operational protocols for malaria case and foci investigations and responses in very low transmission settings. Lessons learned from these surveillance strengthening activities are being documented through an ongoing adaptive learning cycle, to inform improvements of surveillance system performance and guide further rollout of activities.

Fig. B.9.3. Reporting completeness

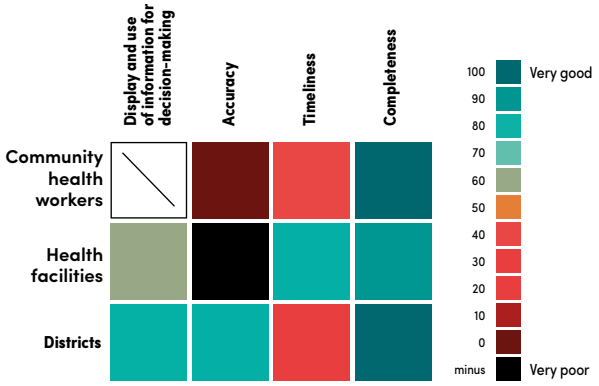
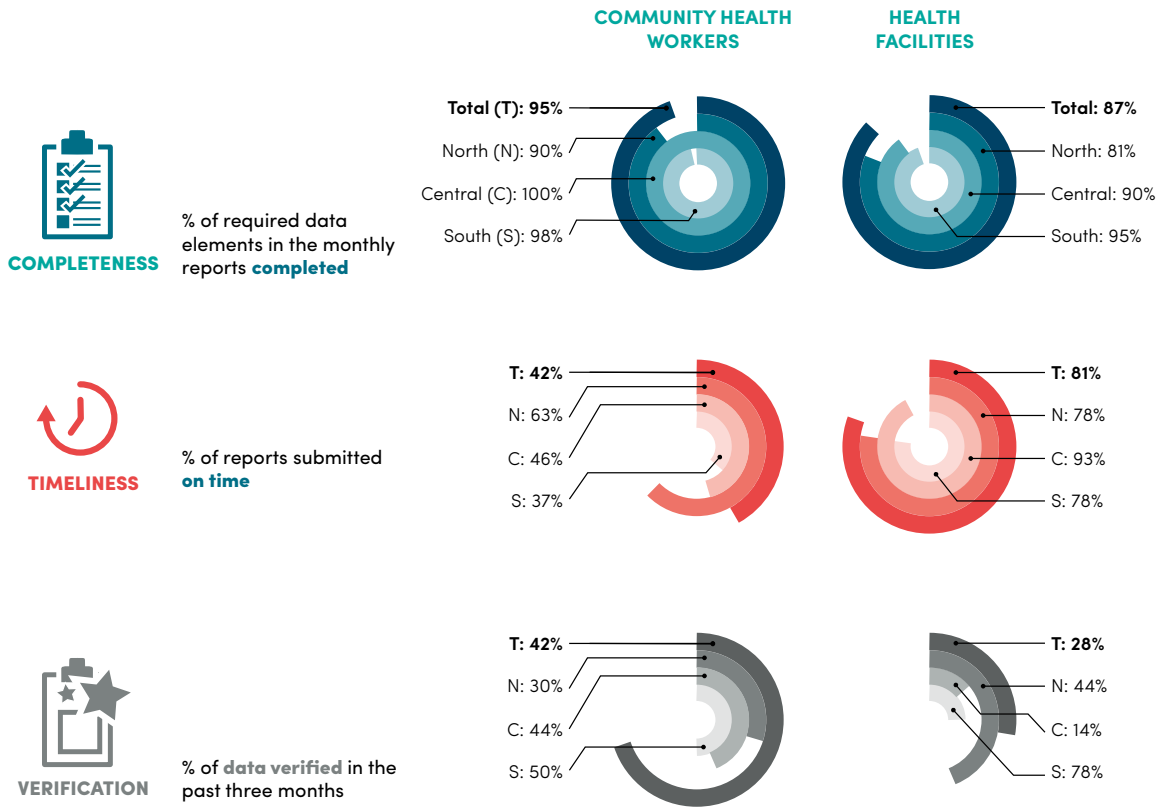


Fig. B.9.4. Proportion of health facilities with data verification carried out in the past 3 months



10 Responding to biological threats to the fight against malaria

The GTS (*1*) recognizes challenges in the fight against malaria, including the lack of robust, predictable and sustained international and domestic financing; the risks posed by conflict and other complex situations; the emergence of parasite resistance to antimalarial medicines and of mosquito resistance to insecticides; and the inadequate performance of health systems. One of WHO's major roles is to bring emerging challenges to the attention of the global community and to coordinate responses to address these challenges. This section of the report documents these challenges and proposed responses.

10.1 *PF-HRP2/3* GENE DELETIONS

HRP2 is the predominant target of the 412 million *P. falciparum*-detecting malaria RDTs sold annually. Parasites that no longer express HRP2 may not be detectable by HRP2-based RDTs, and those that no longer express HRP2 and HRP3 are completely invisible to these RDTs. Deletions in the *pfhrp2* and *pfhrp3* (*pfhrp2/3*) genes of clinical isolates were first identified in 2010 in the Peruvian Amazon basin by researchers characterizing blood samples that were negative by HRP2-RDTs but positive by microscopy. In recent years, *pfhrp2/3* deleted parasites have been documented outside of South America, including in East, Central, West and Southern Africa, in Asia and in the Middle East. Prevalence estimates vary widely both within and between countries. The examples of Eritrea and Peru, where the prevalence of dual *pfhrp2* and *pfhrp3* deletions among symptomatic patients reached as high as 80%, demonstrate that these parasites can become dominant in the population, posing a serious global threat to patients and the continued use of HRP2-based RDTs.

WHO has published guidance on investigating suspected *pfhrp2/3* deletions (*40*), and recommends that countries that have reports of *pfhrp2/3* deletions or that border countries with reports should conduct representative baseline surveys among suspected malaria cases, to determine whether the prevalence of *pfhrp2/3* deletions causing false negative RDT results has reached a threshold for RDT change (>5% *pfhrp2* deletions causing false negative RDT results). Alternative RDT options (e.g. based on detection of the parasite's lactate dehydrogenase [pLDH]) are limited; in particular, there is a lack of WHO-prequalified non-HRP2 combination tests that can detect and distinguish between *P. falciparum* and *P. vivax*.

WHO is tracking published reports of *pfhrp2/3* deletions using the Malaria Threat Map mapping tool,[1] and is encouraging a harmonized approach to mapping and reporting *pfhrp2/3* deletions through publicly available survey protocols. To date, 28 countries have reported *pfhrp2* deletions, but owing

[1] https://apps.who.int/malaria/maps/threats/

to variable methods in sample selection and laboratory analysis, the scale and scope of clinically significant *pfhrp2/3* deletions have not been fully elucidated. The WHO Global Response Plan for *pfhrp2/3* deletions outlines several areas for action beyond scaling up surveillance; the plan includes discovery of new biomarkers and improving the performance of non-HRP2 RDTs, as well as market forecasting and strengthened laboratory networks to support the demands of molecular characterization to rule in or rule out the presence of these gene deletions.

10.2 PARASITE RESISTANCE – STATUS OF ANTIMALARIAL DRUG EFFICACY (2010–2018)

Plasmodium resistance to antimalarial medicines is one of the key recurring challenges in the fight against malaria. Monitoring antimalarial drug efficacy supports early detection of changes in how well the recommended treatments work; this enables rapid action to mitigate any impact of resistance and prevent its spread. Therapeutic efficacy studies (TESs) provide a measure of clinical and parasitological patient outcomes, and are the main source of data on which the NMPs base their decisions regarding which treatment to recommend (*41*). In areas implementing malaria elimination activities, the routine surveillance system can track treatment and follow-up of all malaria cases, and use the data generated for integrated drug efficacy surveillance (iDES) (*38*). Information from TESs and iDES is supplemented by information on the prevalence and spread of molecular markers – genetic changes in the parasite – that are found to be associated with resistance. *PfKelch13* mutations have been identified as molecular markers of partial artemisinin resistance. *PfKelch13* mutations associated with artemisinin resistance are widespread in the GMS in South-East Asia, and have also been detected at a significant prevalence (over 5%) in Guyana, Papua New Guinea and Rwanda.

The WHO global database on antimalarial drug efficacy and resistance contains data from TESs conducted on *P. falciparum*, *P. vivax*, *P. knowlesi*, *P. malaria* and *P. ovale*, as well as molecular marker studies of *P. falciparum* drug resistance (*PfKelch13*, *PfPlasmepsin 2-3*, *Pfmdr1* and *Pfcrt* in Mesoamerica). Summary reports are regularly updated and are available on the WHO website (*42*). In addition, the Malaria Threats Maps provide a geographical representation of drug efficacy and resistance data.[1]

This section outlines the status of antimalarial drug efficacy in the WHO regions for 2010–2018.

WHO African Region

The first-line treatments used in most African countries for *P. falciparum* are artemether-lumefantrine (AL) and artesunate-amodiaquine (AS-AQ), with some countries' treatment policies also allowing for the use of dihydroartemisinin-piperaquine (DHA-PPQ). Between 2010 and 2018, treatment efficacy data for AL were available from 28 countries, for AS-AQ from 26 and for DHA-PPQ from 14. The overall average efficacy rates of AL, AS-AQ and DHA-PPQ for *P. falciparum* were 98.0%, 98.5% and 99.3%, respectively. When the failure rates of all three treatments were analysed separately by year, it was found that their high efficacy has remained constant over time. Treatment failure rates above 10% detected in Gambia and Malawi in 2010 are likely to be statistical outliers; recent studies show that most treatment failure rates remain low. The high reported failure rate from two studies in Angola was probably due to methodological issues. For all other medicines, treatment failure rates remain below 10%.

In Africa, artemisinin partial resistance has not yet been confirmed. Surveys are detecting a number of different validated and unvalidated *PfKelch13* mutations at low prevalence, except in Rwanda, where clearance and efficacy of the first-line treatment AL does not seem to be affected. There have been unconvincing case reports of travellers returning from Africa with malaria and not responding as expected to treatment. These include a Vietnamese male returning in 2013 to Viet Nam from Angola, who developed malaria that did not respond to intravenous artesunate, clindamycin or DHA-PPQ (*43*). Another case was reported in a Chinese male, who developed malaria 8 weeks after returning from Equatorial Guinea in 2013. The patient responded to treatment with DHA-PPQ but had low-level parasitaemia on day 3 after the start of treatment, and the infection was identified as carrying the *PfKelch13* mutation M579I, previously only reported once in Myanmar (*44, 45*). Three recent surveys conducted in Equatorial Guinea did not identify M579 among a total of 721 samples.

Eleven cases of treatment failure were reported in European travellers returning from different locations in Africa and treated with DHA-PPQ or AL (*46-48*). The patients were infected with parasites not carrying *PfKelch13* mutations, and molecular markers or blood levels of the partner medicines could not confirm resistance. Combined, these cases do not provide convincing evidence for the presence of resistance to artemisinin or ACT partner drugs in Africa. Nevertheless, reporting on these cases is important because

[1] https://apps.who.int/malaria/maps/threats/

resistance or treatment failures in travellers could be an early warning signal, supplementing the information collected in the endemic countries.

The *P. vivax* species is only endemic in a few countries in the WHO African Region. TESs with chloroquine (CQ) were conducted in Ethiopia, Madagascar and Mauritania. Ethiopia confirmed high rates of treatment failure for both CQ and AL. The high failure rate of AL without primaquine (PQ) is probably caused by the short half-life of artemisinin, which fails to prevent the first relapse. Madagascar monitored the efficacy of AS-AQ in 2012 and 2013, and Mauritania monitored CQ in 2012. The efficacy in these studies was found to be 100%.

WHO Region of the Americas

The first-line treatments for *P. falciparum* in the Amazon region are AL and artesunate-mefloquine (AS-MQ). Treatment efficacy was high for both medicines. One treatment failure was detected in a TES of AL, conducted in Suriname, among 11 patients. In Guatemala, Haiti, Honduras and Nicaragua, where the first-line treatment is CQ, molecular marker studies of *Pfcrt* are conducted to supplement TESs. Between 2010 and 2018, a low prevalence of *Pfcrt* mutation was observed in Haiti, Honduras and Nicaragua. TESs almost always confirmed the high efficacy of CQ in these countries.

A retrospective study of Guyanese samples collected in 2010 identified the *PfKelch13* mutation C580Y in five out of 98 samples (5.1%). A larger survey done in 2016–2017 found C580Y in 14 out of 877 samples (1.6%). Genetic studies have confirmed that these parasites were not imported from South-East Asia; rather, the mutation emerged in parasites of South American origin.

The first-line treatment policy for *P. vivax* in all endemic countries in this region is CQ. Between 2010 and 2018, TESs of *P. vivax* were conducted in Bolivia (Plurinational State of), Brazil, Colombia, Peru and Venezuela (Bolivarian Republic of). All countries conducted studies for *P. vivax* with CQ alone or with CQ and PQ. One study conducted in the Plurinational State of Bolivia confirmed CQ resistance. Additionally, Brazil conducted studies of AS-AQ, AL+PQ and AS-MQ+PQ. None of these resulted in treatment failures above 10%.

WHO South-East Asia Region

In Bhutan, Nepal and Timor-Leste, the first-line treatment policy for *P. falciparum* is AL. TESs conducted in these countries between 2010 and 2013 found high treatment efficacy, with less than 10% treatment failure.

Indonesia monitored DHA-PPQ efficacy between 2010 and 2017. All studies resulted in less than 10% treatment failures.

In Bangladesh, the first-line treatment policy includes AL, AS-AQ, AS-MQ and DHA-PPQ. Bangladesh monitored AL treatment failure between 2010 and 2018, and found rates above 10% in two studies, each with a small number of patients.

India's first-line treatment policy includes AL and AS-SP. India has extensively monitored the efficacy of AS-SP and found treatment failure rates ranging from 0% to 21.4%. Failure rates above 10% in north-eastern parts of India led to the treatment policy in this region changing to AL. All studies conducted for AL in India between 2011 and 2017 found treatment failure rates to be less than 10%.

Thailand's first-line treatment policy was AS-MQ until treatment failure rates began to progressively increase. The first-line treatment was changed to DHA-PPQ in 2015. Treatment failure for DHA-PPQ was monitored between 2014 and 2017, and treatment failure rates as high as 92.9% (13/14) were detected in 2017 in the north-eastern part of the country, probably from importation of malaria from Cambodia. As a result, the first-line treatment has since been changed to artesunate-pyronaridine (AS-PY) in eastern Thailand.

Myanmar's first-line treatment policy includes AL, AS-MQ and DHA-PPQ. Treatment failure rates were less than 10% despite the high prevalence of artemisinin partial resistance. In addition, Myanmar monitored AS-PY efficacy in four studies in 2017 and 2018, and found the treatment to be 100% efficacious.

The presence of molecular markers of artemisinin resistance has been reported in Bangladesh, India, Myanmar and Thailand. In Myanmar, seven different validated mutations have been reported, and the most frequently identified since 2010 is F446I. In Thailand, eight different validated mutations have been reported. In western Thailand, it is still possible to identify a range of different K13 mutations, whereas C580Y is becoming dominant in eastern Thailand. In Bangladesh, one C580Y mutation has been identified in a sample collected in 2018. Recently, two articles reported the emergence of artemisinin resistance in West Bengal, India based on the results from a TES with AS-SP done in the period 2014–2016 (*49, 50*). Among the 226 patients in the study, 10.6% (24/226) were found to have parasite clearance half-lives of more than 5 hours, 5.8% (13/226) were found to carry the *PfKelch13* mutation G625R, and 0.9% (2/226) carried R539T. The treatment failure rate was 8% (18/226). These results should be interpreted with caution (*51*). The data contrast with other available data on drug efficacy from India, including from West Bengal. *PfKelch13* mutations are rare in India, and the G625R mutation has not yet been validated as an artemisinin resistance marker; further investigation is needed to examine the role of G625R in delayed parasite clearance. TESs are

now being conducted in West Bengal, with an evaluation of parasite clearance times and analysis of *PfKelch13* mutations. Until appropriate validation and external quality control is completed, it is premature to claim that artemisinin resistance has emerged in India.

For *P. vivax*, CQ is the first-line treatment in Bangladesh, Bhutan, the Democratic People's Republic of Korea, India, Myanmar, Nepal, Sri Lanka and Thailand. DHA-PPQ is the first-line treatment in Indonesia, and AL in Timor-Leste. Although most studies demonstrated high efficacy of CQ, high failure rates of treatment with CQ were confirmed in Myanmar and Timor-Leste.

WHO Eastern Mediterranean Region

Studies conducted in Somalia and Sudan between 2011 and 2015 detected high failure rates of treatment with AS-SP, ranging from 12.3% to 22.2%. The evidence prompted a decision to change the new first-line treatment policy to AL. Therefore, the first-line treatment for *P. falciparum* in Afghanistan, Djibouti, Pakistan, Somalia and Sudan is AL. The efficacy of AL has been monitored in each of these countries, except in Djibouti. All TESs show low rates of AL treatment failure (<5%).

For infection with *P. vivax*, the first-line treatment policy is AL in Somalia and Sudan, and CQ in Afghanistan, Djibouti, Iran (Islamic Republic of), Pakistan, Saudi Arabia and Yemen. TESs of AL were conducted in Afghanistan and Sudan, and TESs of CQ were conducted in Iran (Islamic Republic of) and Pakistan. All studies showed high treatment efficacy. A study conducted in Pakistan in 2013 for DHA-PPQ detected one treatment failure among 103 cases (1%).

WHO Western Pacific Region

For *P. falciparum*, AL is the first-line treatment policy in countries outside the GMS as well as in Lao People's Democratic Republic. All studies conducted outside of the GMS resulted in failure rates of less than 10% for treatment with AL. In Lao People's Democratic Republic, treatment failure rates above 10% were found in three of nine studies between 2011 and 2017. However, the recommended samples sizes were not achieved.

In Cambodia, AS-MQ is the current first-line treatment. AS-MQ replaced DHA-PPQ after high rates of treatment failure were observed. Of the 17 studies conducted with AS-MQ since 2014, the treatment failure rate has been less than 2%. One study of AL found a treatment failure rate of 5% (3/60). The most recent studies with AS-PY in 2017 and 2018 showed efficacy of more than 95%. Treatment failure rates for AS-AQ ranged between 13.8% and 22.6%.

In Viet Nam, the first-line treatment policy is DHA-PPQ. Of the 42 TESs of DHA-PPQ conducted between 2010 and 2017, five studies detected treatment failure rates between 14.3% and 46.3%, all from 2015 to 2017. These studies were concentrated in the south, in the neighbouring provinces of Dak Nong and Binh Phuoc. Most recently, high failure rates for treatment with DHA-PPQ were observed in a third province, Dak Lak. Viet Nam has also monitored the efficacy of AL and AS-PY, with overall efficacies of 100% and 95.5%, respectively. Papua New Guinea monitored the efficacy of DHA-PPQ, and Malaysia monitored that of AS-MQ; both countries found 100% treatment efficacy for these medicines.

Artemisinin resistance has been confirmed in Cambodia, Lao People's Democratic Republic and Viet Nam through several studies conducted between 2001 and 2018. Between 2010 and 2018, eight *PfKelch13* mutations were identified in Cambodia and Lao People's Democratic Republic. C580Y was the most frequent, with about 71.7% of the genotypes carrying this mutation. In Viet Nam, six *PfKelch13* mutations were identified, and C580Y was also the most predominant, appearing on an average of 33.3% of the genotypes. The *PfKelch13* mutation C580Y has been identified twice in Papua New Guinea: in a survey in 2017 where 2.3% (3/132) of the samples carried the mutation (the percentage was higher in 2018) and in one traveller. No validated molecular markers of artemisinin resistance were found in studies conducted in Malaysia, the Philippines, Solomon Islands or Vanuatu.

The first-line treatment for *P. vivax* in Lao People's Democratic Republic, Malaysia, Papua New Guinea, Solomon Islands and Vanuatu is AL. High failure rates of treatment with AL were observed in Papua New Guinea (35% in 2011), Solomon Islands (31.6% in 2011), and Vanuatu (12.1% in 2013). These high rates in areas where early relapses occur are possibly explained by the short half-life of lumefantrine. In China, the Republic of Korea and Viet Nam, the first-line treatment for *P. vivax* is CQ. China and Viet Nam conducted TESs of CQ; only Viet Nam detected a treatment failure rate above 10% in 2015. In the Philippines, the recommended first-line treatments for *P. vivax* are AL and CQ. The nine studies in the Philippines conducted on CQ between 2010 and 2016 all showed treatment failure rates below 10%. In Cambodia, the first-line treatment for *P. vivax* is AS-MQ. Three recent TESs conducted in Cambodia showed 100% efficacy for AS-MQ. The efficacy of AS-MQ was also monitored in Lao People's Democratic Republic and Malaysia between 2012 and 2018. Both studies showed 100% efficacy. The efficacy of DHA-PPQ was monitored in Cambodia, Papua New Guinea and Viet Nam between 2010 and 2015. All studies found treatment failure rates below 10%.

10.3 VECTOR RESISTANCE TO INSECTICIDES

Resistance of malaria vectors to insecticides commonly used for malaria vector control – namely, pyrethroids, organophosphates, carbamates and the occasionally used organochlorine dichlorodiphenyltrichloroethane (DDT) – threatens malaria control and elimination efforts.

From 2010 through 2018, some 81 countries reported data from a total of 3075 sites to WHO, 10% more sites than in the period 2010–2017. The extent and frequency of insecticide resistance monitoring continue to vary considerably between countries. Of these 81 countries, 63 reported insecticide resistance monitoring data at least once within the past 3 years and 18 did not. Only 59 out of the 81 countries reported on their insecticide resistance status consistently every year for the past 3 years. The number of sites per country for which resistance monitoring data were reported between 2010 and 2018 varied widely, from a single site to 271 sites.

A total of 73 countries confirmed resistance to at least one insecticide in one malaria vector species from one mosquito collection site within the period 2010–2018, an increase of five countries compared with the previous reporting period (2010–2017). The number of countries that reported insecticide resistance to all four main insecticide classes used to date in at least one malaria vector species increased from 22 to 26, and the number of countries that reported resistance to three of these four classes in at least one malaria vector species increased from 16 to 18. Of those countries that reported insecticide resistance monitoring data to WHO, the proportion of countries that confirmed resistance to each of these insecticide classes was 87.5% for pyrethroids, 81.5% for organochlorines, 68% for carbamates and 56% for organophosphates. Only eight of the countries that reported data did not confirm resistance to any insecticide class.

Resistance to the four insecticide classes mentioned above was detected in all WHO regions except for the WHO European Region. Globally, resistance to pyrethroids was detected in at least one malaria vector in 68% of the sites for which data were available, and resistance to organochlorines was detected in 63% of the sites. Resistance to carbamates and organophosphates was less prevalent, being detected in 31% and 26%, respectively, of the sites that reported monitoring data. However, the geographical extent of confirmed resistance to each insecticide class differed considerably across regions (**Fig. 10.1**).

Collection and reporting of data to guide deployment of recently prequalified vector control tools covered by WHO policy recommendations have significantly improved. Further enhancement will be needed to guide strategic deployment of tools currently undergoing WHO evaluation. Until 2018, a total of 17 countries had monitored the involvement of metabolic resistance mechanisms in pyrethroid resistance by means of piperonyl butoxide (PBO) pre-exposure bioassays. By 2018, the number of countries reporting data from these bioassays to WHO rose to 23, all of which detected partial or full involvement of metabolic resistance mechanisms in phenotypic resistance to pyrethroids in at least one monitoring site for at least one vector species and one pyrethroid insecticide. Of the 190 sites for which data were reported until 2018, 187 detected full or partial involvement of metabolic resistance mechanisms for at least one vector species and one pyrethroid insecticide.

Results of biochemical and molecular assays conducted to detect metabolic resistance mechanisms are available for 24 countries and 160 sites for the period 2010–2018. Mono-oxygenases were detected in 64% of the sites for which reports are available (84/160), glutathione-S-transferases were detected in 76% of the sites (83/160) and esterases in 77% of the sites (114/160). Results of assays conducted to detect target-site resistance mechanisms are now available for 43 countries and 628 sites. *Kdr L1014F* was detected in 76% of the sites (514/628) and *Kdr L1014S* in 42% of the sites (311/628).

Recently, WHO Member States and their implementing partners have started to explore procedures and dosages to monitor resistance to neonicotinoid and pyrrole insecticides. A formal WHO process to establish discriminating dosages and test procedures for these two insecticide classes is ongoing and will be completed in 2020. The data on mosquito mortality after exposure to neonicotinoid and pyrrole insecticides reported so far to WHO will be assessed against these discriminating dosages once they have been finalized. WHO test procedures for insecticide resistance monitoring will be updated in 2020 to incorporate the new discriminating dosages and potential changes to the test procedures.

All the standard insecticide resistance data reported to WHO are included in the WHO Global Insecticide Resistance Database and are available for exploration via the online mapping tool, Malaria Threats Map.[1] This tool was extended in 2019 to cover a fourth threat to malaria control and elimination: invasive mosquito vector species. At present, this new theme shows the geographical extent of reports on the detection of *Anopheles stephensi*; it may be further extended to other invasive vector species as reported to WHO.

[1] https://apps.who.int/malaria/maps/threats/

10.3.1 Mitigating and managing insecticide resistance

Among other considerations, the selection of effective vector-control interventions needs to be based on routine and representative data on the susceptibility of local vectors to insecticides recommended and prequalified by WHO. In addition, insecticide resistance data are crucial for assessing the potential impact that resistance may have on the effectiveness of malaria vector control, an area that continues to be poorly understood. To meet these data needs, countries and their partners are advised to conduct regular insecticide resistance monitoring following the WHO-recommended *Test procedures for insecticide resistance monitoring in malaria vector mosquitoes* (*52*), and to report and share results in a timely manner. To facilitate reporting, WHO has developed and supports the rollout of data-reporting templates and DHIS2 modules for use by its Member States and their implementing partners.

Ultimately, it is likely that insecticide resistance will reduce the efficacy of currently available interventions. Countries should therefore not delay the development and application of policies and practices for resistance prevention, mitigation and management. Two relatively

FIG. 10.1.

Reported insecticide resistance status as a proportion of sites for which monitoring was conducted, by WHO region, 2010–2018, (a) Pyrethroids, (b) Organochlorines, (c) Carbamates, (d) Organophosphates Status was based on mosquito mortality where <90% = confirmed resistance, 90–97% = possible resistance, and ≥98% = susceptibility. Where multiple insecticide classes or types, mosquito species or time points were tested at an individual site, the highest resistance status was considered. Numbers above bars indicate the total number of sites for which data were reported (n). *Sources: reports from NMPs and national health institutes, their implementation partners, research institutions and scientific publications.*

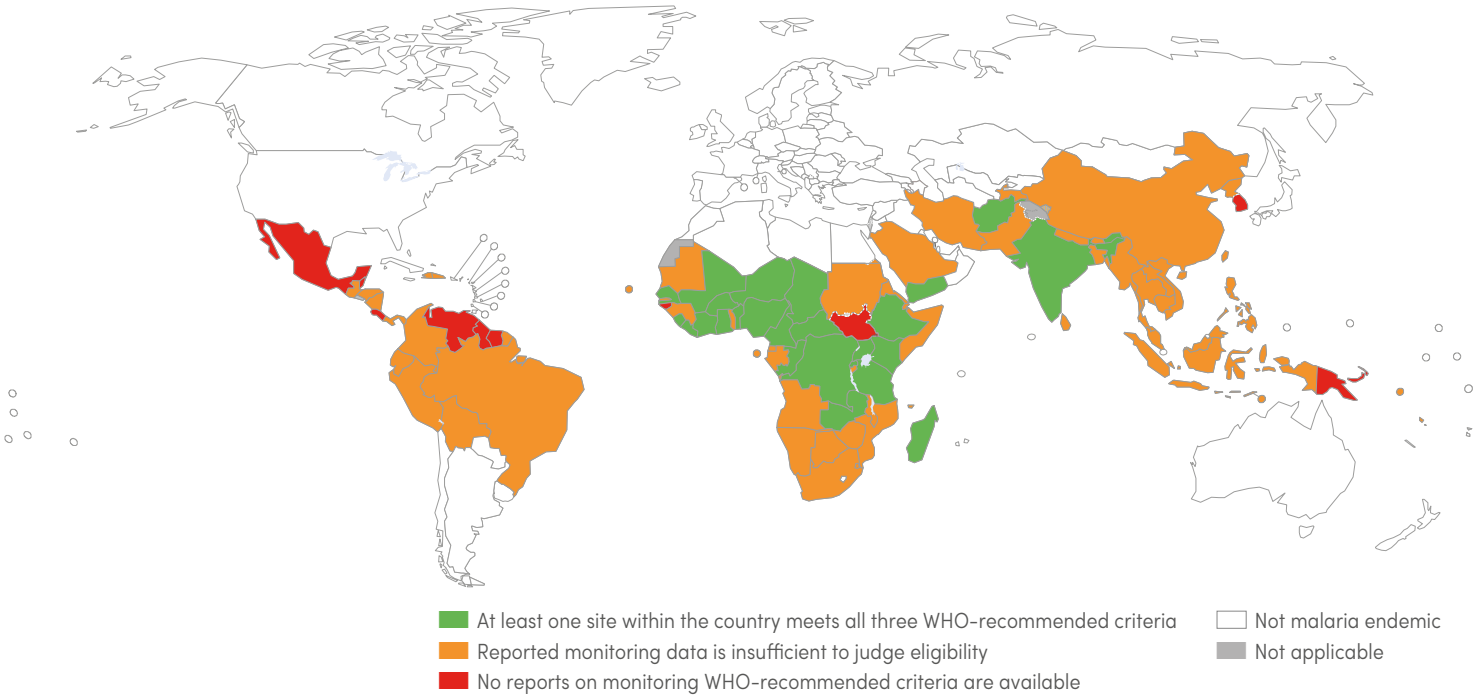
AFR: WHO African Region; AMR: WHO Region of the Americas; EMR: WHO Eastern Mediterranean Region; EUR: WHO European Region; n: number; NMP: national malaria programme; SEAR: WHO South-East Asia Region; WHO: World Health Organization; WPR: WHO Western Pacific Region.

new vector control options that should be considered as part of a strategy to mitigate or manage insecticide resistance – pyrethroid-PBO nets and neonicotinoid insecticides for IRS – have been recommended by WHO in the past 2 years; a number of prequalified products are now available, as well as a high-level map to support in-country discussion on pyrethroid-PBO net deployment (**Fig. 10.2**). Additional vector-control interventions to provide options for insecticide resistance management or to address outdoor transmission are under development; a number of these are already under WHO evaluation, supported by the WHO Vector Control Advisory Group.

To guide resistance management, countries should develop and implement a national plan for insecticide-resistance monitoring and management, drawing on the WHO *Framework for a national plan for monitoring and management of insecticide resistance in malaria vectors* (*53*). Through 2018, some countries have made progress in developing such plans. By the end of 2018 a total of 45 countries had finalized plans for resistance monitoring and management, and 36 were developing them. Further effort and support will be required to ensure that every country has such a plan, updates it regularly and has the necessary resources to implement it.

FIG. 10.2.

Status of monitoring WHO-recommended criteria for pyrethroid-PBO net deployment, 2010–2018 NMPs and their partners should consider the deployment of pyrethroid-PBO nets in areas where the main malaria vectors meet the criteria recommended by WHO in 2017 (*54*). Deployment of pyrethroid-PBO nets should be guided by whether geographical areas of operational relevance (e.g. districts or provinces) – rather than the whole country – meet the criteria specified by WHO and should be considered in the context of resource availability and potential for deployment of alternative malaria control interventions. *Sources: reports from NMPs and national health institutes, their implementation partners, research institutions and scientific publications.*



NMP: national malaria programme; PBO: piperonyl butoxide; WHO: World Health Organization.

11 Conclusion

WHO's *World malaria report 2019* summarizes global progress in the fight against malaria up to the end of 2018. This is the fourth world malaria report since the launch of the GTS (*1*). From a baseline of 2015, the GTS aims to achieve, by 2020, a reduction of 40% of malaria morbidity incidence and mortality rate, elimination in at least 10 countries and prevention of reintroduction in all countries that achieved elimination (*1*). To this end, the analysis shows that in 2018 there were an estimated 228 million cases and 405 000 deaths globally, concentrated mainly in Africa and India. This represents about 3 million fewer cases and 11 000 fewer deaths compared with 2017.

On the one hand, the analysis shows that if malaria case incidence and mortality rate remained the same as those in 2000, globally there would be 320 million cases and nearly 1 million malaria deaths in 2018. Instead, there were an estimated 228 million malaria cases and 405 000 malaria deaths in 2018. These represent about 30% fewer cases and 60% fewer deaths in 2018 than would have been the case had levels of malaria incidence and malaria death remained similar to those in 2000. While the gains to date are impressive, the global malaria challenge remains enormous, and the rate of progress is slowing. For example, on the current trajectory, globally, the 2020 GTS milestones for morbidity will not be achieved, and unless there is accelerated change, the 2025 and 2030 milestones will not be achieved. A global malaria case incidence of 45 per 1000 population at risk in 2018 would have been required to get the world on target for the 2020 milestones, but current estimated incidence is 57 cases per 1000 population at risk. If the current trend in incidence is maintained, estimated malaria case incidence (per 1000 population at risk) would be 54 in 2020, 48 in 2025 and 42 in 2030, instead of the 35, 14 and 6 required to achieve the GTS milestones.

Progress towards the GTS elimination goals is on track. At least 10 countries that are part of the WHO E-2020 initiative are on track to reach the 2020 elimination milestone of our global malaria strategy. In 2015, all of these countries were malaria endemic; now they have either achieved zero malaria cases or are nearing the finish line. Across the six countries of the GMS – Cambodia, China (Yunnan Province), Lao People's Democratic Republic, Myanmar, Thailand and Viet Nam – there was a 76% reduction in malaria cases and a 95% reduction in deaths in the period 2010–2018. Notably, the report shows a steep decline in cases of *P. falciparum* malaria, the primary target in view of the ongoing threat of antimalarial drug resistance. In 2018, Cambodia reported zero malaria-related deaths for the first time in the country's history, China reported its second consecutive year of zero indigenous malaria cases and Thailand reported a 38% drop in *P. falciparum* cases compared with the previous year.

By November 2019, the HBHI approach had been initiated in nine high-burden countries in Africa. Countries have developed detailed activity plans to address the challenges revealed during the assessments. Two HBHI countries achieved significant reductions in malaria cases in 2018 compared with previous year – India (2.6 million fewer cases) and Uganda (1.5 million fewer cases). Notable increases were estimated in Ghana and Nigeria; however, overall, malaria case incidence and mortality rates continued to decline, but at a slower rate in recent years.

In 2018, total funding for malaria control and elimination reached an estimated US$ 2.7 billion, falling far short of the US$ 5 billion funding target of the GTS. Moreover, the funding gap widened between 2017 and 2018, from US $1.3 billion to US $2.3 billion. Over the period 2010–2018, nearly 70% of total malaria funding in 2018 was provided by international sources. Governments of malaria endemic countries contributed about 30% of total funding, with investments reaching US $0.9 billion in 2018. Of the US $2.7 billion invested in 2018, the government of the USA contributed about $1 billion; the United Kingdom contributed about $200 million; and France, Japan and Germany each contributed about $100 million. About US $1 billion in malaria funding was channelled through the Global Fund. Approximately three quarters of total funding benefited the WHO African Region, followed by the WHO Region of the Americas (7%), the WHO South-East Asia Region (6%), and the WHO Eastern Mediterranean Region and the WHO Western Pacific Region (5% each).

The scourge of malaria continues to strike hardest against pregnant women and children in Africa. The *World malaria report 2019* includes a special section focused on the burden and consequences of the disease among these two most-at-risk groups. In 2018, an estimated 11 million pregnant women in sub-Saharan Africa were infected with malaria, and 872 000 children were born with a low birthweight. About 24 million children in the region were estimated to be infected with the *P. falciparum* parasite in 2018; of these, 12 million had moderate anaemia and 1.8 million had severe anaemia. An estimated 70% of all malaria deaths globally, most of which were in sub-Saharan Africa, were of children aged under 5 years.

In 2018, 31% of pregnant women in 36 African countries received the recommended three or more doses of IPTp, up from 22% in 2017 and 0% in 2010. Notably, Burkina Faso and the United Republic of Tanzania reached IPTp coverage of more than 50% in 2018. Nearly 40% of pregnant women and children aged under 5 years did not sleep under an ITN in 2018. In the same year, two thirds of pregnant women also did not receive the recommended three or more doses of preventive therapy. In Africa's Sahel subregion, WHO recommends SMC during the peak transmission season. More than 60% of children living in SMC-eligible areas benefited from this preventive therapy in 2018. A high proportion of febrile children in sub-Saharan Africa (36%) do not receive any medical attention. Although impressive gains have been made in preventing and treating malaria in pregnant women and children, important gaps in access to care remain. Effective and equitable delivery of primary health care interventions is required to rapidly reduce the burden of malaria among these vulnerable groups.

References

1. Global technical strategy for malaria 2016–2030. Geneva: World Health Organization; 2015 (https://www.who.int/malaria/areas/global_technical_strategy/en, accessed 20 October 2019).

2. Roll Back Malaria Partnership Secretariat. Action and investment to defeat malaria 2016–2030. For a malaria-free world. Geneva: World Health Organization; 2015 (https://endmalaria.org/sites/default/files/RBM_AIM_Report_0.pdf, accessed 20 October 2019).

3. Sustainable Development Goals: 17 goals to transform our world [website]. United Nations; 2015 (https://www.un.org/sustainabledevelopment/sustainable-development-goals, accessed 20 October 2019).

4. Thirteenth general programme of work 2019–2023 [website]. Geneva: World Health Organization; 2018 (https://www.who.int/about/what-we-do/gpw-thirteen-consultation/en/, accessed 20 October 2019).

5. Malaria and the UN Sustainable Development Goals (SDGs) 2030. Swiss Tropical and Public Health Institute (TPH) Swiss TPH for the Swiss Malaria Group; 2018 (https://www.swissmalariagroup.ch/fr/assets/uploads/files/New%20factsheet%20Malaria%20and%20the%20UN%20Sustainable%20Development%20Goals%20x.pdf, accessed 20 October 2019).

6. Country profiles [website]. Geneva: World Health Organization; (https:///www.who.int/malaria/publications/country-profiles/en/, accessed 20 October 2019).

7. Malaria in pregnant women. Geneva: World Health Organization; 2017 (https://www.who.int/malaria/areas/high_risk_groups/pregnancy/en/, accessed 20 October 2019).

8. Stevens GA, Finucame MM, De-Regil LM, Paciorek CJ, Flaxman SR, Branca F et al. Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995-2011: a systematic analysis of population-representative data. Lancet Glob Health. 2013 Jul;1(1):e16-25 (https://www.ncbi.nlm.nih.gov/pubmed/25103581, accessed 14 November 2019).

9. Guyatt HL, Snow RW. The epidemiology and burden of *Plasmodium falciparum*-related anemia among pregnant women in sub-Saharan Africa. Am J Trop Med Hyg. 2001 Jan-Feb;64(1-2 Suppl):36-44 (https://www.ncbi.nlm.nih.gov/pubmed/11425176, accessed 14 November 2019).

10. Guyatt HL, Snow RW. Impact of malaria during pregnancy on low birth weight in sub-Saharan Africa. Clin Microbiol Rev. 2004;17(4):760–9 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC523568/, accessed 20 October 2019).

11. Guyatt HL, Snow RW. Malaria in pregnancy as an indirect cause of infant mortality in sub-Saharan Africa. Trans R Soc Trop Med Hyg. 2001;95(6):569–76 (https://academic.oup.com/trstmh/article-abstract/95/6/569/1905057?redirectedFrom=fulltext, accessed 20 October 2019).

12. Menendez C. Malaria during pregnancy. Curr Mol Med. 2006 Mar;6(2):269-73.

13. Bardaji A, Martinez-Espinosa FE, Arevalo-Herrera M, Padilla N, Kochar S, Ome-Kaius M et al. Burden and impact of *Plasmodium vivax* in pregnancy: A multi-centre prospective observational study. PLoS Negl Trop Dis. 2017 Jun 12;11(6):e0005606.

14. WHA Global Nutrition Targets 2015: Anaeamia Policy Brief. Geneva: World Health Organization; 2014 (https://www.who.int/nutrition/topics/globaltargets_anaemia_policybrief.pdf, accessed 14 November 2019).

15. Crawley J. Reducing the burden of anemia in infants and young children in malaria-endemic countries of Africa: from evidence to action. Am J Trop Med Hyg. 2004;71(2_suppl):25–34 (https://www.ajtmh.org/content/journals/10.4269/ajtmh.2004.71.25, accessed 20 October 2019).

16. Walker PG, ter Kuile FO, Garske T, Menendez C, Ghani AC. Estimated risk of placental infection and low birthweight attributable to *Plasmodium falciparum* malaria in Africa in 2010: a modelling study. Lancet Glob Health. 2014;2(8):e460–e7.

17. Walker PGT, Griffin JT, Cairns M, Rogerson SJ, van Eijk AM; Ter Kuile F, Ghani AC. A model of parity-dependent immunity to placental malaria. Nat Commun. 2013;4:1609.

18. World Population Prospects. The 2019 Revision [website]. United Nations Population Division; 2019 (http://data.un.org/Data.aspx?d=PopDiv&f=variableID%3A54, accessed 14 November 2019).

19. Antimalarial drug efficacy and drug resistance (updated 27 April 2018) [website]. Geneva: World Health Organization; 2018 (https://www.who.int/malaria/areas/treatment/drug_efficacy/en/, accessed 15 October 2018).

20. UNICEF-WHO. Low birthweight estimates: Levels and trends 2000–2015. Geneva: World Health Organization; 2019 (https://www.unicef.org/media/53711/file/UNICEF-WHO%20Low%20birthweight%20estimates%202019%20.pdf, accessed 14 November 2019).

21. World health statistics overview 2019: monitoring health for the SDGs, sustainable development goals. Geneva: World Health Organization; 2019 (https://apps.who.int/iris/bitstream/handle/10665/311696/WHO-DAD-2019.1-eng.pdf, accessed 14 November 2019).

22. UNICEF Data: Monitoring the situation of children and women [website]. UNICEF; 2019 (https://data.unicef.org/topic/maternal-health/antenatal-care/, accessed 14 November 2019).

23. High burden to high impact: a targeted malaria response. Geneva: World Health Organization; 2019 (https://www.who.int/malaria/publications/atoz/high-impact-response/en/, accessed 22 October 2019).

24. World malaria report. Geneva: World Health Organization; 2017 (https://www.who.int/malaria/publications/world-malaria-report-2017/en/, accessed 20 October 2019).

25. World malaria report. Geneva: World Health Organization; 2018 (https://www.who.int/malaria/publications/world-malaria-report-2018/en/, accessed 20 October 2019).

26. Zero Malaria Starts with Me Toolkit. RBM Partnership to End Malaria African and the African Union Commission (https://endmalaria.org/sites/default/files/Zero%20Malaria%20Toolkit%20Final.pdf, accessed 15 November 2019).

27. WHO Malaria Policy Advisory Committee (MPAC): meeting report. Geneva: World Health Organization Global Malaria Programme; 2019 (https://www.who.int/publications-detail/malaria-policy-advisory-committee-meeting-report-october-2019, accessed 15 November 2019).

28. Malaria elimination: report from the inaugural global forum of countries with potential to eliminate malaria by 2020. Wkly Epidemiol Rec. 2017;92(39):578–86 (https://www.ncbi.nlm.nih.gov/pubmed/28960948, accessed 16 October 2018).

29. Guidelines for malaria vector control. Geneva: World Health Organization; 2019 (https://www.who.int/malaria/publications/atoz/9789241550499/en/, accessed 25 October 2019).

30. Intermittent preventive treatment in pregnancy (IPTp) (updated 21 June 2018) [website]. Geneva: World Health Organization; 2018 (https://www.who.int/malaria/areas/preventive_therapies/pregnancy/en/, accessed 15 October 2018).

31. Intermittent preventive treatment in infants (updated 1 May 2017) [website]. Geneva: World Health Organization; 2017 (https://www.who.int/malaria/areas/preventive_therapies/infants/en/, accessed 15 October 2018).

32. Seasonal malaria chemoprevention with sulfadoxine-pyrimethamine plus amodiaquine in children: a field guide. Geneva: World Health Organization; 2013 (https://apps.who.int/iris/bitstream/handle/10665/85726/9789241504737_eng.pdf?sequence=1, accessed 15 October 2018).

33. Mass drug administration for falciparum malaria: a practical field manual. Geneva: World Health Organization; 2017 (https://extranet.who.int/iris/restricted/handle/10665/259367, accessed 20 October 2019).

34. Acosta A, Obi E, Selby RA, Ugot I, Lynch M, Maire M et al. Design, implementation, and evaluation of a school insecticide-treated net distribution program in Cross River State, Nigeria. J Glob Health Sci. 2018;6(2):272–87.

35. Bhatt S, Weiss DJ, Cameron E, Bisanzio D, Mappin B, Dalrymple U et al. The effect of malaria control on *Plasmodium falciparum* in Africa between 2000 and 2015. Nature. 2015;526(7572):207–11.

36. Guidelines for the treatment of malaria, third edition. Geneva: World Health Organization; 2015 (https://apps.who.int/iris/bitstream/handle/10665/162441/9789241549127_eng.pdf;sequence=1, accessed 20 October 2010).

37. Sadruddin S, Pagnoni P, Baugh G. Lessons from the integrated community case management (iCCM) Rapid Access Expansion Program. JoGH 2019;9: 020101 (http://www.jogh.org/documents/issue201902/jogh-09-020101.pdf, accessed 15 November 2019).

References

38. Malaria surveillance, monitoring & evaluation: a reference manual. Geneva: World Health Organization; 2018 (https://apps.who.int/iris/bitstream/handle/10665/272284/9789241565578-eng.pdf?ua=1, accessed 15 October 2018).

39. Adapted Performance Review Information System Management (PRISM) [website]. Measure Evaluation; (https://www.measureevaluation.org/resources/tools/health-information-systems/prism, accessed 21 October 2019).

40. False-negative RDT results and implications of new reports of *P. falciparum* histidine-rich protein 2/3 gene deletions World Health Organization; 2017 (https://apps.who.int/iris/bitstream/10665/258972/1/WHO-HTM-GMP-2017.18-eng.pdf, accessed 27 October 2017).

41. Methods for surveillance of antimalarial drug efficacy. Geneva: World Health Organization; 2009 (https://www.who.int/malaria/publications/atoz/9789241597531/en/, accessed 20 October 2019).

42. Global database on antimalaria drug efficacy and resistance (updated 27 April 2018). Geneva: World Health Organization; 2018 (https://www.who.int/malaria/areas/drug_resistance/drug_efficacy_database/en/, accessed 15 November 2019).

43. Van Hong N, Amambua-Ngwa A, Quang Tuan N, Duy Cuong D, Thi Huong Giang N, Van Dung N et al. Severe malaria not responsive to artemisinin derivatives in man returning from Angola to Vietnam. Emerg Infect Dis. 2014. 20(7):1199-202 (https://wwwnc.cdc.gov/eid/article/20/7/14-0155_article, accessed 15 November 2019).

44. Lu F, Culleton R, Zhang M, Ramaprasad A, von Seidlein L, Zhou H et al. Emergence of indigenous artemisinin-resistant *Plasmodium falciparum* in Africa. N Engl J Med. 2017 Mar 9;376(10):991-993 (https://www.nejm.org/doi/10.1056/NEJMc1612765, accessed 15 November 2019).

45. Rasmussen C, Nyunt MM, Ringwald P. Artemisinin-resistant *Plasmodium falciparum* in Africa. N Engl J Med. 2017 Jul 20;377(3):305-306 (https://www.nejm.org/doi/10.1056/NEJMc1705789, accessed 15 November 2019).

46. Russo G, L'Episcopia M, Menegon M, Souza SS, Dongho BGD, Vullo V et al. Dihydroartemisinin-piperaquine treatment failure in uncomplicated *Plasmodium falciparum* malaria case imported from Ethiopia. Infection. 2018 Dec;46(6):867-870 (https://link.springer.com/article/10.1007%2Fs15010-018-1174-9, accessed 15 November 2019).

47. Sonden K, Wyss K, Jovel I, Vieira da Silva A, Pohanka A, Asghar M et al. High rate of treatment failures in nonimmune travelers treated with artemether-lumefantrine for uncomplicated *Plasmodium falciparum* malaria in Sweden: retrospective comparative analysis of effectiveness and case series. Clin Infect Dis. 2017 Jan 15;64(2):199-206 (https://academic.oup.com/cid/article/64/2/199/2698880, accessed 15 November 2019).

48. Sutherland CJ, Lansdell P, Sanders M, Muwanguzi J, van Schalkwyk DA, Kaur H et al. Pfk13-independent treatment failure in four imported cases of *Plasmodium falciparum* malaria treated with artemether-lumefantrine in the United Kingdom. Antimicrob Agents Chemother. 2017 Feb 23;61(3): e02382-16 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5328508/, accessed 15 November 2019).

49. Das S, Saha B, Hati AK, Roy S. Evidence of artemisinin-resistant *Plasmodium falciparum* malaria in Eastern India. N Engl J Med. 2018 Nov 15;379(20):1962-1964 (https://www.nejm.org/doi/10.1056/NEJMc1713777, accessed 15 November 2019).

50. Das S, Manna S, Saha B, Hati AK, Roy S. Novel pfkelch13 gene polymorphism associates with artemisinin resistance in Eastern India. Clin Infect Dis. 2019 Sep 13;69(7):1144-1152 (https://academic.oup.com/cid/article/69/7/1144/5236823, accessed 15 November 2019).

51. Rasmussen C, Valecha N, Ringwald P. Lack of convincing evidence of artemisinin resistance in India. Clin Infect Dis. 2019, 1461-1462 (https://academic.oup.com/cid/article-abstract/69/8/1461/5367393?redirectedFrom=fulltext, accessed 15 November 2019).

52. Test procedures for insecticide resistance monitoring in malaria vector mosquitoes (second edition). Geneva: World Health Organization; 2018 (https://apps.who.int/iris/bitstream/handle/10665/250677/9789241511575-eng.pdf, accessed 15 November 2019).

53. Framework for a national plan for monitoring and management of insecticide resistance in malaria vectors. Geneva: World Health Organization; 2017 (https://apps.who.int/iris/bitstream/handle/10665/254916/9789241512138-eng.pdf, accessed 15 November 2019).

54. Conditions for deployment of mosquito nets treated with a pyrethroid and piperonyl butoxide. Geneva: World Health Organization; 2017 (https://apps.who.int/iris/bitstream/handle/10665/258939/WHO-HTM-GMP-2017.17-eng.pdf, accessed 15 November 2019).

Annexes

Annex 1 - Data sources and methods

Annex 2 - Regional profiles

- A. WHO African Region
  - a. West Africa
  - b. Central Africa
  - c. Countries with high transmission in East and Southern Africa
  - d. Countries with low transmission in East and Southern Africa
- B. WHO Region of the Americas
- C. WHO Eastern Mediterranean Region
- D. WHO South-East Asia Region
- E. WHO Western Pacific Region

Annex 3 - Data tables

- A. Policy adoption, 2018
- B. Antimalarial drug policy, 2018
- C. Funding for malaria control, 2016–2018
- D. Commodities distribution and coverage, 2016–2018
- Ea. Household survey results, 2015–2018, compiled through STATcompiler
- Eb. Household survey results, 2015–2018, compiled through WHO calculations
- F. Population at risk and estimated malaria cases and deaths, 2010–2018
- G. Population at risk and reported malaria cases by place of care, 2018
- H. Reported malaria cases by method of confirmation, 2010–2018
- I. Reported malaria cases by species, 2010–2018
- J. Reported malaria deaths, 2010–2018

Annex 1 – Data sources and methods

Fig. 1.1. Countries with indigenous cases in 2000 and their status by 2018

Data on the number of indigenous cases (an indicator of whether countries are endemic for malaria) were as reported to the World Health Organization (WHO) by national malaria programmes (NMPs). Countries with 3 consecutive years of zero indigenous cases are considered to have eliminated malaria.

Table 1.1. GTS: global targets for 2030 and milestones for 2020 and 2025

Targets and milestones are as described in the *Global technical strategy for malaria 2016–2030* (GTS) (*1*) and *Action and investment to defeat malaria 2016–2030* (AIM) (*2*).

Fig. 1.2. Malaria and the SDGs 2016–2030

This figure was adapted from a fact sheet on malaria and the Sustainable Development Goals (SDGs) (*3*) produced by the Swiss Tropical and Public Health Institute (a WHO Collaborating Centre) for the Swiss Malaria Group.

Fig. 1.3. The WHO triple billion targets and the contribution of the fight against malaria

This figure is extracted from the document *Informal Member States Consultation GPW 13 WHO Impact Framework* (*4*).

Table 2.1. Estimated malaria cases by WHO region, 2010–2018

The number of malaria cases was estimated by one of the following two methods:

Method 1

Method 1 was used for countries and areas outside Africa and for low-transmission countries and areas in Africa: Afghanistan, Bangladesh, Bolivia (Plurinational State of), Botswana, Brazil, Cambodia, Colombia, Dominican Republic, Eritrea, Ethiopia, French Guiana, Gambia, Guatemala, Guyana, Haiti, Honduras, India, Indonesia, Lao People's Democratic Republic, Madagascar, Mauritania, Myanmar, Namibia, Nepal, Nicaragua, Pakistan, Panama, Papua New Guinea, Peru, Philippines, Rwanda, Senegal, Solomon Islands, Timor-Leste, Vanuatu, Venezuela (Bolivarian Republic of), Viet Nam, Yemen and Zimbabwe.

Estimates were made by adjusting the number of reported malaria cases for completeness of reporting, the likelihood that cases were parasite positive, and the extent of health service use. The procedure, which is described in the *World malaria report 2008* (*5*), combines data reported by NMPs (reported cases, reporting completeness and likelihood that cases are parasite positive) with data obtained from nationally representative household surveys on health service use. Briefly:

$T = (a + (c \times e))/d \times (1+f/g+(1-g-f)/2/g)$

where:

a is malaria cases confirmed in public sector

b is suspected cases tested

c is presumed cases (not tested but treated as malaria)

d is reporting completeness

e is test positivity rate (malaria positive fraction) = a/b

f is fraction seeking treatment in private sector

g is fraction seeking treatment in public sector

No treatment seeking factor: $(1-g-f)$

Cases in public sector: $(a + (c \times e))/d$

Cases in private sector: $(a + (c \times e))/d \times f/g$

To estimate the uncertainty around the number of cases, the *test positivity rate* was assumed to have a normal distribution centred on the test positivity rate value and standard deviation, defined as $0.244 \times f^{0.5547}$, and truncated to be in the range 0, 1. *Reporting completeness* (*d*), when reported as a range or below 80%, was assumed to have one of three distributions, depending on the value reported by the NMP. If the value was greater than 80%, the distribution was assumed to be triangular, with limits of 0.8 and 1 and the peak at 0.8. If the value was greater than 50%, then the distribution was assumed to be rectangular, with limits of 0.5 and 0.8. Finally, if the value was lower than 50%, the distribution was assumed to be triangular, with limits of 0 and 0.5 and the peak at 0.5 (*6*). If the reporting completeness was reported as a value and was greater than 80%, a beta distribution was assumed with a mean value of the reported value (maximum of 95%) and confidence intervals (CIs) of 5% round the mean value. The fraction of children brought for care in the public sector and in the private sector were assumed to have a beta distribution, with the mean value being the estimated value in the survey and the standard deviation calculated from the range of the estimated 95% CIs divided by 4. The fraction of children not brought for care was assumed to have a rectangular distribution, with the lower limit being 0 and the upper limit calculated as 1 minus the proportion that were brought for care in the public and private sectors. The three distributions (fraction seeking treatment in public sector, fraction seeking treatment in private sector only and fraction not seeking treatment) were constrained to add up to 1.

Values for the fractions seeking care were linearly interpolated between the years that had a survey, and were extrapolated for the years before the first or after the last survey. Missing values for the distributions were imputed in a similar way or, if there was no value for any year in the country or area, a mixture of the distribution of

the region for that year. CIs were obtained from 10 000 draws of the convoluted distributions. The data were analysed using the R statistical software (*7*).

For India, the values were obtained at subnational level using the same methodology, but adjusting the private sector for an additional factor due to the active case detection, estimated as the ratio of the test positivity rate in active case detection over the test positivity rate for passive case detection. This factor was assumed to have a normal distribution, with mean value and standard deviation calculated from the values reported in 2010.

No adjustment for private sector treatment seeking was made for the following countries and areas, because they report cases from the private and public sector together: Bangladesh, Bolivia (Plurinational State of), Botswana, Brazil, Colombia, Dominican Republic, French Guiana, Guatemala, Guyana, Haiti, Honduras, Myanmar (since 2013), Nicaragua, Panama, Peru, Rwanda, Senegal (70% of private sector reported together with public sector in 2018) and Venezuela (Bolivarian Republic of).

Method 2

Method 2 was used for high-transmission countries in Africa and for some countries in the WHO Eastern Mediterranean Region in which the quality of surveillance data did not permit a robust estimate from the number of reported cases: Angola, Benin, Burkina Faso, Burundi, Cameroon, Central African Republic, Chad, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Equatorial Guinea, Gabon, Ghana, Guinea, Guinea-Bissau, Kenya, Liberia, Malawi, Mali, Mozambique, Niger, Nigeria, Sierra Leone, Somalia, South Sudan, Sudan, Togo, Uganda, United Republic of Tanzania and Zambia. In this method, estimates of the number of malaria cases were derived from information on parasite prevalence obtained from household surveys.

First, data on parasite prevalence from nearly 60 000 survey records were assembled within a spatio-temporal Bayesian geostatistical model, along with environmental and sociodemographic covariates, and data distribution on interventions such as insecticide-treated mosquito net (ITNs), antimalarial drugs and indoor residual spraying (IRS). The geospatial model enabled predictions of *Plasmodium falciparum* prevalence in children aged 2–10 years, at a resolution of 5 × 5 km^2, throughout all malaria endemic African countries for each year from 2000 to 2018.[1] Second, an ensemble model was developed to predict malaria incidence as a function of parasite prevalence. The model was then applied to the estimated parasite prevalence in order to obtain estimates of the malaria case incidence at 5 × 5 km^2 resolution for each year from 2000 to 2018.[1] Data for each 5 × 5 km^2 area were then aggregated within country and regional boundaries, to obtain both national and regional estimates of malaria cases (*8*).

Other methods

For most of the elimination countries and countries in prevention of reintroduction, the number of indigenous cases registered by the NMPs are reported without further adjustments. The countries in this category were Algeria, Argentina, Armenia, Azerbaijan, Belize, Bhutan, Cabo Verde, China, Comoros, Costa Rica, Democratic People's Republic of Korea, Djibouti, Ecuador, Egypt, El Salvador, Eswatini, Georgia, Iran (Islamic Republic of), Iraq, Kazakhstan, Kyrgyzstan, Malaysia, Mexico, Morocco, Oman, Paraguay, Republic of Korea, Sao Tome and Principe, Saudi Arabia, South Africa, Sri Lanka, Suriname, Syrian Arab Republic, Tajikistan, Thailand, Turkey, Turkmenistan, United Arab Emirates and Uzbekistan.

For some years, information was not always available or was not of sufficient quality to be used. For those countries, the number of cases was imputed from other years where the quality of the data was better, adjusting for population growth, as follows: for Ethiopia, the values were taken from a mixed distribution between values from Method 1 and Method 2 (50% from each method); for Gambia, 2010 values were imputed from 2011 to 2013 values; for Haiti, 2010 values were imputed from 2006 to 2008 values; for Namibia, 2012 values were imputed from 2010 and 2013 values; and for Papua New Guinea, 2012 values were imputed from 2009 to 2011 values. Estimated rates from 2017 were extrapolated to 2018 for Angola, Burundi, Central African Republic and Sudan. For Djibouti, 2011 and 2012 values were extrapolated from cases reported in 2009 and 2013. For Kenya, Mali, Niger and Somalia, the estimated series up to 2017 in the *World malaria report 2018* was used and extrapolated to 2018. To follow the current trends in reported cases in the public sector, modelled cases were adjusted for a factor of 1.1 in Uganda in 2018.

The number of malaria cases caused by *P. vivax* in each country was estimated by multiplying the country's reported proportion of *P. vivax* cases, computed as 1 – *P. falciparum*, by the total number of estimated cases for the country. For countries where the estimated proportion was not 0 or 1, the proportion of *P. falciparum* cases was assumed to have a beta distribution estimated from the proportion of *P. falciparum* cases reported by NMPs.

To transform malaria cases into incidence, a population at risk estimate was used. The proportion of the population at high, low or no risk of malaria was provided by NMPs. This was applied to United Nations (UN) population estimates, to compute the number of people at risk of malaria.

[1] For methods on the development of maps by the Malaria Atlas Project, see https://www.map.ox.ac.uk/making-maps/.

Table 2.2. Estimated *P. vivax* malaria cases by WHO region, 2018

See methods notes for **Table 2.1**.

Fig. 2.1. Estimated country share of (a) total malaria cases and (b) *P. vivax* malaria cases, 2018

See methods notes for **Table 2.1**.

Fig. 2.2. Trends in malaria case incidence rate (cases per 1000 population at risk) globally and by WHO region, 2010–2018

See methods notes for **Table 2.1**.

Fig. 2.3. Map of malaria case incidence rate (cases per 1000 population at risk) by country, 2018

See methods notes for **Table 2.1**.

Fig. 2.4. Trends in malaria mortality rate (deaths per 100 000 population at risk), globally and in the WHO African Region, 2010–2018

See methods notes for **Table 2.3**.

Fig. 2.5. Trends in malaria mortality rate (deaths per 100 000 population at risk) in WHO regions, 2010–2018

See methods notes for **Table 2.3**.

Table 2.3. Estimated number of malaria deaths by WHO region, 2010–2018

Numbers of malaria deaths were estimated using methods from Category 1, 2 or 3, as outlined below.

Category 1 method

A Category 1 method was used for low-transmission countries and areas outside Africa and for low-transmission countries and areas in Africa: Afghanistan, Bangladesh, Bolivia (Plurinational State of), Botswana, Cambodia, Comoros, Dominican Republic, Eritrea, Eswatini, Ethiopia, French Guiana, Guatemala, Guyana, Haiti, Honduras, India, Indonesia, Lao People's Democratic Republic, Madagascar, Myanmar, Namibia, Nepal, Nicaragua, Pakistan, Papua New Guinea, Philippines, Solomon Islands, Somalia, Sudan, Timor-Leste, Vanuatu, Venezuela (Bolivarian Republic of), Viet Nam, Yemen and Zimbabwe.

A case fatality rate of 0.256% was applied to the estimated number of *P. falciparum* cases, which represents the average of case fatality rates reported in the literature (*9–11*) and rates from unpublished data from Indonesia, 2004–2009.[1] The proportion of deaths then follows a categorical distribution of 0.01%, 0.19%, 0.30%, 0.38% and 0.40%, each one with equal probability. A case fatality rate of 0.0375% was applied to the estimated number of *P. vivax* cases, representing the midpoint of the range of case fatality rates reported in a study by Douglas et al. (*12*), following a rectangular distribution between 0.012% and 0.063%. Following the nonlinear association explained for the Category 2 method below, the proportion of deaths in children aged under 5 years was estimated as:

$$\text{Proportion of deaths}_{\text{under 5}} = -0.2288 \times \text{Mortality}_{\text{overall}}^{2} + 0.823 \times \text{Mortality}_{\text{overall}} + 0.2239$$

where the $\text{Mortality}_{\text{overall}}$ is the number of estimated deaths over the estimated population at risk per 1000 (see **Annex 3.F** for national estimates of population at risk).

Category 2 method

A Category 2 method was used for countries in Africa with a high proportion of deaths due to malaria: Angola, Benin, Burkina Faso, Burundi, Cameroon, Central African Republic, Chad, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Equatorial Guinea, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Liberia, Malawi, Mali, Mauritania, Mozambique, Niger, Nigeria, Rwanda, Senegal, Sierra Leone, South Sudan, Togo, Uganda, United Republic of Tanzania and Zambia.

In this method, child malaria deaths were estimated using a verbal autopsy multicause model that was developed by the WHO Maternal and Child Health Epidemiology Estimation Group (MCEE) to estimate causes of death in children aged 1–59 months (*13*). Mortality estimates (and 95% CI) were derived for seven causes of post-neonatal death (pneumonia, diarrhoea, malaria, meningitis, injuries, pertussis and other disorders), four causes arising in the neonatal period (prematurity, birth asphyxia and trauma, sepsis, and other conditions of the neonate), and other causes (e.g. malnutrition). Deaths due to measles, unknown causes and HIV/AIDS were estimated separately. The resulting cause-specific estimates were adjusted, country by country, to fit the estimated mortality envelope of 1–59 months (excluding HIV/AIDS and measles deaths) for corresponding years. Estimated prevalence of malaria parasites (see methods notes for **Table 2.1**) was used as a covariate within the model. It was assumed that the number of deaths follows a rectangular distribution, with limits being the estimated 95% CI. The malaria mortality rate in children aged under 5 years estimated with this method was then used to infer malaria-specific mortality in those aged over 5 years, using the relationship between levels of malaria mortality in a series of age groups and the intensity of malaria transmission (*14*), and assuming a nonlinear association between under-5-years mortality and over-5-years mortality, as follows:

[1] Dr Ric Price, Menzies School of Health Research, Australia, personal communication (November 2014).

$$\text{Proportion of deaths}_{\text{over 5}} = -0.293 \times \text{Mortality}_{\text{under 5}}^{2} + 0.8918 \times \text{Mortality}_{\text{under 5}} + 0.2896$$

where $\text{Mortality}_{\text{under 5}}$ is estimated from the number of deaths from the MCEE model over the population at risk per 1000.

Category 3 method

For the Category 3 method, the number of indigenous malaria deaths registered by the NMPs is reported without further adjustments. This category includes the following countries: Algeria, Argentina, Armenia, Azerbaijan, Belize, Bhutan, Brazil, Cabo Verde, China, Colombia, Costa Rica, Democratic People's Republic of Korea, Djibouti, Ecuador, Egypt, El Salvador, Georgia, Iran (Islamic Republic of), Iraq, Kazakhstan, Kyrgyzstan, Malaysia, Mexico, Morocco, Oman, Panama, Paraguay, Peru, Republic of Korea, Sao Tome and Principe, Saudi Arabia, South Africa, Sri Lanka, Suriname, Syrian Arab Republic, Tajikistan, Thailand, Turkey, Turkmenistan, United Arab Emirates and Uzbekistan.

Fig. 2.6. Percentage of estimated malaria deaths attributable to the 21 countries with nearly 85% of malaria deaths globally in 2018

See methods notes for **Table 2.3**.

Fig. 2.7. Comparison of current estimated malaria cases with expected cases had malaria incidence remained at 2000 levels globally

Number of malaria cases by year was estimated using methods described for **Table 2.1**. Expected malaria cases if case incidence remained the same as the year 2000 were estimated using the 2000 incidence per 1000 population to estimated population at risk each year.

Fig. 2.8. Comparison of current estimated malaria deaths with expected deaths had malaria incidence remained at 2000 levels globally

Number of malaria deaths by year was estimated using methods described for **Table 2.3**. Expected malaria deaths if mortality rate remained the same as the year 2000 were estimated using the 2000 rate per 100 000 population to estimated population at risk each year.

Fig. 2.9. Comparison of progress in malaria case incidence considering three scenarios: current trajectory maintained (blue), GTS targets achieved (green) and worst case scenario, that is a return to mean peak past incidence in the period 2000–2007 (red)

GTS target 90% reduction of malaria incidence and mortality rate by 2030 with milestones of 40% and 75% reductions in both indicator for the years 2020 and 2025 respective (*1*). A curve based on a quadratic fit is used for the malaria incidence milestones. For projection of malaria incidence under current estimated trend, the same year on year trend observed from latest years (2016–2018) is forecast up to 2030. For the regress scenario, the trend in mean peak incidence of the 'pre-intervention scale-up' years (2000–2007) is projected forward to 2030.

Fig. 3.1. Estimated prevalence of exposure to malaria infection during pregnancy overall and by subregion in 2018 in moderate to high transmission sub-Saharan Africa

Estimates of malaria-exposed pregnancies and preventable malaria-attributable low birthweight (LBW) deliveries in the absence of pregnancy-specific malaria prevention (i.e. LLIN delivery based on intermittent preventive treatment in pregnancy [IPTp] or antenatal care [ANC]) were obtained using a model of the relationship between these outcomes with slide microscopy prevalence in the general population and age- and gravidity-specific fertility patterns. This model was developed by fitting an established model of the relationship between malaria transmission and malaria infection by age (*15*) to patterns of infection in placental histology (*16*) and attributable LBW risk by gravidity in the absence of IPTp or other effective chemoprevention (*17*). The model was run across a 0.2 degree (5 km^2) longitude/latitude grid for 100 realisations of the MAP joint posterior estimated slide prevalence in 2-10 year olds in 2018 (*8*). Country-specific age-specific or gravidity-specific fertility rates, stratified by urban rural status, were obtained from demographic health surveys (DHS) and malaria indicator surveys (MIS) where such surveys had been carried out since 2014 and were available from the DHS program website (*18*). Countries where surveys were not available were allocated fertility patterns from a survey from a different country matched on the basis of total fertility rate (*19*) and geography. Fertility patterns of individual women within simulations at each grid-point were simulated according to the proportion of women estimated to be living in urban or rural locations. Urban/rural attribution at a 1 km^2 was conducted based upon WorldPop 1 km^2 2018 population estimates (*20*) and an urban/rural threshold of 386/km^2 (*21*) which were then aggregated to the 0.2 degree (5 km^2) resolution of the MAP surfaces. This provided a risk of malaria infection and malaria-attributable LBW in the absence of prevention, along with a modelled per capita pregnancy rate for each grid-point, which was aggregated to country level, using WorldPop population estimates, to provide a per pregnancy risk of malaria infection and per livebirth estimate of malaria-attributable LBW in the absence of prevention. These were then multiplied by [X data source] country-level estimates of pregnancies and [Y data source] estimates of LBW in 2018.

Table 3.1. Estimates of pregnancies, livebirths, low birthweights, exposure to malaria infection in pregnancy and malaria-attributable low birthweights in 2018 in moderate to high transmission sub-Saharan Africa

Methods for estimating malaria infection in pregnancy and malaria-attributable LBWs are described in Walker et al. (*17*). Number of pregnancies and infection rates were estimated from latest UN population estimates and total fertility rates, while the underlying *P. falciparum* parasite prevalence estimates were the updated MAP series, methods described in Bhatt et al. (2015) (*8*).

Fig. 3.2. Estimated maternal anaemia versus exposure to malaria infection in pregnancy in 2018 in moderate to high transmission countries in sub-Saharan Africa

Malaria-related maternal anaemia prevalence estimates were derived from WHO, Global Health Observatory Data Repository/World Health Statistics.[1] The estimates have not been updated since 2016 and, for the purpose of this analysis, these estimates were maintained. For the methods used to compute malaria infection during pregnancy, see methods for **Table 3.1**.

Fig. 3.3. Estimated low birthweights due to exposure to malaria infection during pregnancy overall and by subregion in 2018 in moderate to high transmission sub-Saharan Africa

Overall LBW prevalence was obtained from a United Nations Children's Fund (UNICEF)–WHO publication (*22*). These rates have not been updated since 2015 and, for the purpose of the analysis, were applied to the number of livebirths in 2018 based on UN estimates of pregnancies and livebirths. For methods on low birthweights attributable to malaria infection during pregnancy, see methods for **Table 3.2**.

Fig. 3.4. Prevalence of severe anaemia (<7 g/dL), moderate anaemia (7–9.9 g/dL) and mild anaemia (10–10.9 g/dL) in children aged under 5 years in sub-Saharan Africa, 2015–2018, by age and malaria infection status

Estimates were derived from 16 nationally representative household surveys – demographic health surveys (DHS) and malaria indicator surveys (MIS) – conducted between 2015 and 2017 in Angola, Burundi, Ghana, Kenya, Liberia, Madagascar, Malawi, Mali, Mozambique, Nigeria, Rwanda, Senegal, Sierra Leone, Togo, Uganda and United Republic of Tanzania.

The numerator is the number of children in each category: not anaemic (Hb >11 g/dL), mild anaemia (Hb 10–10.9 g/dL), moderate anaemia (Hb 7–9.9 g/dL) and severe anaemia (Hb <7 g/dL). The denominator is the number of children aged under 5 years. Please refer to the methods for **Section 8** for more details about the limitations related to the use of DHS and MIS data.

Fig. 3.5. Prevalence of severe anaemia (<7 g/dL), moderate anaemia (7–9.9 g/dL) and mild anaemia (10–10.9 g/dL) in children aged under 5 years in sub-Saharan Africa, 2015–2018, by country

See methods notes for **Fig. 3.4**.

Table 3.2. Estimated number of children aged 1–59 months infected with *P. falciparum* parasites in 2018 by subregion and overall in sub-Saharan Africa

These were estimated from geospatial models of *P. falciparum* infection prevalence by age (*8*). These models use a combination of household parasite survey data, climatic and malaria intervention covariates, and information on age-specific patterns of parasite prevalence in diverse transmission settings (*23*). Prevalence estimates were applied to age-structured UN population estimates for 38 moderate to high malaria transmission countries in sub-Saharan Africa. Data were aggregated to the WHO African Region.

Fig. 3.6. Country comparison of coverage of ANC4 and IPTp3 in moderate and high transmission sub Saharan Africa, 2018

Estimates of at least four visits to ANC (ANC4) coverage were obtained from the UNICEF data on antenatal care coverage. This data are posted on https://data.unicef.org/topic/maternal-health/antenatal-care/ and contain a measure of ANC coverage by visit from household surveys. IPTp3 coverage was estimated using methods described for **Figure 7.6**.

Fig. 4.1. HBHI: a targeted malaria response to get countries back on target for the 2025 GTS milestones

This was taken from a recent WHO publication (*24*).

Fig. 4.2a. Estimated malaria cases and deaths, 2010–2018

See methods notes for **Table 2.1** and **Table 2.3**.

Fig. 4.2b. Estimated malaria cases in India, showing seven states that contributed a combined 90% of cases, 2010 versus 2018

See methods notes for **Table 2.1**.

[1] https://apps.who.int/gho/data/node.main.1?lang=en

Fig. 4.3. Distribution and coverage of preventive interventions: (a) Number of LLINs distributed, 2016–2018, (b) Percentage of population with access to LLINs, 2018, (c) Percentage of population sleeping under an LLIN, 2018, (d) Percentage of children sleeping under an LLIN, 2018; (e) Percentage of pregnant women who received IPTp3, 2018; (f) SMC targeted children and mean treatments per cycle, 2018

See methods notes for **Fig. 6.8**, **Fig. 7.1**, **Fig. 7.2**, **Fig. 7.6** and **Fig. 7.7**, respectively.

Fig. 4.4. Diagnosis and treatment of febrile children in HBHI African countries: (a) Treatment seeking for fevers in children aged under 5 years, and source of treatment by health sector, (b) Percentage of children aged under 5 years with fever who sought treatment and were diagnosed with a parasitological test

Data obtained from household surveys such as DHS, MIS and multiple indicator cluster surveys (MICS).

Fig. 4.5. Total international and domestic direct funding for malaria in the 11 HBHI countries, (a) 2010–2018 and (b) 2016–2018

See methods notes for **Fig. 6.3**.

Table 5.1. Countries eliminating malaria since 2000

Countries are shown by the year in which they attained zero indigenous cases for 3 consecutive years, according to reports submitted by NMPs.

Fig. 5.1. Number of countries that were malaria endemic in 2000 with fewer than 10, 100, 1000 and 10 000 indigenous malaria cases between 2010 and 2018

For the 16 countries that attained zero indigenous cases for 3 consecutive years between 2000 and 2018, the number of NMP-reported indigenous cases was tabulated according to the number of years preceding the attainment of zero cases. Data from years before the peak number of cases were excluded. Thus, if a country had experienced zero cases and malaria returned, cases were only included from the year in which they peaked. This inclusion criterion generates a slope that is steeper than it would be if cases from all years were included (because some increases are excluded). In some earlier years where data on indigenous cases were not available, the total number of reported cases was used (i.e. for country–years with larger numbers of cases, in which the proportion of imported cases is expected to be low).

Fig. 5.2. Trends in indigenous malaria cases in E-2020 countries, 2010–2018

Data were derived from NMP reports.

Fig. 5.3. *P. falciparum* cases in the GMS, 2010–2018

Data were derived from NMP reports to the Greater Mekong subregion (GMS) Malaria Elimination Database (MEDB).

Fig. 5.4. Regional map of malaria incidence in the GMS by area, 2018

Data were derived from NMP reports to the GMS MEDB.

Fig. 6.1. Funding for malaria control and elimination over the period 2010–2018 (% of total funding), by source of funds (constant 2018 US$)

Total funding for malaria control and elimination over the period 2010–2018 was estimated using data obtained from several sources.

Contributions from governments of endemic countries were estimated as the sum of government contributions reported by NMPs for the world malaria report of the relevant year plus the estimated costs of patient care delivery services at public health facilities. If NMP contributions were missing for 2018, data reported from previous years were used after conversion in constant 2018 US$. The number of reported malaria cases attending public health facilities was sourced from NMP reports, adjusted for diagnosis and reporting completeness. Between 1% and 3% of uncomplicated reported malaria cases were assumed to have moved to the severe stage of disease, and 50–80% of these severe cases were assumed to have been hospitalized. Costs of outpatient visits and inpatient bed-stays were estimated from the perspective of the public health care provider, using unit cost estimates[1] from WHO-CHOosing Interventions that are Cost-Effective (WHO-CHOICE). For each country, WHO-CHOICE 2010 unit cost estimates expressed in national currency were estimated for the period 2011–2018 using the gross domestic product (GDP) annual price deflator published by the World Bank[2] on 28 August 2019 and converted in base year 2010. Country-specific unit cost estimates were then converted from national currency to constant 2018 US$ for each year during 2010–2018. For each country, the number of adjusted reported malaria cases attending public health facilities was then multiplied by the estimated unit costs. In the absence of information on the level of care at which

[1] https://www.who.int/choice/en/
[2] https://data.worldbank.org/indicator

malaria patients attend public facilities, uncertainty around unit cost estimates was handled through probabilistic uncertainty analysis. The mean total cost of patient care service delivery was calculated from 1000 estimations.

International bilateral funding data were obtained from several sources. Data on planned funding from the government of the United States of America (USA) were sourced from the US government Foreign Assistance website,[1] with the technical assistance of the Kaiser Family Foundation. Country-level planned funding data were available for the United States Agency for International Development (USAID) for the period 2010–2018. Country-specific planned funding data from other agencies, such as the US Centers for Disease Control and Prevention (CDC) and the US Department of Defense, were not available; therefore, data on total annual planned funding from each of these two agencies were used for the period 2010–2018. For the government of the United Kingdom of Great Britain and Northern Ireland (United Kingdom), funding data towards malaria control for 2017 and 2018 were sourced from the Statistics on International Development: Final UK Aid Spend 2018[2] (UK Aid Spend) with the technical assistance of the United Kingdom Department for International Development. UK Aid Spend data do not capture all spending from the United Kingdom that may impact on malaria outcomes. The United Kingdom supports malaria control and elimination through a broad range of interventions; for example, via support to overall health systems in malaria endemic countries and research and development, which are not included in these data.

For the period 2010–2016, United Kingdom spending data were sourced from the Organisation for Economic Co-operation and Development (OECD) creditor reporting system (CRS) database on aid activity.[3] For all other donors, disbursement data were also obtained from the OECD CRS database on aid activity for the period 2010–2018. For each year and each funder, the country-level and regional-level project-type interventions and other technical assistance were extracted. All data were converted to constant 2018 US$.

Malaria-related annual funding from donors through multilateral agencies was estimated from data on (i) donors' contributions published by the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund)[4] and annual disbursements by the Global Fund to malaria endemic countries between 2010 and 2018 as reported by the Global Fund; and (ii) donors' disbursements to malaria endemic countries published in the OECD CRS and in the OECD Development Assistance Committee members' total use of the multilateral system.[5] All funding flows were converted to constant 2018 US$.

For (i), the amount of funding contributed by each donor was estimated as the proportion of funding paid by each donor out of the total amount received by the Global Fund in a given year, multiplied by the total amount disbursed by the Global Fund in the same year. Equal contributions were assumed every year by each donor over the 3-year periods for which data were available.

For (ii), contributions from donors to multilateral channels were estimated by calculating the proportion of the core contributions received by a multilateral agency each year by each donor, then multiplying that amount by the multilateral agency's estimated investment in malaria control in the same year.

Contributions from malaria endemic countries to multilateral agencies were allocated to governments of endemic countries under the "funding source" category. Contributions from non-DAC countries and other sources to multilateral agencies were not available and were, therefore, not included.

Annual estimated investments were summed up to estimate the total amount each funder contributed to malaria control and elimination over the period 2010–2018, and the relative percentage of the total spending contributed by each funder calculated for the period 2010–2018.

Fig. 6.1 excludes household spending on malaria prevention and treatment in malaria endemic countries.

Fig. 6.2. Funding for malaria control and elimination 2010–2018, by source of funds (constant 2018 US$)

See methods notes for **Fig. 6.1** for sources of information on total funding for malaria control and elimination from governments of malaria endemic countries and on international funding flows. **Fig. 6.2** excludes household spending on malaria prevention and treatment in malaria endemic countries.

Fig. 6.3. Funding for malaria control and elimination 2010–2018, by channel (constant 2018 US$)

See methods notes for **Fig. 6.1** for sources of information on total funding for malaria control and elimination from governments of malaria endemic countries and on international funding flows. **Fig. 6.3** excludes household spending on malaria prevention and treatment in malaria endemic countries.

[1] https://foreignassistance.gov/
[2] https://www.gov.uk/government/statistics/statistics-on-international-development-final-uk-aid-spend-2018 (purpose code 12262)
[3] https://stats.oecd.org/Index.aspx?DataSetCode=CRS1
[4] https://www.theglobalfund.org/en/financials/
[5] https://stats.oecd.org/Index.aspx?DataSetCode=CRS1

Fig. 6.4. Funding for malaria control and elimination 2010–2018, by World Bank 2018 income group and source of funding (constant 2018 US$)

See methods notes for **Fig. 6.1** for sources of information on total funding for malaria control and elimination from governments of malaria endemic countries and on international funding flows. Data on income group classification for 2018 were sourced from the World Bank.[1] **Fig. 6.4** excludes household spending on malaria prevention and treatment in malaria endemic countries.

Fig. 6.5. Funding for malaria control and elimination 2010–2018, by WHO region (constant 2018 US$)

See methods notes for **Fig. 6.1** for sources of information on total funding for malaria control and elimination from governments of malaria endemic countries and on international funding flows. The "Unspecified" category includes all funding data for which there was no geographical information on the recipient. **Fig. 6.5** excludes household spending on malaria prevention and treatment in malaria endemic countries.

Fig. 6.6. Funding for malaria-related R&D 2010–2018, by product type (constant 2018 US$)

Data on funding for malaria-related research and development for 2010–2018 were sourced directly from Policy Cures Research as advance preview of the forthcoming 2019 G-FINDER report.[2]

Fig. 6.7. Malaria R&D funding in 2018, by sector (constant 2018 US$)

See methods notes for **Fig. 6.6**.

Fig. 6.8. Number of ITNs delivered by manufacturers and distributed by NMPs, 2010–2018

Data on the number of ITNs delivered by manufacturers to countries were provided to WHO by Milliner Global Associates. Data from NMP reports were used for the number of ITNs distributed within countries.

Fig. 6.9. Total LLINs distributed to communities by country in the period 2016–2018, in countries accounting for about 90% of global distributions by NMPs

Data on long-lasting insecticidal nets (LLINs) were derived from NMP reports.

Fig. 6.10. Number of RDTs sold by manufacturers and distributed by NMPs for use in testing suspected malaria cases, 2010–2018

The numbers of rapid diagnostic tests (RDTs) distributed by WHO region are the annual totals reported as having been distributed by NMPs. Numbers of RDT sales were reported by 41 manufacturers that participated in RDT product testing by WHO, the Foundation for Innovative New Diagnostics (FIND), the CDC, and the Special Programme for Research and Training in Tropical Diseases. The number of RDTs reported by manufacturers represents total sales to the public and private sectors worldwide.

Fig. 6.11. Number of ACT treatment courses delivered by manufacturers and distributed by NMPs to patients, 2010–2018

Data on artemisinin-based combination therapy (ACT) sales were provided by eight manufacturers eligible for procurement by WHO or UNICEF. ACT sales were categorized as being to either the public sector or the private sector. Data on ACTs distributed within countries through the public sector were taken from NMP reports.

Fig. 7.1. Percentage of population at risk with access to an ITN, and percentage of households with at least one ITN and enough ITNs for all occupants, sub-Saharan Africa, 2010–2018

Estimates of ITN coverage were derived from a model developed by MAP,[3] using a two-stage process. First, a mechanism was designed for estimating net crop (i.e. the total number of ITNs in households in a country at a given time), taking into account inputs to the system (e.g. deliveries of ITNs to a country) and outputs (e.g. loss of ITNs from households). Second, empirical modelling was used to translate estimated net crops into resulting levels of coverage (e.g. access within households, use in all ages and use among children aged under 5 years).

The model incorporates data from three sources:

- the number of ITNs delivered by manufacturers to countries, as provided to WHO by Milliner Global Associates;
- the number of ITNs distributed within countries, as reported to WHO by NMPs; and
- data from nationally representative household surveys from 39 countries in sub-Saharan Africa, from 2001 to 2018.

[1] https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups, accessed 1 October 2019
[2] https://www.policycuresresearch.org/, forthcoming
[3] https://www.map.ox.ac.uk/

Annex 1 – Data sources and methods

Countries for analysis

The main analysis covered 40 of the 47 malaria endemic countries or areas of sub-Saharan Africa. The islands of Mayotte (for which no ITN delivery or distribution data were available) and Cabo Verde (which does not distribute ITNs) were excluded, as were the low-transmission countries of Eswatini, Namibia, Sao Tome and Principe, and South Africa, for which ITNs comprise a small proportion of vector control. Analyses were limited to populations categorized by NMPs as being at risk.

Estimating national net crops through time

As described by Flaxman et al. (*25*), national ITN systems were represented using a discrete-time stock-and-flow model. Nets delivered to a country by manufacturers were modelled as first entering a "country stock" compartment (i.e. stored in-country but not yet distributed to households). Nets were then available from this stock for distribution to households by the NMP or other distribution channels. To accommodate uncertainty in net distribution, the number of nets distributed in a given year was specified as a range, with all available country stock (i.e. the maximum number of nets that could be delivered) as the upper end of the range and the NMP-reported value (i.e. the assumed minimum distribution) as the lower end. The total household net crop comprised new nets reaching households plus older nets remaining from earlier times, with the duration of net retention by households governed by a loss function. Rather than the loss function being fitted to a small external dataset, as was done by Flaxman et al. (*25*), the loss function was fitted directly to the distribution and net crop data within the stock-and-flow model itself. Loss functions were fitted on a country-by-country basis, were allowed to vary through time, and were defined separately for conventional ITNs (cITNs) and LLINs. The fitted loss functions were compared to existing assumptions about rates of net loss from households. The stock-and-flow model was fitted using Bayesian inference and Markov chain Monte Carlo methods, which provided time-series estimates of national household net crop for cITNs and LLINs in each country, and an evaluation of under-distribution, all with posterior credible intervals.

Estimating indicators of national ITN access and use from the net crop

Rates of ITN access within households depend not only on the total number of ITNs in a country (i.e. the net crop), but also on how those nets are distributed among households. One factor that is known to strongly influence the relationship between net crop and net distribution patterns among households is the size of households, which varies among countries, particularly across sub-Saharan Africa.

Many recent national surveys report the number of ITNs observed in each household surveyed. Hence, it is possible not only to estimate net crop, but also to generate a histogram that summarizes the household net ownership pattern (i.e. the proportion of households with zero nets, one net, two nets and so on). In this way, the size of the net crop was linked to distribution patterns among households while accounting for household size, in order to generate ownership distributions for each stratum of household size. The bivariate histogram of net crop to distribution of nets among households by household size made it possible to calculate the proportion of households with at least one ITN. Also, because the number of both ITNs and people in each household was available, it was possible to directly calculate two additional indicators: the proportion of households with at least one ITN for every two people, and the proportion of the population with access to an ITN within their household. For the final ITN indicator – the proportion of the population who slept under an ITN the previous night – the relationship between ITN use and access was defined using 62 surveys in which both these indicators were available (ITN $use_{all\ ages}$ = 0.8133 × ITN $access_{all\ ages}$ + 0.0026, R^2 = 0.773). This relationship was applied to the MAP's country–year estimates of household access in order to obtain ITN use among all ages. The same method was used to obtain the country–year estimates of ITN use in children aged under 5 years (ITN $use_{children\ under\ 5}$ = 0.9327 x ITN $access_{children\ under\ 5}$ + 0.0282, R^2 = 0.754).

Fig. 7.2. Percentage of population at risk, pregnant women and children aged under 5 years sleeping under an ITN, sub-Saharan Africa, 2010–2018

See methods notes for **Fig. 7.1**.

Fig. 7.3. Percentage of population at risk with access to an ITN, and percentage of households with enough ITNs for all occupants, sub-Saharan Africa, 2010–2018

See methods notes for **Fig. 7.1**.

Fig. 7.4. Percentage of the population at risk protected by IRS, by WHO region, 2010–2018

The number of persons protected by IRS was reported to WHO by NMPs. The total population of each country was taken from the 2017 revision of the *World population prospects* (*19*), and the proportion at risk of malaria was derived from NMP reports.

Fig. 7.5. Main chemical classes used for IRS by national programmes globally, 2010–2018

Data on the type of insecticide used for IRS were reported to WHO by NMPs. Insecticides were classified into pyrethroids or other classes (carbamates, organochlorines or organophosphates). If data were not reported for a particular year, data from the most recent year were used. For the period 2010–2018, this method of imputation was used for an average of 19 countries each year.

Fig. 7.6. Percentage of pregnant women attending ANC at least once and receiving IPTp, by dose, sub-Saharan Africa, 2010–2018

The total number of pregnant women eligible for intermittent preventive treatment in pregnancy (IPTp) was calculated by adding total live births calculated from UN population data and spontaneous pregnancy loss (specifically, miscarriages and stillbirths) after the first trimester. Spontaneous pregnancy loss has previously been calculated by Dellicour et al. (*26*). Country-specific estimates of IPTp coverage were calculated as the ratio of pregnant women receiving IPTp at antenatal care (ANC) clinics to the estimated number of pregnant women eligible for IPTp in a given year. ANC attendance rates were derived in the same way, using the number of initial ANC visits reported through routine information systems. Local linear interpolation or information for national representative surveys was used to compute missing values. Annual aggregate estimates exclude countries for which a report or interpolation was not available for the specific year. Among 38 countries with IPTp policy, dose coverage could be calculated for 34.

Fig. 7.7. Number of SMC treatments administered in scale-up countries in 2018

Data were provided by the Seasonal Malaria Chemoprevention (SMC) Working Group.

Diagnostic testing and treatment

The first step was to select for inclusion all nationally representative household surveys (DHS and MIS) conducted between 2015 and 2018 (and released before 4 October 2019), for which data on malaria case management were available. Sub-Saharan Africa is the region that carries the highest share of the global malaria burden, and more surveys were available from there than from other regions; hence, only surveys conducted in that region were included in the analyses. Data were only available for children aged under 5 years because DHS and MIS focus on the most vulnerable population groups. Interviewers ask caregivers whether the child has had fever in the 2 weeks preceding the interview and, if so, where care was sought; whether the child received a finger or heel stick as part of the care; what treatment was received for the fever and when; and, in particular, whether the child received an ACT or other antimalarial medicine. In addition to self-reported data, DHS and MIS also include biomarker testing for malaria, using RDTs that detect *P. falciparum* histidine-rich protein 2 (HRP2). Percentages were calculated for each country each year. Median values and interquartile ranges (IQRs) were calculated using country percentages over a 4-year period. For cross-sectional analysis over the period 2015–2018, in cases where more than one dataset were available for a country, the most recent survey was used. For trend analysis from 2010–2013 to 2015–2018, data were calculated over 4-year overlapping intervals and all surveys in all countries for all years were included.

The use of household survey data has several limitations. One issue is that, because of difficulty recalling past events, respondents may not provide reliable information, especially on episodes of fever and the identity of prescribed medicines, resulting in a misclassification of drugs. Also, because respondents can choose more than one source of care for one episode of fever, and because the diagnostic test and treatment question is asked broadly and is, therefore, not linked to any specific source of care, it has been assumed that the diagnostic test and treatment were received in all the selected sources of care. However, only a low percentage (<5%) of febrile children were brought for care in more than one source of care. Data may also be biased by the seasonality of survey data collection because DHS are carried out at various times during the year and MIS are usually timed to correspond with the high malaria transmission season. Another limitation, when undertaking trend analysis, is that DHS and MIS are done intermittently, or not at all in some countries, resulting in a relatively small number of countries for the region of sub-Saharan Africa or for any one 4-year period. Countries are also not the same across each 4-year period. In addition, depending on the sample size of the survey, the denominator for some indicators can be small – countries where the number of children in the denominator was less than 30 were excluded from the calculation.

Fig. 8.1. Median percentage of children who had a fever in the 2 weeks preceding the survey, overall and by age group, sub-Saharan Africa, 2015–2018 (latest survey)

Estimates were derived from 20 nationally representative household surveys (DHS and MIS) conducted between 2015 and 2018 in Angola, Benin, Burkina Faso, Burundi, Ethiopia, Ghana, Kenya, Liberia, Madagascar, Malawi, Mali, Mozambique, Nigeria, Rwanda, Senegal, Sierra Leone, Togo, Uganda, United Republic of Tanzania and Zimbabwe. For each age group, the numerator was the number of children who had a fever in the 2 weeks preceding the survey, and the denominator was the number of children.

Fig. 8.2. Median percentage of febrile children brought for care, by health sector, sub-Saharan Africa, 2015–2018 (latest survey)

Estimates were derived from 20 nationally representative household surveys (DHS and MIS) conducted between 2015 and 2018 in Angola, Benin, Burkina Faso, Burundi, Ethiopia, Ghana, Kenya, Liberia, Madagascar, Malawi,

Mali, Mozambique, Nigeria, Rwanda, Senegal, Sierra Leone, Togo, Uganda, United Republic of Tanzania and Zimbabwe. The numerator was the number of febrile children brought for care in each health sector, and the denominator was the number of febrile children aged under 5 years. Note that respondents could choose more than one source of care for one episode of fever. Community health worker data were based on 12 countries: Burkina Faso, Burundi, Madagascar, Malawi, Mali, Mozambique, Nigeria, Rwanda, Senegal, Togo, Uganda and Zimbabwe.

Fig. 8.3. Malaria patients examined using RDT and microscopy, and percentage of suspected cases tested in health facilities, sub-Saharan Africa, 2010–2018

Data reported by NMPs on the number of tests (RDTs and microscopy) from the public health sector were combined to calculate the number of patients examined in this sector. The number of suspected cases was computed as the number of tests plus number of presumed cases. Percentage of suspected cases who were tested was computed as percentage of number of cases examined divided by number of suspected cases.

Fig. 8.4. Percentage of suspected cases tested in health facilities, sub-Saharan Africa, 2010–2018

See methods notes for **Fig. 8.3**.

Fig. 8.5. Median percentage of febrile children who received a blood test, by health sector, sub-Saharan Africa, 2015–2018 (latest survey)

Estimates were derived from 19 nationally representative household surveys (DHS and MIS) conducted between 2015 and 2018 in Angola, Benin, Burkina Faso, Burundi, Ghana, Kenya, Liberia, Madagascar, Malawi, Mali, Mozambique, Nigeria, Rwanda, Senegal, Sierra Leone, Togo, Uganda, United Republic of Tanzania and Zimbabwe. For each health sector, the numerator was the number of febrile children who received a blood test and the denominator was the number of febrile children aged under 5 years. Community health worker data were based on seven countries: Burundi, Madagascar, Mali, Mozambique, Rwanda, Togo and Uganda.

Fig. 8.6. Trend in the median percentage of febrile children who received a blood test among those treated with an antimalarial drug, by health sector, sub-Saharan Africa, 2010–2018 (all surveys)

Estimates were derived from 61 nationally representative household surveys (DHS and MIS) conducted between 2010 and 2018 in 29 countries: Angola, Benin, Burkina Faso, Burundi, Chad, Comoros, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Gabon, Gambia, Ghana, Guinea, Kenya, Liberia, Madagascar, Malawi, Mali, Mozambique, Namibia, Niger, Nigeria, Rwanda, Senegal, Sierra Leone, Togo, Uganda, United Republic of Tanzania and Zambia. For each health sector, the numerator was the number of febrile children who received a blood test, and the denominator was the number of febrile children aged under 5 years who were treated with an antimalarial drug.

Fig. 8.7. Median percentage of febrile children who were treated with an antimalarial drug, by health sector, sub-Saharan Africa, 2015–2018 (latest survey)

Estimates were derived from 20 nationally representative household surveys (DHS and MIS) conducted between 2015 and 2017 in Angola, Benin, Burkina Faso, Burundi, Ethiopia, Ghana, Kenya, Liberia, Madagascar, Malawi, Mali, Mozambique, Nigeria, Rwanda, Senegal, Sierra Leone, Togo, Uganda, United Republic of Tanzania and Zimbabwe. For each health sector, the numerator was the number of febrile children who received an antimalarial drug, and the denominator was the number of febrile children aged under 5 years. Community health worker data were based on eight countries: Burundi, Madagascar, Mali, Mozambique, Nigeria, Rwanda, Togo and Uganda.

Fig. 8.8. Trend in the median percentage of febrile children who were treated with an antimalarial drug, by health sector, sub-Saharan Africa, 2010–2018 (all surveys)

Estimates were derived from 71 nationally representative household surveys (DHS and MIS) conducted between 2010 and 2018 in 32 countries: Angola, Benin, Burkina Faso, Burundi, Cameroon, Chad, Comoros, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Ethiopia, Gabon, Gambia, Ghana, Guinea, Kenya, Liberia, Madagascar, Malawi, Mali, Mozambique, Namibia, Niger, Nigeria, Rwanda, Senegal, Sierra Leone, Togo, Uganda, United Republic of Tanzania, Zambia and Zimbabwe. For each health sector, the numerator was the number of febrile children who received an antimalarial drug, and the denominator was the number of febrile children aged under 5 years.

Fig. 8.9. Median percentage of febrile children who received an ACT among those treated with an antimalarial drug, by health sector, sub-Saharan Africa, 2015–2018 (latest survey)

Estimates were derived from 19 nationally representative household surveys (DHS and MIS) conducted between 2015 and 2018 in Angola, Benin, Burkina Faso, Burundi, Ethiopia, Ghana, Kenya, Liberia, Madagascar, Malawi,

Mali, Mozambique, Nigeria, Rwanda, Senegal, Sierra Leone, Togo, Uganda and United Republic of Tanzania. The numerator was the number of febrile children who received an ACT, and the denominator was the number of febrile children aged under 5 years who were treated with an antimalarial drug.

Fig. 8.10. Trend in the median percentage of febrile children who received an ACT among those treated with an antimalarial drug, by health sector, sub-Saharan Africa, 2010–2018 (all surveys)

Estimates were derived from 70 nationally representative household surveys (DHS and MIS) conducted between 2010 and 2018 in 32 countries: Angola, Benin, Burkina Faso, Burundi, Cameroon, Chad, Comoros, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Ethiopia, Gabon, Gambia, Ghana, Guinea, Kenya, Liberia, Madagascar, Malawi, Mali, Mozambique, Namibia, Niger, Nigeria, Rwanda, Senegal, Sierra Leone, Togo, Uganda, United Republic of Tanzania, Zambia and Zimbabwe. The numerator was the number of febrile children who received an ACT, and the denominator was the number of febrile children aged under 5 years who were treated with an antimalarial drug.

Fig. 9.1. Status of malaria surveillance modules implemented in DHIS2, October 2019

Data on the implementation of District Health Information Software 2 (DHIS2) were obtained from communications with NMPs and WHO GMP project reports.

Fig. 9.2. Proposed structure and examples of thematic areas for national malaria data repositories

The aim of national malaria data repositories is to assemble, in a structured way with ability for dynamic update, existing malaria-related databases in a malaria endemic country. These databases will be installed centrally and sub nationally by HMIS to allow for effective intervention against malaria. This figure illustrates the structure and some of the proposed content of such a database.

Fig. 10.1. Reported insecticide resistance status as a proportion of sites for which monitoring was conducted, by WHO region, 2010–2018, (a) Pyrethroids, (b) Organochlorines, (c) Carbamates, and (d) Organophosphates

Insecticide resistance monitoring results were collated from data submissions to WHO by NMPs, the African Network for Vector Resistance, national public health institutes, universities and research centers, MAP and the US President's Malaria Initiative, and extracted from scientific publications. Only data from standard WHO tube tests or CDC bottle bioassays with discriminating concentrations of insecticides were considered. Where multiple insecticide classes or types, mosquito species or time points were tested at an individual site, the highest resistance status was considered.

Fig. 10.2. Status of monitoring of the WHO-recommended criteria for pyrethroid-PBO net deployment, 2010–2018

The status of each country was judged based on whether their monitoring sites fulfill the following criteria, namely 1) resistance to pyrethroids was confirmed in at least one key malaria vector, 2) resistance was of moderate intensity and 3) it was conferred (at least in part) by monooxygenase-based resistance mechanism. Monitoring data was reported to WHO by NMPs, the US President's Malaria Initiative and extracted from scientific publications.

References for Annex 1

1. Global technical strategy for malaria 2016–2030. Geneva: World Health Organization; 2015 (https://www.who.int/malaria/areas/global_technical_strategy/en, accessed 20 October 2019).

2. Roll Back Malaria Partnership Secretariat. Action and investment to defeat malaria 2016–2030. For a malaria-free world. Geneva: World Health Organization; 2015 (https://endmalaria.org/sites/default/files/RBM_AIM_Report_0.pdf, accessed 20 October 2019).

3. Malaria and the UN Sustainable Development Goals (SDGs) 2030. Swiss Tropical and Public Health Institute (TPH) Swiss TPH for the Swiss Malaria Group; 2018 (https://www.swissmalariagroup.ch/fr/assets/uploads/files/New%20factsheet%20Malaria%20and%20the%20UN%20Sustainable%20Development%20Goals%20x.pdf, accessed 20 October 2019).

4. Informal Member States Consultation GPW 13 WHO Impact Framework. Geneva: World Health Organization; 2019.

5. World malaria report 2008. Geneva: World Health Organization; 2008 (https://www.who.int/malaria/publications/atoz/9789241563697/en, accessed 15 October 2013).

6. Cibulskis RE, Aregawi M, Williams R, Otten M, Dye C. Worldwide incidence of malaria in 2009: estimates, time trends, and a critique of methods. PLoS Med. 2011;8(12):e1001142.

7. The R Core Team. R: A language and environment for statistical computing: reference index. Vienna, Austria: R Foundation for Statistical Computing.

8. Bhatt S, Weiss DJ, Cameron E, Bisanzio D, Mappin B, Dalrymple U et al. The effect of malaria control on *Plasmodium falciparum* in Africa between 2000 and 2015. Nature. 2015;526(7572):207–11.

9. Alles HK, Mendis KN, Carter R. Malaria mortality rates in South Asia and in Africa: implications for malaria control. Parasitol Today. 1998;14(9):369–75.

10. Luxemburger C, Ricci F, Nosten F, Raimond D, Bathet S, White NJ. The epidemiology of severe malaria in an area of low transmission in Thailand. Trans R Soc Trop Med Hyg. 1997;91(3):256–62.

11. Meek SR. Epidemiology of malaria in displaced Khmers on the Thai-Kampuchean border. SE Asian J Trop Med. 1988;19(2):243–52.

12. Douglas NM, Pontororing GJ, Lampah DA, Yeo TW, Kenangalem E, Poespoprodjo JR et al. Mortality attributable to *Plasmodium vivax* malaria: a clinical audit from Papua, Indonesia. BMC Medicine. 2014;12(1):217.

13. Liu L, Oza S, Hogan D, Perin J, Rudan I, Lawn JE et al. Global, regional, and national causes of child mortality in 2000–13, with projections to inform post-2015 priorities: an updated systematic analysis. Lancet. 2015;385(9966):430–40.

14. Ross A, Maire N, Molineaux L, Smith T. An epidemiologic model of severe morbidity and mortality caused by *Plasmodium falciparum*. Am J Trop Med Hyg. 2006;75(2 Suppl):63–73.

15. Griffin QJ, Ferguson NM, Ghani AC. Estimates of the changing age-burden of *Plasmodium falciparum* malaria disease in sub-Saharan Africa. Nat Commun. 2014;5:3136.

16. Walker PGT, Griffin JT, Cairns M, Rogerson SJ, van Eijk AM, Ter Kuile F, Ghani AC. A model of parity-dependent immunity to placental malaria. Nat Commun. 2013;4:1609.

17. Walker PGT, Ter Kuile FO, Garske T, Menendez C, Ghani AC. Estimated risk of placental infection and low birthweight attributable to *Plasmodium falciparum* malaria in Africa in 2010: a modelling study. Lancet Glob Health. 2014;2(8):e460–e7.

18. The DHS Program: Demographic and Health Surveys [website]. (httpp://dhsprogram.com/, accessed 22 October 2019).

19. World population prospects [website]. United Nations; 2017 (https://population.un.org/wpp/, accessed 24 October 2018).

20. WorldPop [website]. (https://www.worldpop.org/, accessed 22 October 2019).

21. Cairns M, Roca-Felter A, Garske T, Wilson AL, Diallo D, Milligan PJ et al. Estimating the potential public health impact of seasonal malaria chemoprevention in African children. Nat Commun. 2012;3:881.

22. UNICEF-WHO. Low birthweight estimates: levels and trends 2000–2015. Geneva: World Health Organization; 2015 (https://www.who.int/nutrition/publications/UNICEF-WHO-lowbirthweight-estimates-2019/en/, accessed 22 October 2019).

23. Cameron E, Battle KE, Bhatt S, Weiss DJ, Bisanzio D, Mappin B et al. Defining the relationship between infection prevalence and clinical incidence of *Plasmodium falciparum* malaria. Nat Commun. 2015;6:8170.

24. High burden to high impact: a targeted malaria response. Geneva: World Health Organization; 2019 (https://www.who.int/malaria/publications/atoz/high-impact-response/en/, accessed 22 October 2019).

25. Flaxman AD, Fullman N, Otten MW, Menon M, Cibulskis RE, Ng M et al. Rapid scaling up of insecticide-treated bed net coverage in Africa and its relationship with development assistance for health: a systematic synthesis of supply, distribution, and household survey data. PLoS Med. 2010;7(8):e1000328.

26. Dellicour S, Tatem AJ, Guerra CA, Snow RW, ter Kuile FO. Quantifying the number of pregnancies at risk of malaria in 2007: a demographic study. PLoS Med. 2010;7(1):e1000221.

Annex 2 - A. WHO African Region, a. West Africa

EPIDEMIOLOGY

Population at risk: 381 million

Parasites: *P. falciparum* (almost 100%)

Vectors: *An. arabiensis, An. coluzzi, An. funestus s.l., An. gambiae s.l., An. hispaniola, An. labranchiae, An. melas, An. moucheti, An. multicolor, An. nili s.l., An. pharoensis* and *An. sergentii s.l.*

FUNDING (US$), 2010–2018

547.6 million (2010), 558.9 million (2015), 675.6 million (2017); increase 2010–2018: 23%

Proportion of domestic source* in 2018: 9%

Regional funding mechanisms: Senegal River Basin Development Organization (OMVS): Guinea, Mali, Mauritania and Senegal

* Domestic source excludes patient service delivery costs and out-of-pocket expenditure.

INTERVENTIONS, 2018

Countries with ≥80% coverage with either LLIN or IRS in 2018: Côte d'Ivoire and Togo

Countries with ≥50% coverage with either LLIN or IRS in 2018: Benin, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Senegal and Sierra Leone

Countries implemented IPTp in 2018: Benin, Burkina Faso, Côte d'Ivoire, Gambia, Ghana, Guinea, Guinea-Bissau, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone and Togo

Countries with >30% IPTp3+ in 2018: Burkina Faso, Côte d'Ivoire, Gambia, Ghana, Guinea, Guinea-Bissau, Mali, Niger, Senegal, Sierra Leone and Togo

Percentage of suspected cases tested (reported): 44% (2010), 71% (2015), 81% (2018)

Number of ACT courses distributed: 32.2 million (2010), 47.4 million (2015), 75.8 million (2018)

Number of any antimalarial treatment courses (incl. ACT) distributed: 32.2 million (2010), 49.3 million (2015), 75.8 million (2018)

REPORTED CASES AND DEATHS IN PUBLIC SECTOR, 2010–2018

Total (presumed and confirmed) cases: 29.4 million (2010), 52.3 million (2015), 61.1 million (2018)

Confirmed cases: 7.1 million (2010), 33.3 million (2015), 46.5 million (2018)

Percentage of total cases confirmed: 24.3% (2010), 63.6% (2015), 76.2% (2018)

Deaths*: 39 000 (2010), 21 600 (2015), 19 600 (2018)

* No data reported for Nigeria

Children aged under 5 years, presumed and confirmed cases: 11.9 million (2010), 21.0 million (2015), 24.6 million (2018)

Children aged under 5 years, percentage of total cases: 40.6% (2010), 40.2% (2015), 40.2% (2018)

Children aged under 5 years, deaths: 214 100 (2010), 22 100 (2015), 27 700 (2018)

ESTIMATED CASES AND DEATHS, 2010–2018

Cases: 118.9 million (2010), 107.6 million (2015), 111.1 million (2018); decrease 2010–2018: 7%

Deaths: 304 000 (2010), 220 000 (2015), 194 000 (2018); decrease 2010–2018: 36%

ACCELERATION TO ELIMINATION

Countries with nationwide elimination programme: Cabo Verde

Zero indigenous cases for 3 consecutive years (2016, 2017 and 2018): Algeria

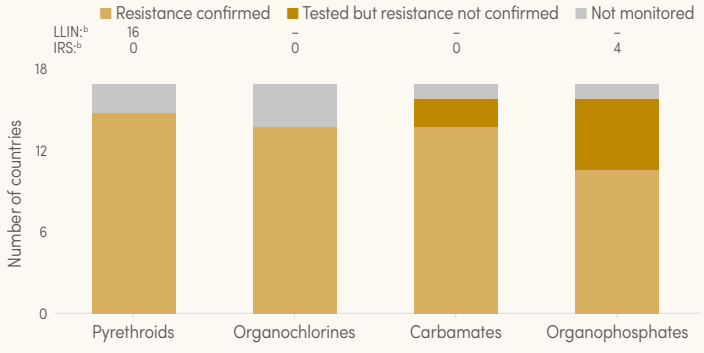
Certified as malaria free since 2010: Algeria (2019)

THERAPEUTIC EFFICACY TESTS (CLINICAL AND PARASITOLOGICAL FAILURE, %)

Medicine	Study years	No. of studies	Min.	Median	Max.	Percentile 25	Percentile 75
AL	2010–2017	69	0.0	0.0	11.9	0.0	2.6
AS-AQ	2010–2017	59	0.0	0.0	6.6	0.0	1.7
AS-PY	2011–2014	6	0.0	0.5	0.6	0.0	0.6
DHA-PPQ	2010–2016	12	0.0	0.0	1.9	0.0	0.2

AL: artemether-lumefantrine; AS-AQ: artesunate-amodiaquine; AS-PY: artesunate-pyronaridine; DHA-PPQ: dihydroartemisinin-piperaquine.

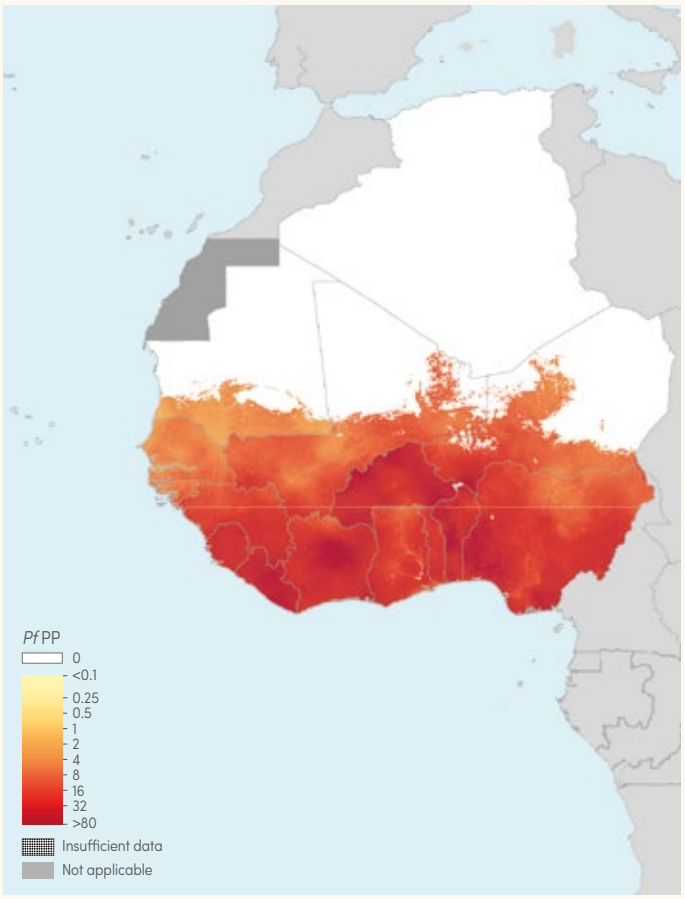
STATUS OF INSECTICIDE RESISTANCE[a] PER INSECTICIDE CLASS (2010–2018) AND USE OF EACH CLASS FOR MALARIA VECTOR CONTROL (2018)



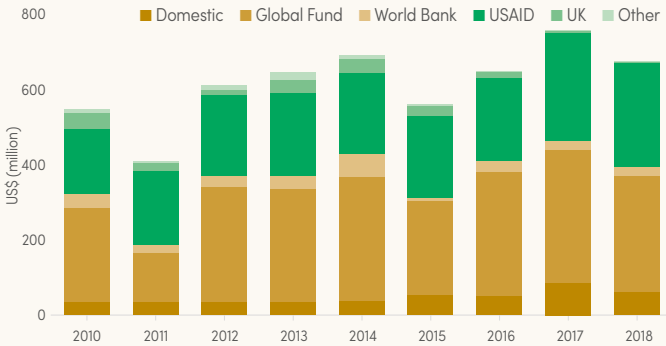
[a] Resistance is considered confirmed when it was detected to one insecticide in the class, in at least one malaria vector from one collection site.

[b] Number of countries that reported using the insecticide class for malaria vector control (2018).

A. *P. falciparum* parasite prevalence (*Pf* PP), 2018



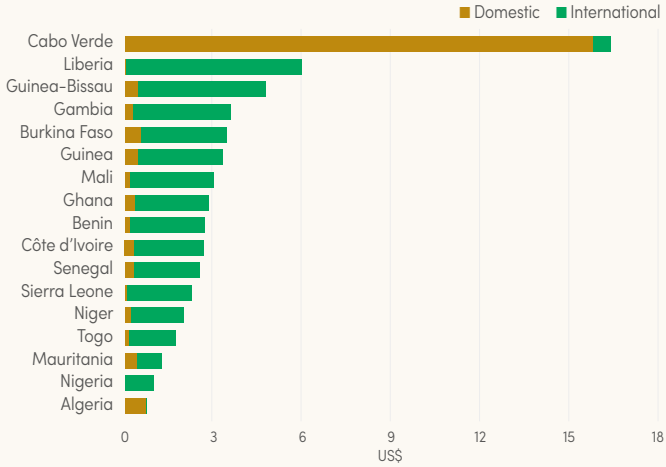
B. Malaria funding* by source, 2010–2018



Global Fund: Global Fund to Fight AIDS, Tuberculosis and Malaria; UK: United Kingdom of Great Britain and Northern Ireland; USAID: United States Agency for International Development.

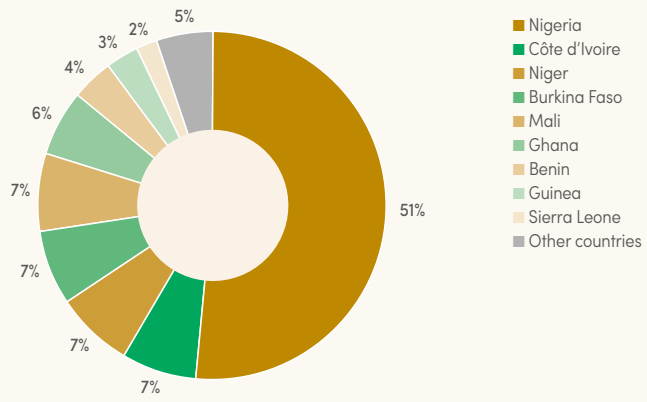
* Excludes patient service delivery costs and out-of-pocket expenditure.

C. Malaria funding* per person at risk, average 2016–2018



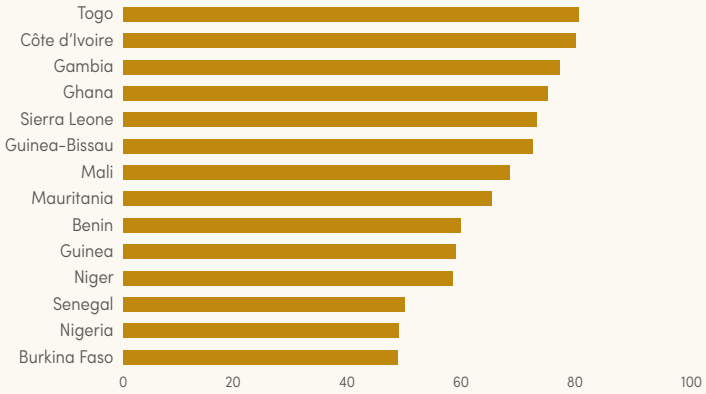
* Excludes costs related to health staff, costs at subnational level and out-of-pocket expenditure.

D. Share of estimated malaria cases, 2018



E. Percentage of population with access to either LLINs or IRS, 2018

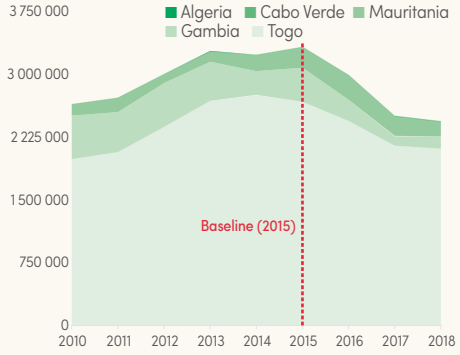
Source: ITN coverage model from MAP



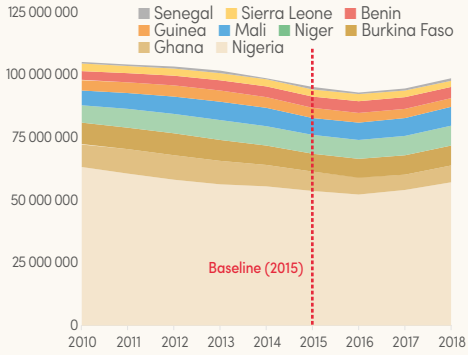
* Cabo Verde is an E-2020 country, vectol control targeted at foci.

IRS: indoor residual spraying; ITN: insecticide-treated mosquito net; LLIN: long-lasting insecticidal net; MAP: Malaria Atlas Project.

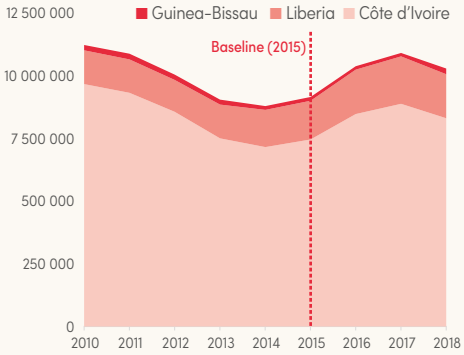
F. Countries on track to reduce case incidence by ≥40% by 2020



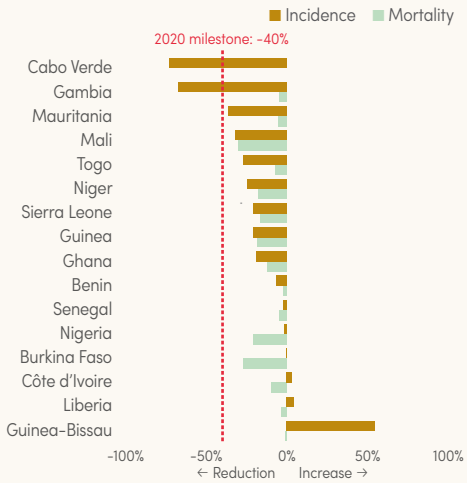
G. Countries likely to reduce case incidence by <40% by 2020



H. Countries with an increase in case incidence, 2015–2018



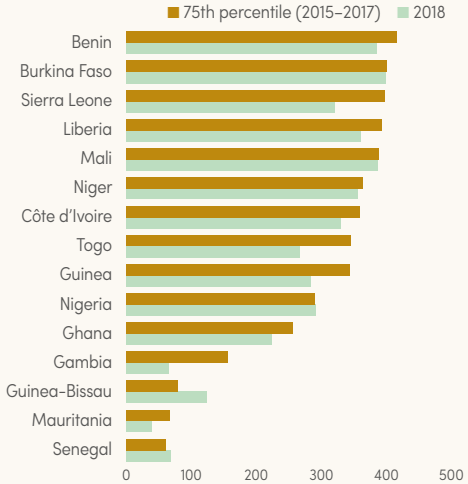
I. Change in estimated malaria incidence and mortality rates, 2015–2018



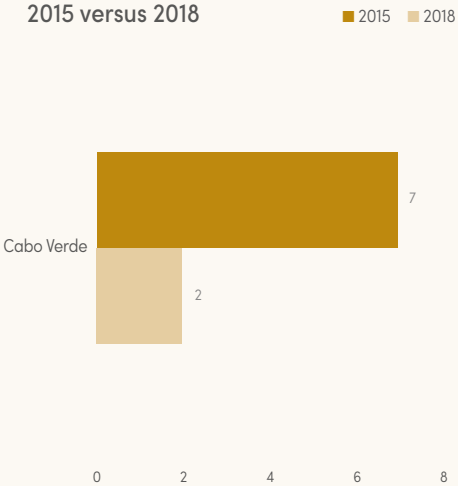
* Cabo Verde already achieved the 40% reduction in mortality rate in 2015; since then there has been no change.

** Zero cases and deaths in Algeria since 2015.

J. Incidence in 2018 compared to baseline (2015–2017)



K. Reported indigenous cases in countries with national elimination activities, 2015 versus 2018



* Zero cases and deaths in Algeria since 2015.

KEY MESSAGES

- About 381 million people living in the 17 countries of West Africa are at high risk. Algeria was certified malaria free in May 2019, following 3 consecutive years with zero indigenous cases. In the rest of the countries in the subregion, malaria transmission is year-round and almost exclusively due to *P. falciparum* in most of the countries, with strong seasonality in the Sahelian countries.
- The subregion had more than 111 million estimated cases and about 194 000 estimated deaths, representing a 7% and 36% decrease compared with 2010, respectively. Six countries accounted for over 80% of the estimated cases: Nigeria (51%), Côte d'Ivoire (7%), Burkina Faso (7%), Mali and Niger (each 7%) and Ghana (6%). In the public health sector, about 61 million cases were reported, of which 40.2% were in children aged under 5 years and 46.5 million (76.2%) were confirmed. The proportion of total cases that were confirmed improved substantially over time, from only 24.3% in 2010. A total of 27 700 malaria deaths were reported in children aged under 5 years; this figure exceeded the total malaria deaths, indicating that there are challenges in the surveillance of malaria mortality in some countries.
- In 12 of the 15 countries in which routine distribution of LLINs or use of IRS is still applicable, at least 50% of the population had access to these interventions. Seven countries are on track to meet the GTS target by reducing case incidence by at least 40% by 2020 compared with 2015: Algeria (already certified malaria free), Cabo Verde, Gambia, Mali, Mauritania, Niger and Togo. Nine countries showed progress towards meeting the target but need efforts to be accelerated to achieve the 40% reduction: Benin, Burkina Faso, Ghana, Guinea, Mali, Niger, Nigeria, Senegal and Sierra Leone. Despite Senegal's progress in malaria reduction in recent years, the country saw an increase in 2017 and 2018. In Côte d'Ivoire, Guinea-Bissau and Liberia, incidence increased in 2018 compared with 2015. Following a large increase in indigenous cases in Cabo Verde between 2016 and 2017, the country reported only two indigenous cases in 2018, similar to 2015. In addition to Algeria and Cabo Verde, only Burkina Faso and Mali are on track to reduce malaria mortality rates by at least 40%.
- In line with the Nouakchott Declaration and the Sahel Malaria Elimination Initiative (SaME), eight ministers of the Sahelian countries (Burkina Faso, Cabo Verde, Chad, Gambia, Mali, Mauritania, Niger and Senegal) committed on 31 August 2018 to accelerate implementation, with the aim of eliminating malaria by 2030. In addition to Cabo Verde as an eliminating country, Gambia, Mauritania, Niger and Senegal are reorienting their programmes towards malaria subnational elimination.
- Vector resistance to pyrethroids was confirmed in most of the countries, and resistance to organochlorines and carbamates was confirmed in more than half of the countries. Guinea-Bissau has not reported standard resistance monitoring to any of the four insecticide classes.
- Challenges include inadequate political commitment and leadership, weak malaria programme management, insufficient prioritization and sustainability of interventions, inappropriate application of larviciding, inadequate domestic financing and weak surveillance systems, including a lack of well-functioning vital registration systems.

Annex 2 - A. WHO African Region, b. Central Africa

EPIDEMIOLOGY

Population at risk: 180 million

Parasites: *P. falciparum* (100%)

Vectors: *An. arabiensis, An. funestus s.l., An. gambiae s.l., An. melas, An. moucheti, An. nili s.l.* and *An. pharoensis.*

FUNDING (US$), 2010–2018

246.2 million (2010), 370.0 million (2015), 318.7 million (2018); increase 2010–2018: 29%

Proportion of domestic source* in 2018: 20%

Regional funding mechanisms: none

* Domestic source excludes patient service delivery costs and out-of-pocket expenditure.

INTERVENTIONS, 2018

Countries with ≥80% coverage with either LLIN or IRS in 2018: Burundi and Sao Tome and Principe

Countries with ≥50% coverage with either LLIN or IRS in 2018: Cameroon, Central African Republic, Chad and Democratic Republic of the Congo

Countries implemented IPTp in 2018: Angola, Burundi, Cameroon, Central African Republic, Chad, Congo, Democratic Republic of the Congo, Equatorial Guinea and Gabon

Countries with >30% IPTp3+ in 2018: Burundi, Cameroon, Central African Republic, Chad and Democratic Republic of the Congo

Percentage of suspected cases tested (reported): 41% (2010), 92% (2015), 92% (2018)

Number of ACT courses distributed: 18.2 million (2010), 22.4 million (2015), 26.8 million (2018)

Number of any antimalarial treatment courses (incl. ACT) distributed: 19.0 million (2010), 22.4 million (2015), 26.9 million (2018)

REPORTED CASES AND DEATHS IN PUBLIC SECTOR, 2010–2018

Total (presumed and confirmed) cases: 20.4 million (2010), 24.6 million (2015), 35.1 million (2018)

Confirmed cases: 6.6 million (2010), 22.2 million (2015), 30.9 million (2018)

Percentage of total cases confirmed: 32.6% (2010), 90.1% (2015), 88.2% (2018)

Deaths: 40 400 (2010), 58 200 (2015), 39 500 (2018)

Children aged under 5 years, presumed and confirmed cases: 9.1 million (2010), 11.3 million (2015), 16.3 million (2018)

Children aged under 5 years, percentage of total cases: 44.9% (2010), 46.1% (2015), 46.4% (2018)

Children aged under 5 years, deaths: 26 000 (2010), 37 100 (2015), 25 100 (2018)

ESTIMATED CASES AND DEATHS, 2010–2018

Cases: 46.0 million (2010), 42.8 million (2015), 49.2 million (2018); increase 2010–2018: 7%

Deaths: 118 400 (2010), 92 000 (2015), 89 900 (2018); decrease 2010–2018: 24%

ACCELERATION TO ELIMINATION

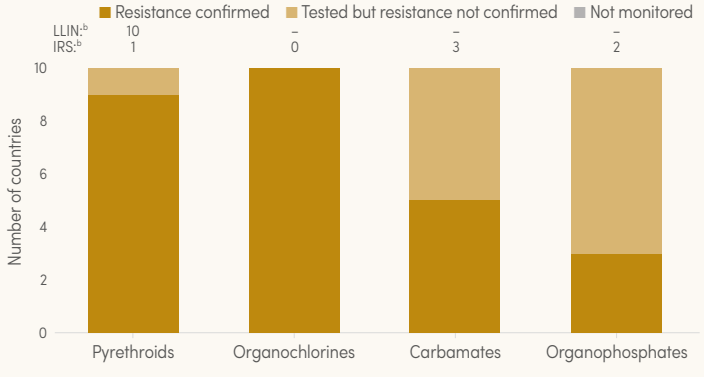
Countries with subnational/territorial elimination programme: Sao Tome and Principe

THERAPEUTIC EFFICACY TESTS (CLINICAL AND PARASITOLOGICAL FAILURE, %)

Medicine	Study years	No. of studies	Min.	Median	Max.	Percentile 25	Percentile 75
AL	2010–2018	27	0.0	2.1	13.6	0.0	3.6
AS-AQ	2010–2018	28	0.0	1.4	7.7	0.0	3.9

AL: artemether-lumefantrine; AS-AQ: artesunate-amodiaquine.

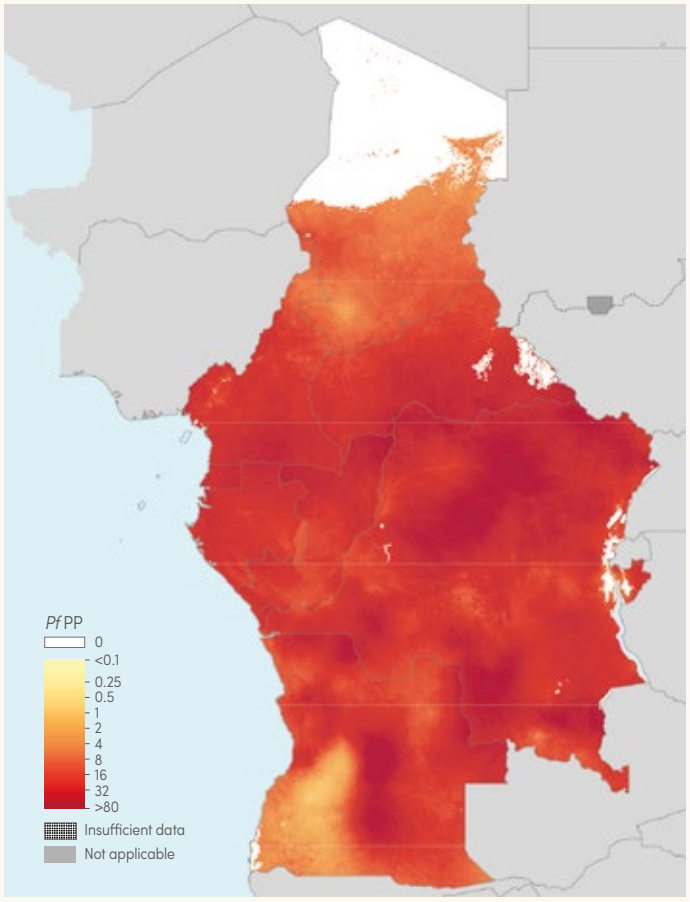
STATUS OF INSECTICIDE RESISTANCE[a] PER INSECTICIDE CLASS (2010–2018) AND USE OF EACH CLASS FOR MALARIA VECTOR CONTROL (2018)



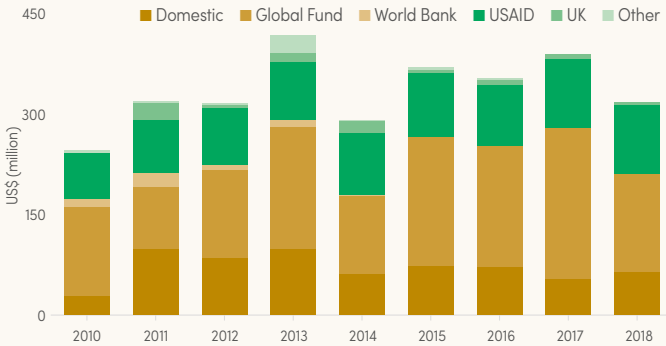
[a] Resistance is considered confirmed when it was detected to one insecticide in the class, in at least one malaria vector from one collection site.

[b] Number of countries that reported using the insecticide class for malaria vector control (2018).

A. *P. falciparum* parasite prevalence (*Pf* PP), 2018



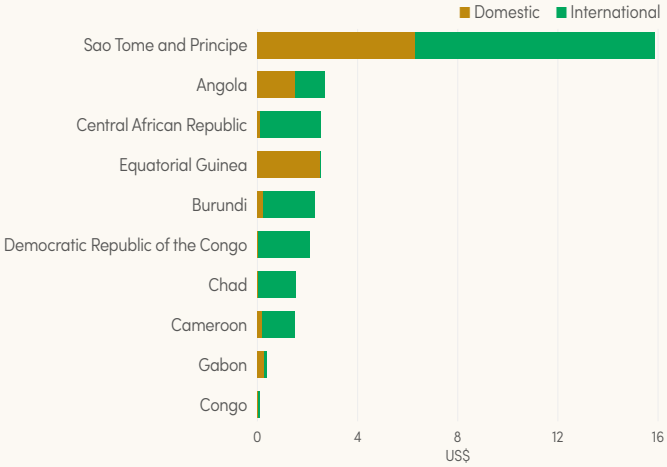
B. Malaria funding* by source, 2010–2018



Global Fund: Global Fund to Fight AIDS, Tuberculosis and Malaria; UK: United Kingdom of Great Britain and Northern Ireland; USAID: United States Agency for International Development.

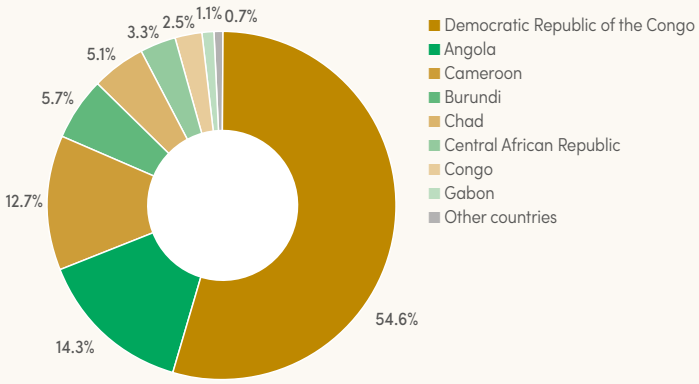
* Excludes patient service delivery costs and out-of-pocket expenditure.

C. Malaria funding* per person at risk, average 2016–2018



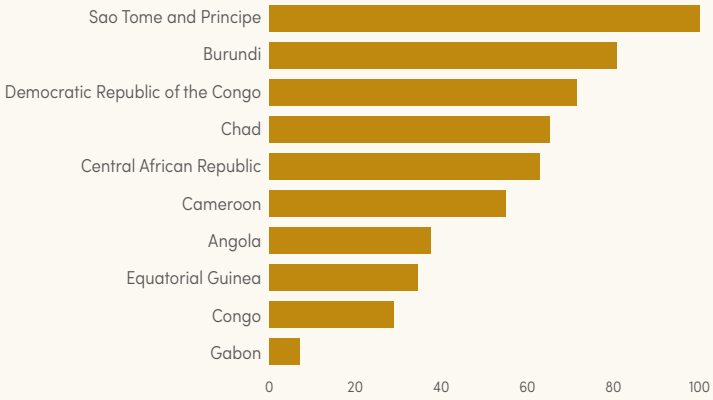
* Excludes costs related to health staff, costs at subnational level and out-of-pocket expenditure.

D. Share of estimated malaria cases, 2018



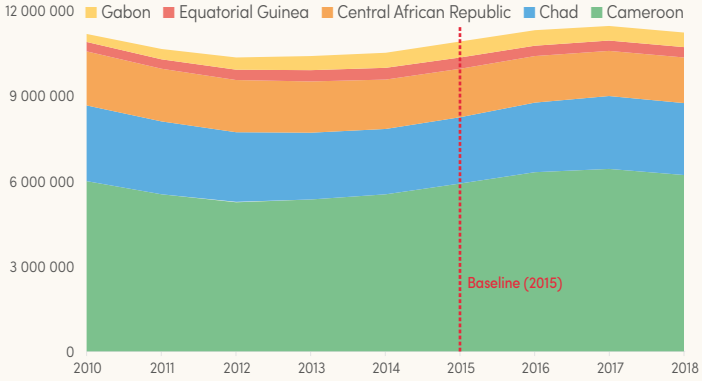
E. Percentage of population with access to either LLINs or IRS, 2018

Source: ITN coverage model from MAP

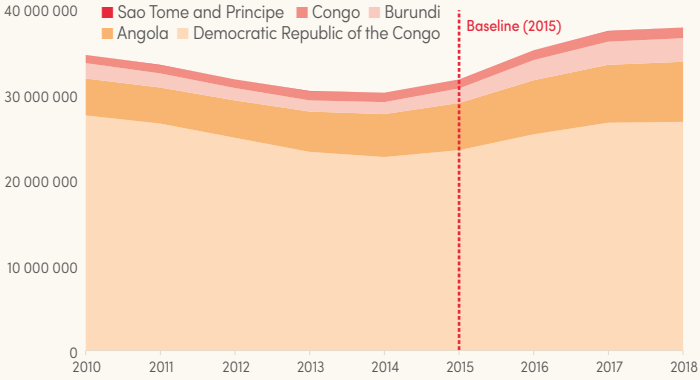


IRS: indoor residual spraying; ITN: insecticide-treated mosquito net; LLIN: long-lasting insecticidal net; MAP: Malaria Atlas Project.

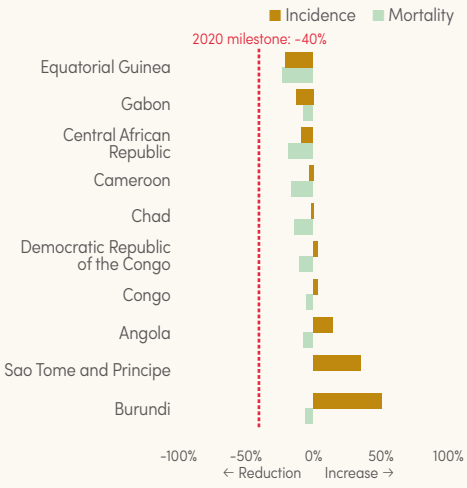
F. Countries likely to reduce case incidence by <40% by 2020



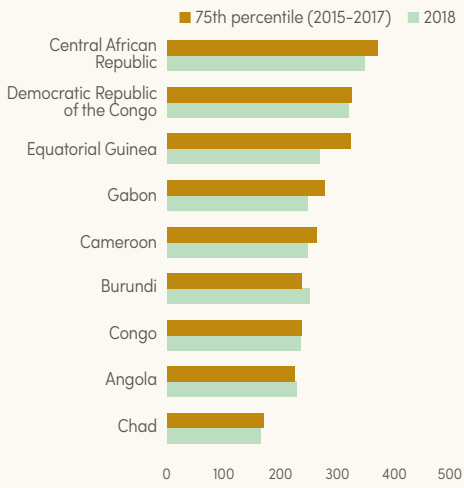
G. Countries with an increase in case incidence, 2015–2018



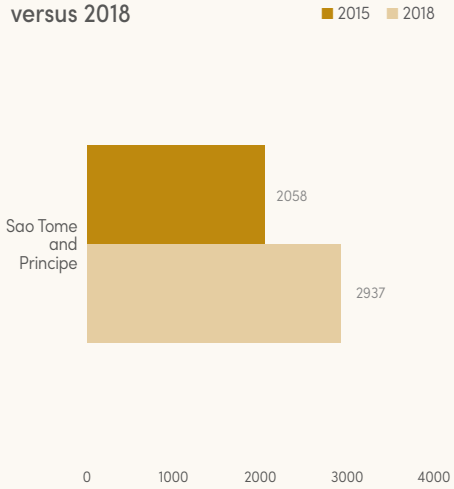
H. Change in estimated malaria incidence and mortality rates, 2015–2018



I. Incidence in 2018 compared to baseline (2015–2017)



J. Reported indigenous cases in countries with national elimination activities, 2015 versus 2018



* Sao Tome and Principe already achieved the 40% reduction in mortality rate in 2015; since then there has been no change.

KEY MESSAGES

- About 180 million people living in the 10 countries of Central Africa are at high risk. Malaria transmission, almost exclusively due to *P. falciparum*, occurs throughout the year, except in Burundi, the highlands of eastern Cameroon, northern Chad and Congo.
- In 2018, the subregion had about 49 million estimated cases and almost 90 000 estimated deaths, representing a 7% increase and a 24% decrease compared with 2010, respectively. The Democratic Republic of the Congo accounted for 55% of estimated cases, followed by Angola (14%), Cameroon (13%), Burundi (6%) and Chad (5%). In the public health sector, about 35 million cases were reported, of which 46% were in children aged under 5 years and 30.9 million (87.7%) were confirmed. The proportion of total cases that were confirmed improved substantially over time from only 32.6% in 2010. There were 39 500 reported malaria deaths, of which 63% were in children aged under 5 years.
- Progress has been made towards achieving the GTS target of a 40% reduction in incidence by 2020 in Cameroon, Central African Republic, Chad, Equatorial Guinea and Gabon, but greater efforts are needed to ensure that these countries meet the target. Five countries saw an increase in cases between 2015 and 2018, with Burundi having the largest increase (51%). Although Sao Tome and Principe also saw a slight increase in reported cases, zero deaths were reported in 2018. In Cameroon, Central African Republic, Chad and the Democratic Republic of the Congo, 50% of the population had access to LLINs or IRS. Burundi and Sao Tome and Principe had more than 80% coverage, which is indicative of a rapid and efficient response to the increasing cases in the countries. In 2018, Angola, Central African Republic, Equatorial Guinea and Sao Tome and Principe conducted LLIN mass campaigns.
- Vector resistance to organochlorines was confirmed in all countries, and to pyrethroids in all countries except Sao Tome and Principe. All countries had standardized monitoring of carbamates and organophosphates, for which resistance is still lower.
- Challenges include weak health systems, insufficient domestic and international funding, and frequent malaria outbreaks. Equatorial Guinea and Gabon are no longer eligible for support from the Global Fund but domestic investments have increased to bridge the funding gap.

Annex 2 - A. WHO African Region, c. Countries with high transmission in East and Southern Africa

EPIDEMIOLOGY

Population at risk: 351 million

Parasites: *P. falciparum* (76%) and *P. vivax* (24%)

Vectors: *An. arabiensis, An. funestus s.l., An. gambiae s.l., An. gambiae s.s., An. leesoni, An. nili, An. pharoensis, An. rivulorum, An. stephesi s.l.** and *An. vaneedeni.*

* A potential vector identified.

FUNDING (US$), 2010–2018

745.6 million (2010), 721.1 million (2015), 698.1 million (2018); decrease 2010–2018: 6%

Proportion of domestic source* in 2018: 11%

Regional funding mechanisms: none

* Domestic source excludes patient service delivery costs and out-of-pocket expenditure.

INTERVENTIONS, 2018

Countries with ≥80% coverage with either LLIN or IRS in 2018: Uganda

Countries with ≥50% coverage with either LLIN or IRS in 2018: Kenya, Malawi, Mozambique, Rwanda, South Sudan, United Republic of Tanzania and Zambia

Countries implemented IPTp in 2018: Kenya, Madagascar, Malawi, Mozambique, South Sudan, Uganda, United Republic of Tanzania, Zambia and Zimbabwe

Countries with >30% IPTp3+ in 2018: Mozambique, United Republic of Tanzania, Zambia and Zimbabwe

Percentage of suspected cases tested (reported): 30% (2010), 80% (2015), 89% (2018)

Number of ACT courses distributed: 84.5 million (2010), 108.2 million (2015), 108.3 million (2018)

Number of any antimalarial treatment courses (incl. ACT) distributed: 84.7 million (2010), 109.9 million (2015), 108.8 million (2018)

REPORTED CASES AND DEATHS IN PUBLIC SECTOR, 2010–2018

Total (presumed and confirmed) cases: 53.2 million (2010), 54.3 million (2015), 56.7 million (2018)

Confirmed cases: 19.9 million (2010), 40.2 million (2015), 47.6 million (2018)

Percentage of total cases confirmed: 37.5% (2010), 74.1% (2015), 83.9% (2018)

Deaths: 70 700 (2010), 38 300 (2015), 14 000 (2018)

Children aged under 5 years, presumed and confirmed cases: 21.6 million (2010), 17.6 million (2015), 11.0 million (2018)

Percentage of total cases under 5: 40.5% (2010), 32.5% (2015), 19.4% (2018)

Children aged under 5 years, deaths: 25 300 (2010), 10 400 (2015), 6500 (2018)

ESTIMATED CASES AND DEATHS, 2010–2018

Cases*: 53.5 million (2010), 48.7 million (2015), 52.2 million (2018); decrease 2010–2018: 2%

Deaths: 12 400 (2010), 5350 (2015), 6500 (2018); decrease 2010–2018: 48%

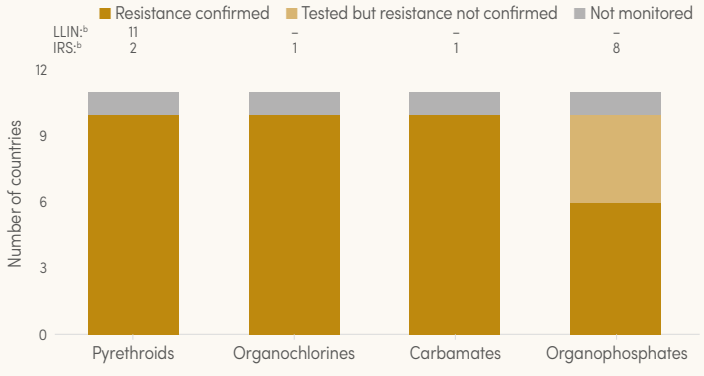
* Estimated cases are derived from the *Pf/Pr*-to-incidence model, which means that estimated cases are lower than reported by the country.

THERAPEUTIC EFFICACY TESTS (CLINICAL AND PARASITOLOGICAL FAILURE, %)

Medicine	Study years	No. of studies	Min.	Median	Max.	Percentile 25	Percentile 75
AL	2010–2016	68	0.0	1.8	19.5	0.0	3.6
AS-AQ	2011–2016	14	0.0	0.0	2.0	0.0	1.2

AL: artemether-lumefantrine; AS-AQ: artesunate-amodiaquine.

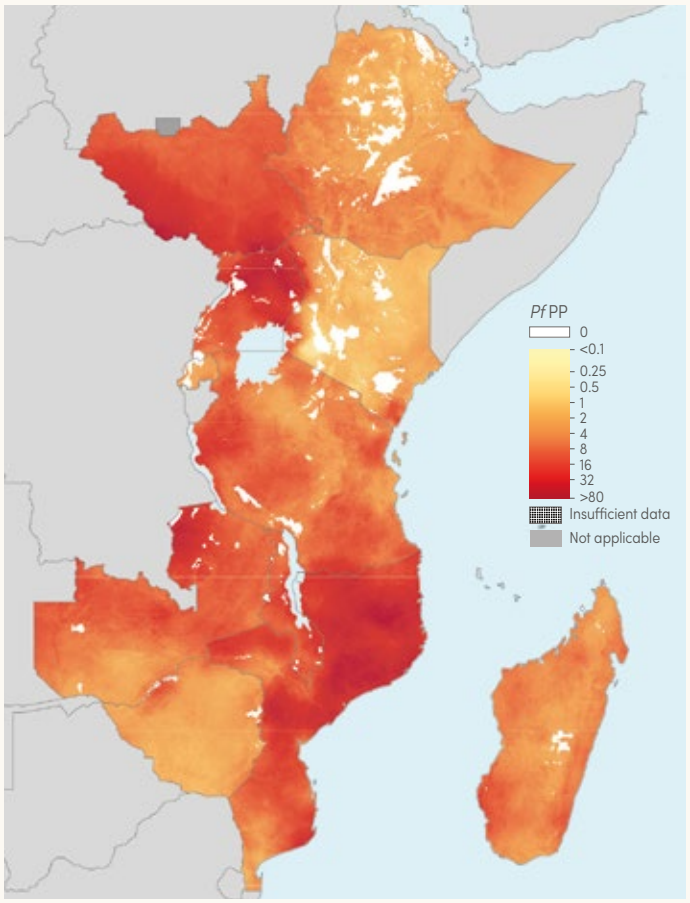
STATUS OF INSECTICIDE RESISTANCE[a] PER INSECTICIDE CLASS (2010–2018) AND USE OF EACH CLASS FOR MALARIA VECTOR CONTROL (2018)



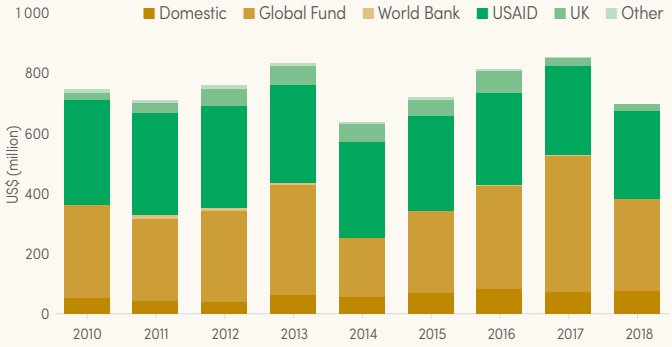
[a] Resistance is considered confirmed when it was detected to one insecticide in the class, in at least one malaria vector from one collection site.

[b] Number of countries that reported using the insecticide class for malaria vector control (2018).

A. *P. falciparum* parasite prevalence (*Pf* PP), 2018



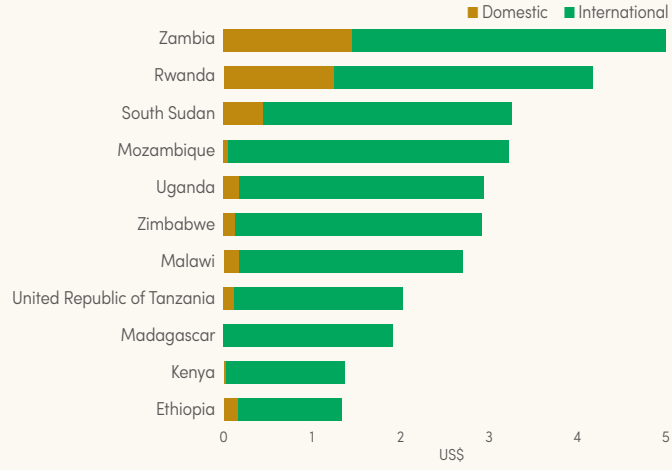
B. Malaria funding* by source, 2010–2018



Global Fund: Global Fund to Fight AIDS, Tuberculosis and Malaria; UK: United Kingdom of Great Britain and Northern Ireland; USAID: United States Agency for International Development.

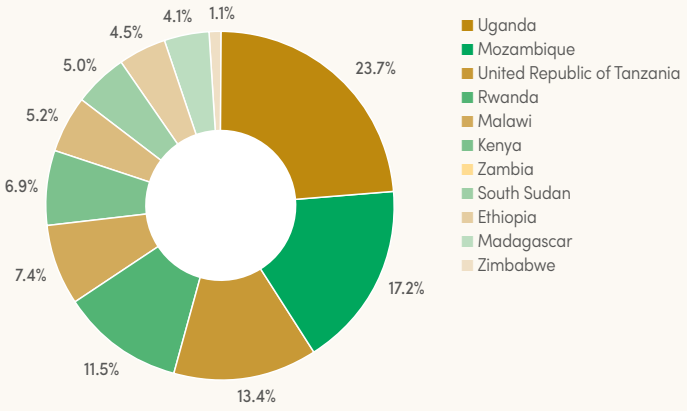
* Excludes patient service delivery costs and out-of-pocket expenditure.

C. Malaria funding* per person at risk, average 2016–2018



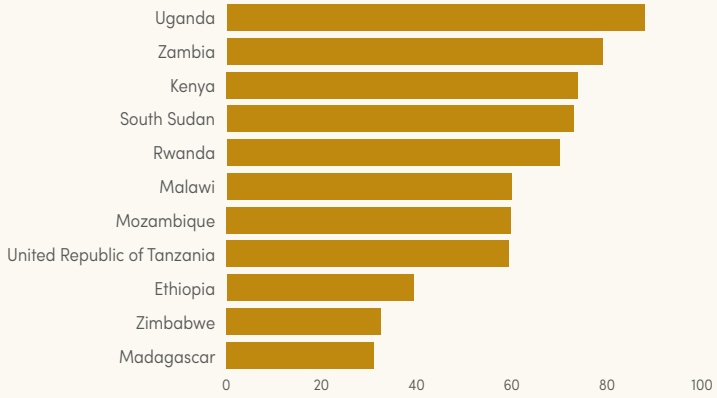
* Excludes costs related to health staff, costs at subnational level and out-of-pocket expenditure.

D. Share of estimated malaria cases, 2018



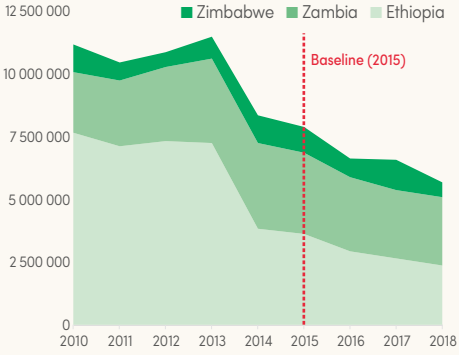
E. Percentage of population with access to either LLINs or IRS, 2018

Source: ITN coverage model from MAP

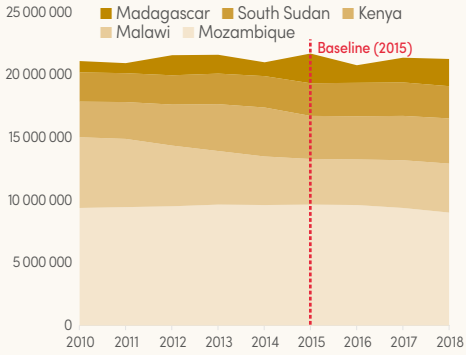


IRS: indoor residual spraying; ITN: insecticide-treated mosquito net; LLIN: long-lasting insecticidal net; MAP: Malaria Atlas Project.

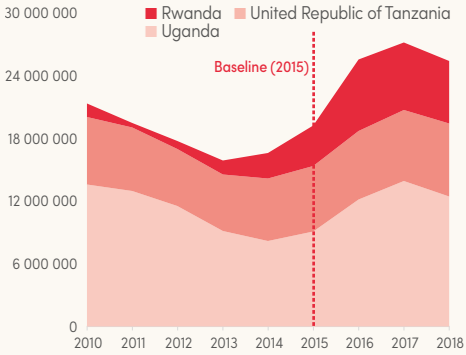
F. Countries on track to reduce case incidence by ≥40% by 2020



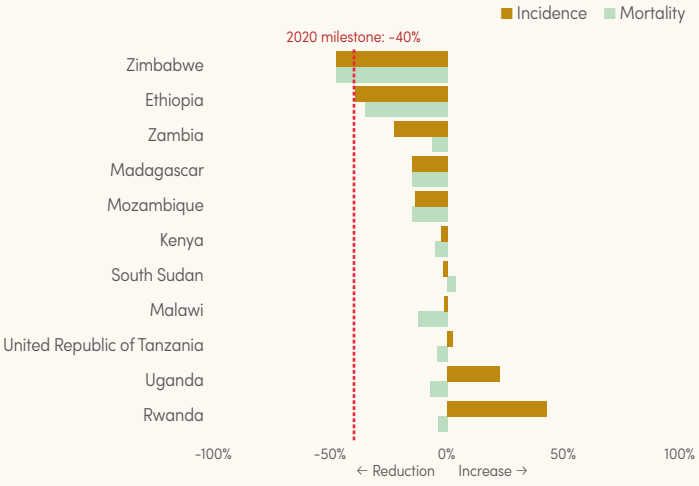
G. Countries likely to reduce case incidence by <40% by 2020



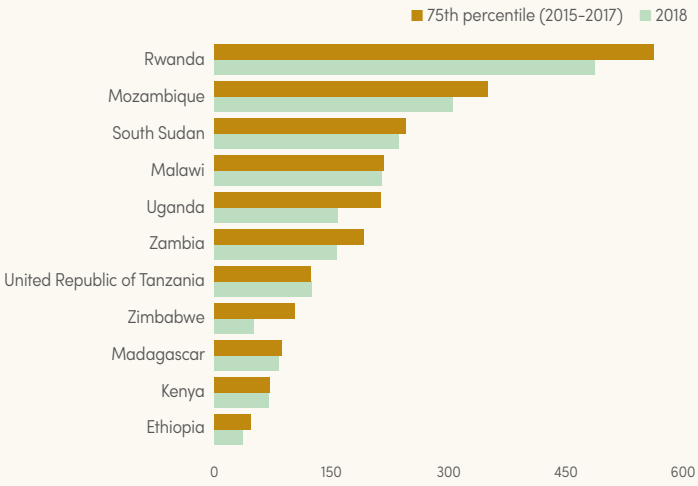
H. Countries with an increase in case incidence, 2015–2018



I. Change in estimated malaria incidence and mortality rates, 2015–2018



J. Incidence in 2018 compared to 75th percentile of 2015–2017



KEY MESSAGES

- About 351 million people in the 11 countries of East and Southern Africa are at high risk. Malaria transmission is almost exclusively due to *P. falciparum* (except in Ethiopia), and is highly seasonal in Ethiopia, Madagascar and Zimbabwe, and in coastal and highland areas of Kenya. Malaria transmission is stable in most of Malawi, Mozambique, South Sudan, Uganda, the United Republic of Tanzania and Zambia.
- The subregion had 52 million estimated cases and about 6500 estimated deaths, representing a 2% and 48% decrease compared with 2010, respectively. Three countries accounted for over 60% of the estimated cases: Uganda (24%), Mozambique (17%) and the United Republic of Tanzania (13%). In the public health sector more than 55 million cases were reported, of which 19.4% were in children aged under 5 years and 47 million (83.9%) were confirmed. The proportion of total cases that were confirmed improved substantially over time, from only 37.5% in 2010. A significantly lower number of malaria deaths were reported in 2018 (14 000) compared with 2010 (70 700) and 2015 (38 300).
- Ethiopia, Rwanda, Zambia and Zimbabwe are all on track for a 40% reduction in incidence by 2020; all other countries either reported small reductions in incidence, or increases (Rwanda, Uganda and the United Republic of Tanzania). Only Ethiopia and Zambia are on track to reduce malaria mortality rates by at least 40%. In more than half of the countries, 50% or more of the population had access to LLINs or IRS in 2018, and Uganda had coverage of more than 80%.
- Reported cases in Rwanda increased from 2.5 million in 2015 to 4.2 million in 2018, an increase of 68%. Madagascar and Mozambique also reported increases of 30% and 20%, respectively, during the period 2015–2018. Causes of such increases can include inadequate vector control; climatic factors and improved reporting. Uganda saw a 51% decrease in 2018 compared with 2017, which may be as a result of a successful rapid public health response to the almost 25% increase in cases that was reported between 2016 and 2017. Zanzibar (United Republic of Tanzania) also reported a 54% decrease in cases (from 3349 to 1532) between 2017 and 2018.
- Vector resistance to pyrethroids, organochlorines and carbamates was confirmed in all countries except South Sudan, which did not report resistance monitoring. Resistance to organophosphates was confirmed in half of the countries.
- Challenges include frequent epidemics, emergencies and inadequate response (South Sudan), inadequate funding and weak surveillance systems in a number of the countries.

Annex 2 - A. WHO African Region, d. Countries with low transmission in East and Southern Africa

EPIDEMIOLOGY

Population at risk: 14 million

Parasites: *P. falciparum* (98%) and *P. vivax* (2%)

Vectors: *An. arabiensis, An. funestus s.l., An. funestus s.s., An. gambiae s.l.* and *An. gambiae s.s.*

FUNDING (US$), 2010–2018

67.7 million (2010), 25.5 million (2015), 42.3 million (2018); decrease 2010–2018: 37%

Proportion of domestic source in 2018: 75%

Regional funding mechanisms: Southern Africa Malaria Elimination Eight Initiative

* Domestic source excludes patient service delivery costs and out-of-pocket expenditure.

INTERVENTIONS, 2018

Countries with ≥80% coverage of at-risk population with either LLIN or IRS in 2018: None

Countries with ≥80% coverage of high risk population with either LLIN or IRS in 2018: Botswana

Countries with >30% IPTp3+ in 2018: Comoros

Percentage of suspected cases tested (reported): 79% (2010), 98% (2015), 99% (2018)

Number of ACT courses distributed: 575 000 (2010), 366 000 (2015), 357 000 (2018)

Number of any antimalarial treatment courses (incl. ACT) distributed: 575 000 (2010), 366 000 (2015), 391 000 (2018)

REPORTED CASES AND DEATHS IN PUBLIC SECTOR, 2010–2018

Total (presumed and confirmed) cases: 205 300 (2010), 47 800 (2015), 99 800 (2018)

Confirmed cases: 82 400 (2010), 33 900 (2015), 79 500 (2018)

Percentage of total cases confirmed: 40.2% (2010), 70.8% (2015), 79.7% (2018)

Deaths: 242 (2010), 178 (2015), 175 (2018)

Children aged under 5 years, presumed and confirmed cases: 56 400 (2010), 7300 (2015), 11 500 (2018)

Children aged under 5 years, percentage of total cases: 27.5% (2010), 15.2% (2015), 11.5% (2018)

Children aged under 5 years, deaths: 37 (2010), 16 (2015), 33 (2018)

ESTIMATED CASES AND DEATHS, 2010–2018

Cases: 133 200 (2010), 87 300 (2015), 177 900 (2018); increase 2010–2018: 34%

Deaths: 344 (2010), 293 (2015), 438 (2018); increase 2010–2018: 27%

ACCELERATION TO ELIMINATION

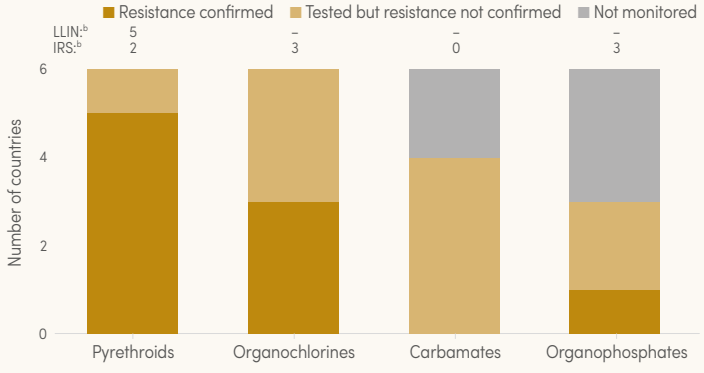
Countries with nationwide elimination programme: Botswana, Comoros, Eswatini, Namibia and South Africa

THERAPEUTIC EFFICACY TESTS (CLINICAL AND PARASITOLOGICAL FAILURE, %)

Medicine	Study years	No. of studies	Min.	Median	Max.	Percentile 25	Percentile 75
AL	2011–2017	18	0.0	0.0	2.5	0.0	0.0
AS-AQ	2010–2016	18	0.0	2.4	7.9	0.0	5.2

AL: artemether-lumefantrine; AS-AQ: artesunate-amodiaquine.

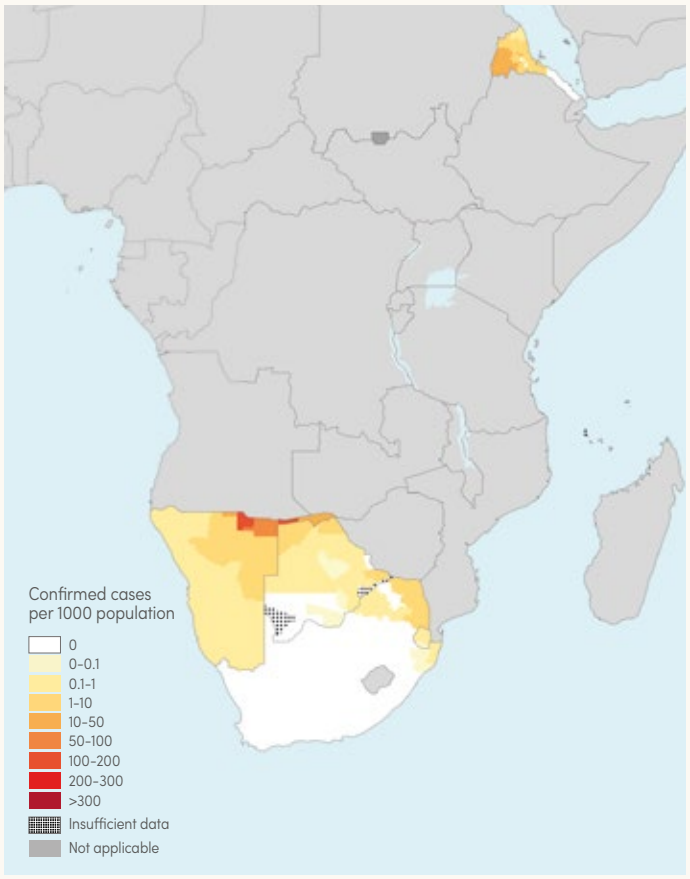
STATUS OF INSECTICIDE RESISTANCE[a] PER INSECTICIDE CLASS (2010–2018) AND USE OF EACH CLASS FOR MALARIA VECTOR CONTROL (2018)



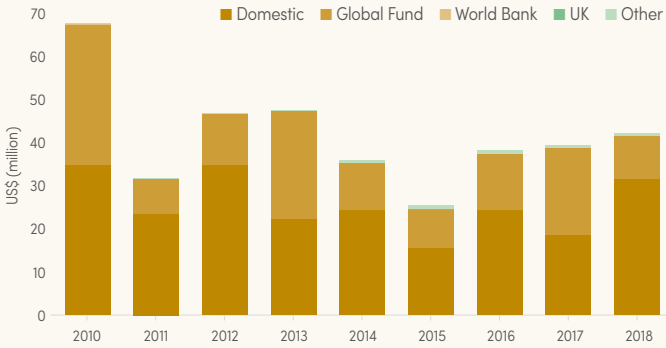
[a] Resistance is considered confirmed when it was detected to one insecticide in the class, in at least one malaria vector from one collection site.

[b] Number of countries that reported using the insecticide class for malaria vector control (2018).

A. Confirmed malaria cases per 1000 population, 2018



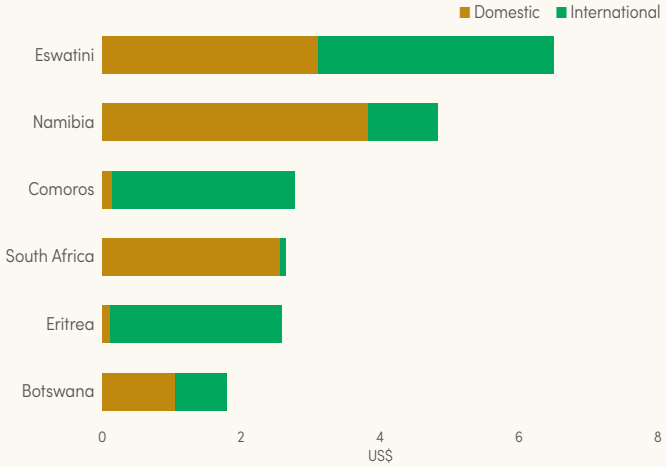
B. Malaria funding* by source, 2010–2018



Global Fund: Global Fund to Fight AIDS, Tuberculosis and Malaria; UK: United Kingdom of Great Britain and Northern Ireland.

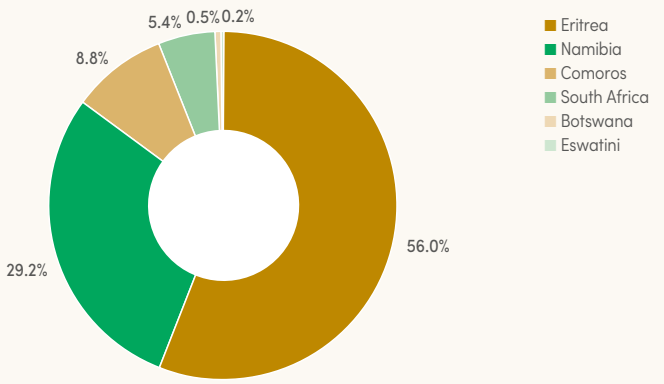
* Excludes patient service delivery costs and out-of-pocket expenditure.

C. Malaria funding* per person at risk, average 2016–2018



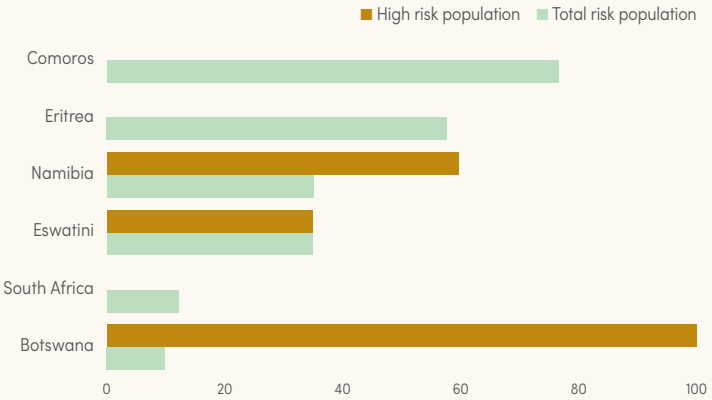
* Excludes costs related to health staff, costs at subnational level and out-of-pocket expenditure.

D. Share of estimated malaria cases, 2018



E. Percentage of population with access to either LLINs or IRS, 2018

Source: ITN coverage model from MAP



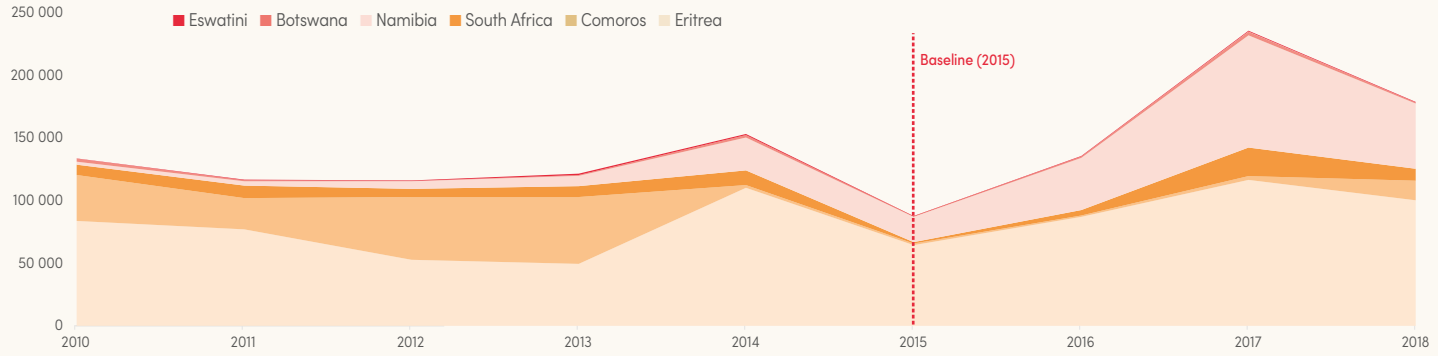
IRS: indoor residual spraying; ITN: insecticide-treated mosquito net; LLIN: long-lasting insecticidal net; MAP: Malaria Atlas Project.

* Comoros and Eritrea have ITN coverage estimated by a model from MAP.

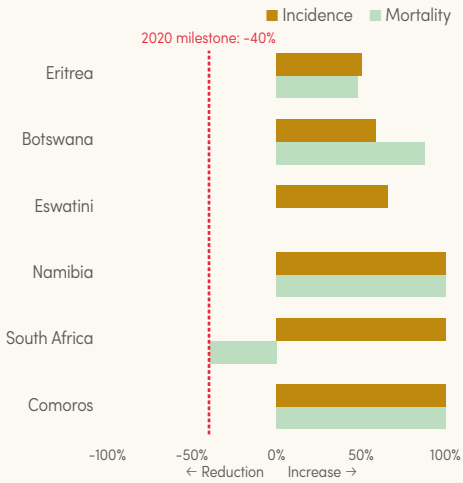
** Namibia and South Africa LLIN and IRS coverage is combined because there is no overlap in the areas where they are used.

*** South Africa has no data for high risk population.

F. Countries with an increase in case incidence, 2015–2018

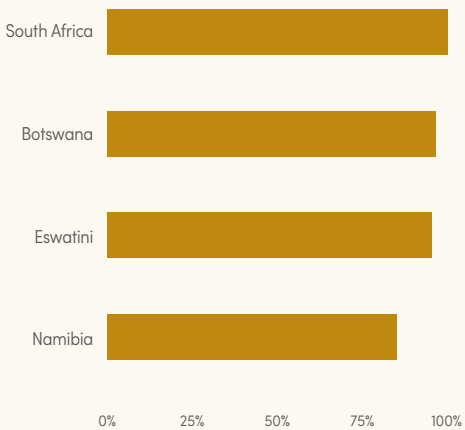


G. Change in estimated malaria incidence and mortality rates, 2015–2018

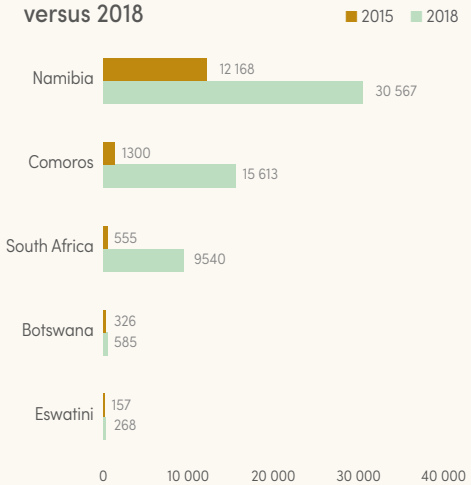


* Eswatini already achieved the 40% reduction in mortality rate in 2015; since then there has been no change

H. Percentage of total confirmed cases investigated, 2018



I. Reported indigenous cases in countries with national elimination activities, 2015 versus 2018



KEY MESSAGES

- About 14 million people in the six countries with low transmission in East and Southern Africa are at high risk of malaria. Malaria transmission is focal, highly seasonal and almost exclusively due to *P. falciparum* (except in Eritrea).
- The subregion had nearly 178 000 estimated malaria cases and about 440 estimated deaths, representing a 34% and 27% increase compared with 2010, respectively. The four frontline countries of the Elimination-8 (E8) initiative in Southern Africa (Botswana, Eswatini, Namibia and South Africa) accounted for almost 50% of cases and Eritrea accounted for almost 40%. In the public health sector almost 103 000 cases were reported, of which 11% were in children aged under 5 years and 79 500 (79.7%) were confirmed. The proportion of total cases that were confirmed improved substantially over time from only 40.2% in 2010.
- Despite previous decreases in case incidence between 2010 and 2015, all of the countries had an increase between 2015 and 2018, which means that currently none are on track to achieve the GTS target of at least a 40% reduction in incidence by 2020. Estimated cases in Namibia increased significantly, from only 2590 cases in 2010 to 89 155 in 2017, and only declined moderately (to 51 898) in 2018. South Africa is the only country on track for reducing the mortality rate by 40%. The proportion of cases investigated was high in all countries except Namibia, possibly because of a lack of resources as a result of the recent resurgence in cases.
- During 2016 and 2017 alone, the number of reported cases in South Africa increased more than fivefold (4323 to 22 061), but decreased to 9540 cases in 2018 (a reduction of 57%). Botswana and Eswatini also saw reductions in reported cases between 2017 and 2018, by 69% and 62%, respectively. Comoros, however, saw a huge increase of reported cases from 2274 in 2017 to 15 613 in 2018; an increase of 587%. There are multiple reasons for the increase in cases: improved diagnosis and reporting, inadequate vector control and climatic factors.
- Vector resistance to pyrethroids was confirmed in more than half of the countries. There are significant gaps in standard resistance monitoring for carbamates and organophosphates.
- Challenges include inadequate coverage of vector control, importation of cases from neighbouring countries and resurgence during the past 3 years.

Annex 2 - B. WHO Region of the Americas

EPIDEMIOLOGY

Population at risk: 138 million

Parasites: *P. vivax* (79.5%), *P. falciparum* and mixed (20.5%), and other (<1%)

Vectors: *An. albimanus, An. albitarsis, An. aquasalis, An. argyritarsis, An. braziliensis, An. cruzii, An. darlingi, An. neivai, An. nuneztovari, An. pseudopunctipennis* and *An. punctimacula.*

FUNDING (US$), 2010–2018

218.5 million (2010), 195.6 million (2015), 168.0 million (2018); decrease 2010–2018: 23%

Proportion of domestic source* in 2018: 84%

Regional funding mechanisms: Regional Malaria Elimination Initiative

* Domestic source excludes patient service delivery costs and out-of-pocket expenditure.

INTERVENTIONS, 2018

Number of people protected by IRS: 2.78 million (2010), 2.81 million (2015), 1.72 million (2018)

Total LLINs distributed: 363 000 (2010), 875 000 (2015), 957 000 (2018)

Number of RDTs distributed: 83 700 (2010), 534 000 (2015), 899 000 (2018)

Number of ACT courses distributed: 148 400 (2010), 209 400 (2015), 220 900 (2018)

Number of any first-line antimalarial treatment courses (incl. ACT) distributed: 1.25 million (2010), 669 000 (2015), 1.26 million (2018)

REPORTED CASES AND DEATHS IN PUBLIC SECTOR*, 2010–2018

Total (presumed and confirmed) cases: 677 100 (2010), 434 000 (2015), 753 700 (2018)

Confirmed cases: 677 100 (2010), 434 000 (2015), 753 700 (2018)

Percentage of total cases confirmed: 100% (2010), 100% (2015), 100% (2018)

Deaths: 190 (2010), 98 (2015), 338 (2018)

* In Belize, Brazil, Colombia, Costa Rica, Ecuador, Haiti, Suriname and Venezuela (Bolivarian Republic of), cases from the private sector and/or community are included in 2018.

ESTIMATED CASES AND DEATHS, 2010–2018

Cases: 814 000 (2010), 566 000 (2015), 929 000 (2018); increase 2010–2018: 14%

Deaths: 460 (2010), 320 (2015), 580 (2018); increase 2010–2018: 26%

ACCELERATION TO ELIMINATION

Countries with nationwide elimination programme: Argentina, Belize, Costa Rica, Ecuador, El Salvador, Mexico and Suriname

Zero indigenous cases for 3 consecutive years (2016, 2017 and 2018): Argentina

Zero indigenous cases in 2018: Argentina and El Salvador

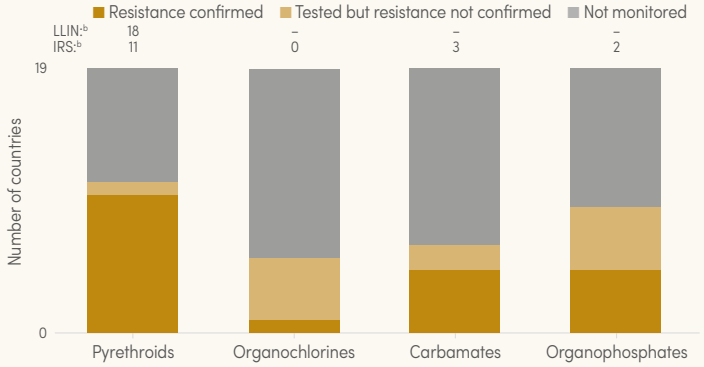
Certified as malaria free since 2010: Argentina (2019) and Paraguay (2018)

THERAPEUTIC EFFICACY TESTS (CLINICAL AND PARASITOLOGICAL FAILURE, %)

Medicine	Study years	No. of studies	Min.	Median	Max.	Percentile 25	Percentile 75
AL	2011–2016	5	0.0	0.0	9.0	0.0	4.5
AS-MQ	2010–2017	6	0.0	0.0	0.0	0.0	0.0

AL: artemether-lumefantrine; AS-MQ: artesunate-mefloquine.

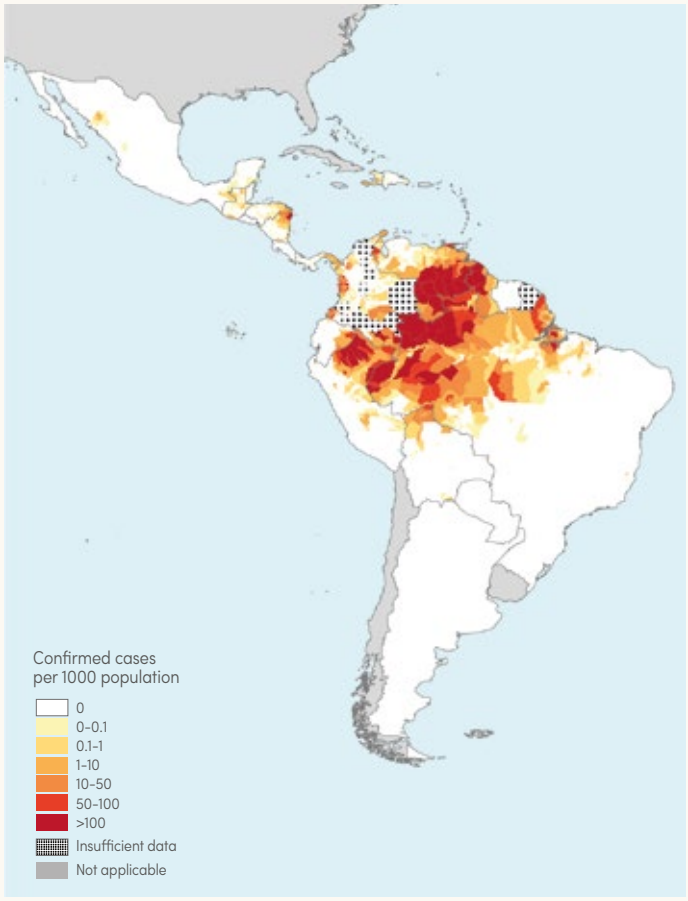
STATUS OF INSECTICIDE RESISTANCE[a] PER INSECTICIDE CLASS (2010–2018) AND USE OF EACH CLASS FOR MALARIA VECTOR CONTROL (2018)



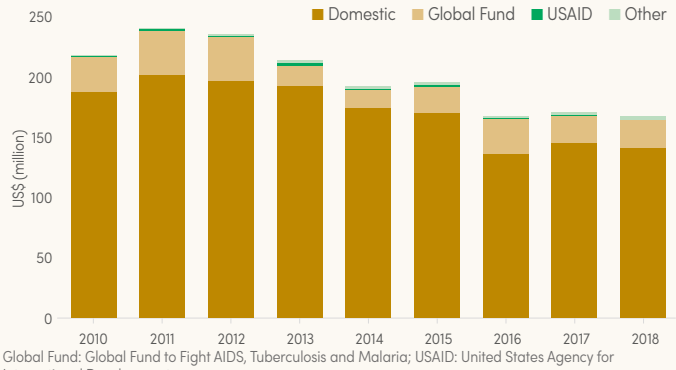
[a] Resistance is considered confirmed when it was detected to one insecticide in the class, in at least one malaria vector from one collection site.

[b] Number of countries that reported using the insecticide class for malaria vector control (2018).

A. Confirmed malaria cases per 1000 population, 2018



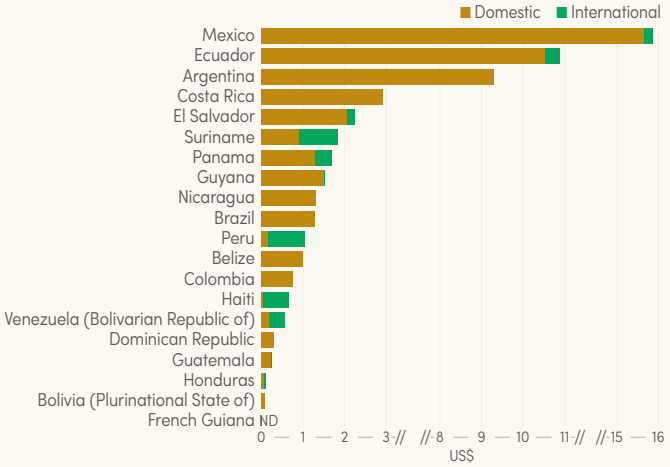
B. Malaria funding* by source, 2010–2018



Global Fund: Global Fund to Fight AIDS, Tuberculosis and Malaria; USAID: United States Agency for International Development.

* Excludes patient service delivery costs and out-of-pocket expenditure.

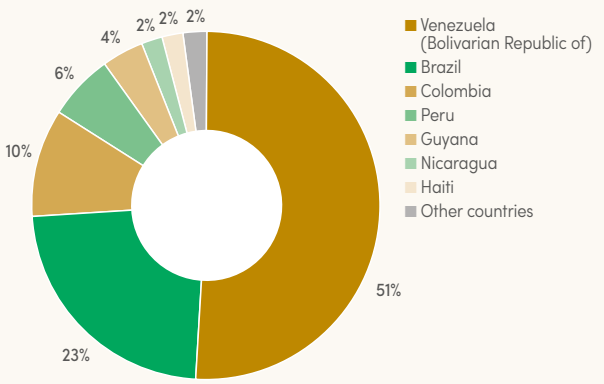
C. Malaria funding* per person at risk, average 2016–2018



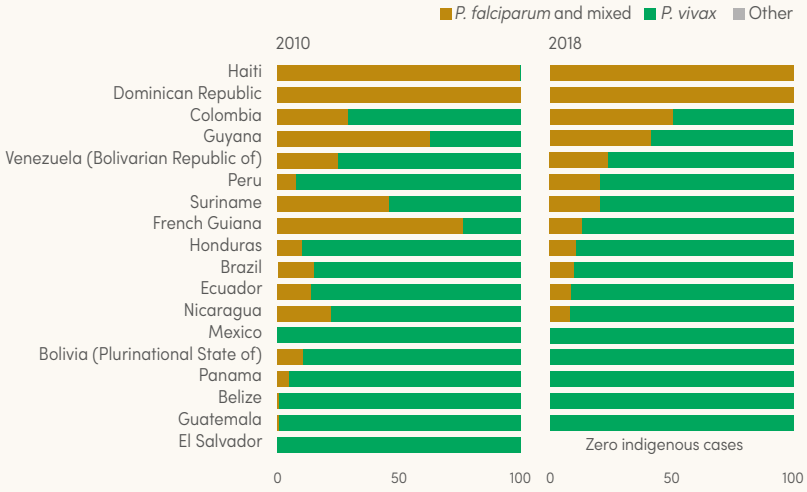
ND: No data.

* Excludes costs related to health staff, costs at subnational level and out-of-pocket expenditure.

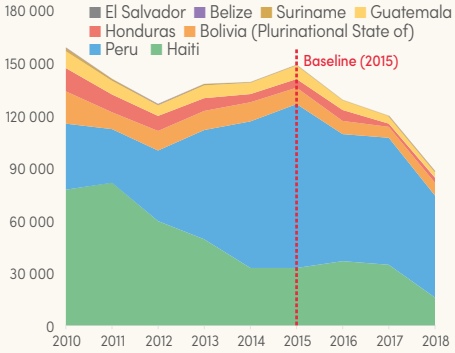
D. Share of estimated malaria cases, 2018



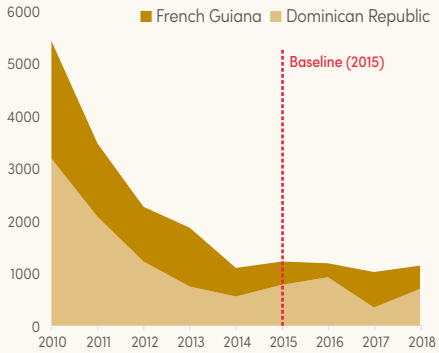
E. Percentage of *Plasmodium* species from indigenous cases, 2010 and 2018



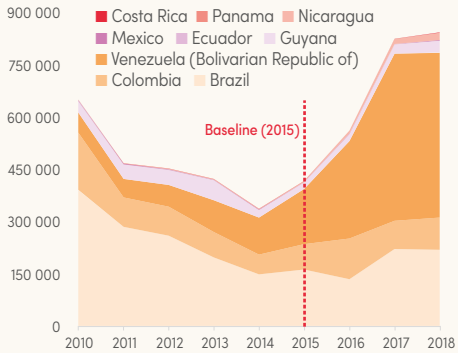
F. Countries on track to reduce case incidence by ≥40% by 2020



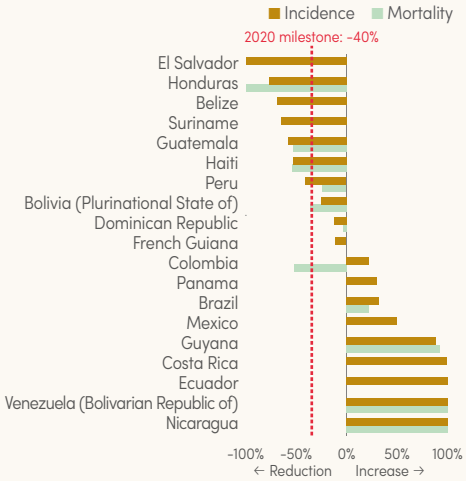
G. Countries and areas likely to reduce case incidence by <40% by 2020



H. Countries with an increase in case incidence, 2015–2018



I. Change in estimated malaria incidence and mortality rates, 2015–2018

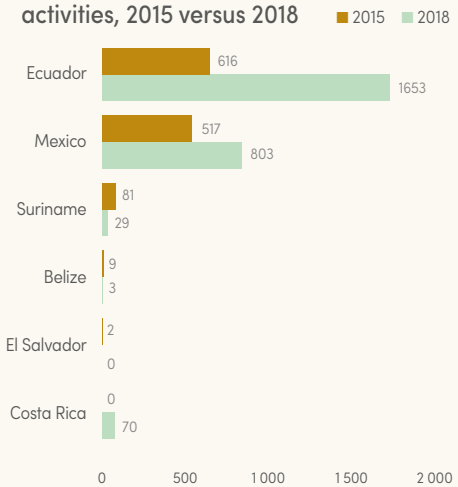


* Belize, Costa Rica, Ecuador, El Salvador, French Guiana, Mexico, Panama and Suriname already achieved the 40% reduction in mortality rate in 2015; since then there has been no change.

J. Percentage of total confirmed cases investigated, 2018

* Countries and areas with no reported case investigation: Bolivia (Plurinational State of), French Guiana, Guyana and Haiti.

K. Number of reported indigenous cases in countries with national elimination activities, 2015 versus 2018



KEY MESSAGES

- About 138 million people in 19 countries and areas are at risk of malaria, of which almost 80% is caused by *P. vivax*. In 2018, the region had almost 1 million estimated malaria cases and about 600 estimated deaths; increases of 14% and 26%, respectively, compared with 2010. Three countries – Brazil, Colombia and Venezuela (Bolivarian Republic of) – account for 80% of all estimated cases. In the public health sector, about 750 000 cases were reported, all of which were confirmed. Reported deaths due to malaria were few, at about 300 deaths.
- Eight out of the 19 malaria endemic countries and areas are on target to achieve a more than 40% reduction in case incidence by 2020, while Dominican Republic and French Guiana are on target to achieve a 20–40% reduction. Nine countries (Brazil, Colombia, Costa Rica, Ecuador, Guyana, Mexico, Nicaragua, Panama and Venezuela [Bolivarian Republic of]) saw increases in incidence in 2018 compared with 2015.
- The number of cases in French Guiana has fluctuated, largely because of variable detection efforts in the hinterland, whereas there have been large increases in Nicaragua (572%) and Venezuela (Bolivarian Republic of) (209%).
- Nevertheless, transmission in countries is focal, being particularly high in Choco in Colombia, Loreto in Peru and Bolivar in Venezuela (Bolivarian Republic of). More than one third of all cases in the region in 2018 were from five municipalities. Increases in other countries in 2018 are attributed to improved surveillance and focal outbreaks. El Salvador has reported zero indigenous cases for the past 2 years. Mexico and Bolivia have reported no local *P. falciparum* cases for more than 3 years, and Belize reported one case in 2018 and only two cases of *P. vivax*. The reported cases due to *P. falciparum* were below 10% in Brazil, Ecuador, Guatemala, Mexico, Nicaragua and Panama. LLIN distribution increased by 9% in 2018 compared with 2015, while the number of people protected by IRS decreased by 39%.
- Paraguay and Argentina were awarded malaria free certification by WHO in 2018 and 2019, respectively. Nine countries in Central America and Hispaniola are taking part in the subregional initiative to eliminate malaria by 2020. Despite Costa Rica reporting zero indigenous cases between 2013 and 2015, there has been a resurgence in cases in recent years, with eight cases being reported in 2016 and 70 cases in 2018, largely related to increased importation of cases from neighbouring countries and consequent re-establishment of transmission. Efforts are underway to enhance access to diagnosis and treatment, investigation of cases and adequate response.
- Vector resistance to pyrethroids was confirmed in more than half of the countries. There are significant gaps in standard resistance monitoring for all the five insecticide classes commonly used for vector control.

Annex 2 - C. WHO Eastern Mediterranean Region

EPIDEMIOLOGY

Population at risk: 317 million

Parasites: *P. falciparum* and mixed (75%), *P. vivax* (25%) and other (<1%)

Vectors: *An. annularis, An. arabiensis, An. culicifacies s.l., An. d'thali, An. fluviatilis, An. funestus s.l., An. gambiae s.s., An. maculipennis s.s., An. pulcherrimus, An. sacharovi, An. sergentii, An. stephensi* and *An. superpictus.*

FUNDING (US$), 2010–2018

127.9 million (2010), 158.2 million (2015), 140.0 million (2018); increase 2010–2018: 9%

Proportion of domestic source* in 2017: 52%

Regional funding mechanisms: none

* Domestic source excludes patient service delivery costs and out-of-pocket expenditure.

INTERVENTIONS, 2018

Number of people protected by IRS: 10.5 million (2010), 27.8 million (2015), 10.2 million (2018)

Total LLINs distributed: 2.8 million (2010), 5.7 million (2015), 10.4 million (2018)

Number of RDTs distributed: 2.0 million (2010), 6.1 million (2015), 8.3 million (2018)

Number of ACT courses distributed: 2.6 million (2010), 3.2 million (2015), 4.7 million (2018)

Number of any first-line antimalarial treatment courses (incl. ACT) distributed: 2.6 million (2010), 4.0 million (2015), 5.9 million (2018)

REPORTED CASES AND DEATHS IN PUBLIC SECTOR*, 2010–2018

Total (presumed and confirmed) cases: 6.4 million (2010), 5.4 million (2015), 5.2 million (2018)

Confirmed cases: 1.2 million (2010), 999 000 (2015), 2.4 million (2018)

Percentage of total cases confirmed: 18.3% (2010), 18.5% (2015), 46.4% (2018)

Deaths: 1140 (2010), 1020 (2015), 3320 (2018)

* In Djibouti, Pakistan and Sudan, cases from the private sector are included in 2018.

ESTIMATED CASES AND DEATHS, 2010–2018

Cases: 4.3 million (2010), 3.8 million (2015), 4.9 million (2018); increase 2010–2018: 12%

Deaths: 8300 (2010), 7120 (2015), 9330 (2018); increase 2010–2018: 13%

* In Iran (Islamic Republic of) and Saudi Arabia, reported malaria cases were used.

ACCELERATION TO ELIMINATION

Countries with nationwide elimination programme: Iran (Islamic Republic of) and Saudi Arabia

Zero indigenous cases in 2018: Iran (Islamic Republic of)

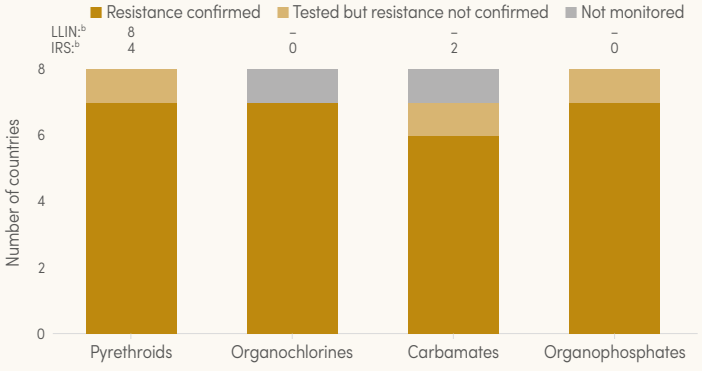
Certified as malaria free since 2010: Morocco (2010)

THERAPEUTIC EFFICACY TESTS (CLINICAL AND PARASITOLOGICAL FAILURE, %)

Medicine	Study years	No. of studies	Min.	Median	Max.	Percentile 25	Percentile 75
AL	2010–2018	27	0.0	0.0	3.3	0.0	1.5
AS-SP	2010–2017	41	0.0	1.0	22.2	0.0	4.4
DHA-PPQ	2013–2016	6	0.0	0.5	2.5	0.0	2.2

AL: artemether-lumefantrine; AS-SP: artesunate-sulfadoxine-pyrimethamine; DHA-PPQ: dihydroartemisinin-piperaquine.

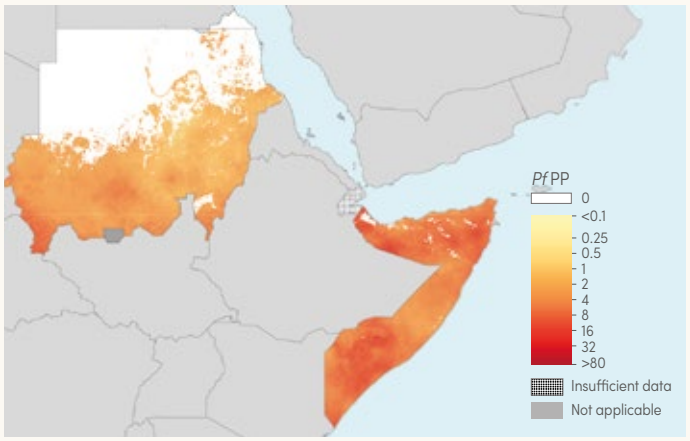
STATUS OF INSECTICIDE RESISTANCE[a] PER INSECTICIDE CLASS (2010–2018) AND USE OF EACH CLASS FOR MALARIA VECTOR CONTROL (2018)

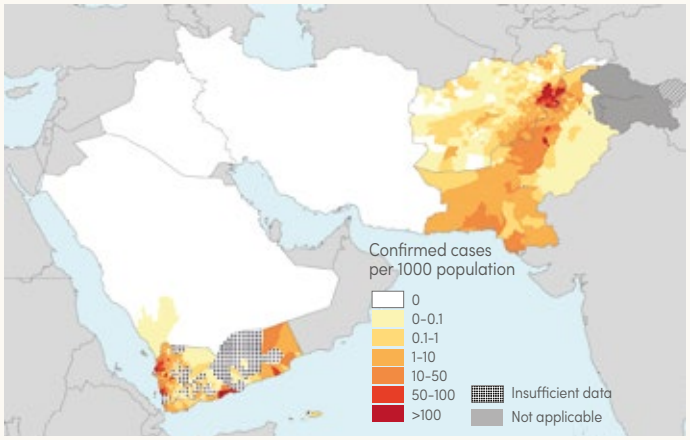


[a] Resistance is considered confirmed when it was detected to one insecticide in the class, in at least one malaria vector from one collection site.

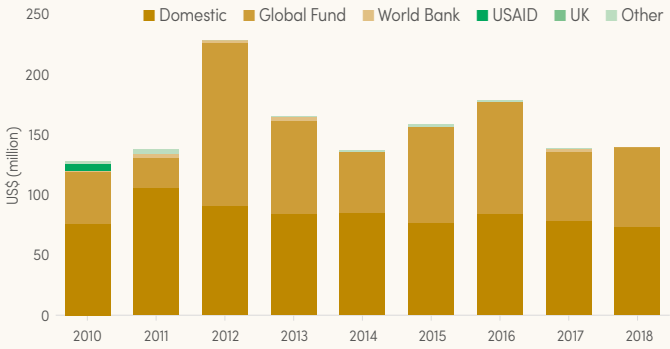
[b] Number of countries that reported using the insecticide class for malaria vector control (2018).

A. *P. falciparum* parasite prevalence (*Pf* PP)/confirmed malaria cases per 1000 population, 2018





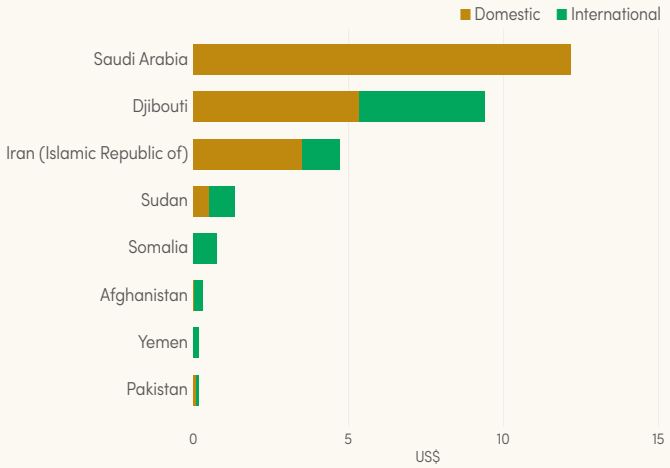
B. Malaria funding* by source, 2010–2018



Global Fund: Global Fund to Fight AIDS, Tuberculosis and Malaria; UK: United Kingdom of Great Britain and Northern Ireland; USAID: United States Agency for International Development.

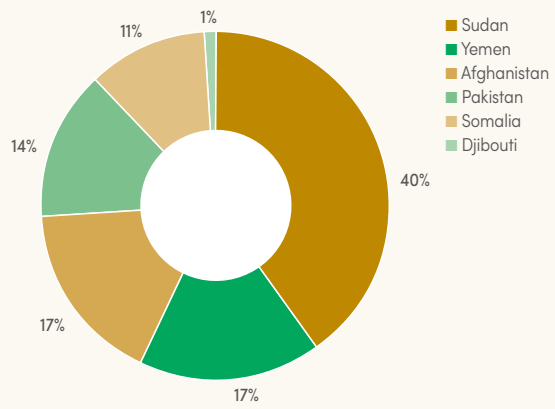
* Excludes patient service delivery costs and out-of-pocket expenditure.

C. Malaria funding* per person at risk, average 2016–2018

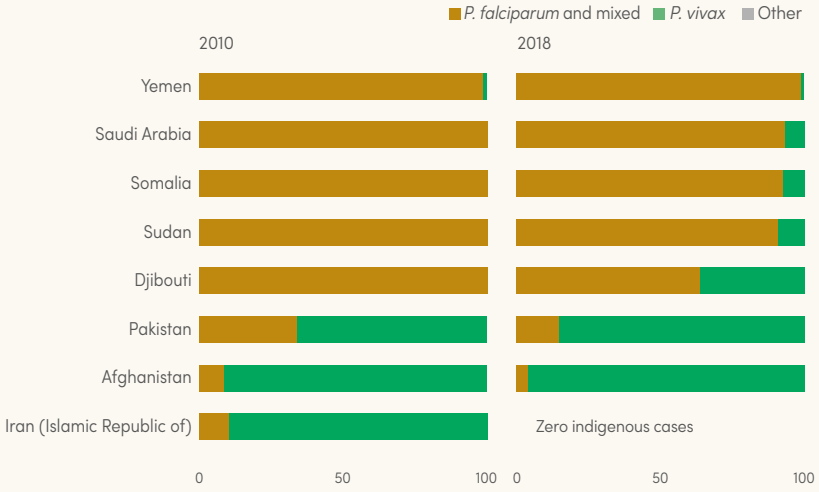


* Excludes costs related to health staff, costs at subnational level and out-of-pocket expenditure.

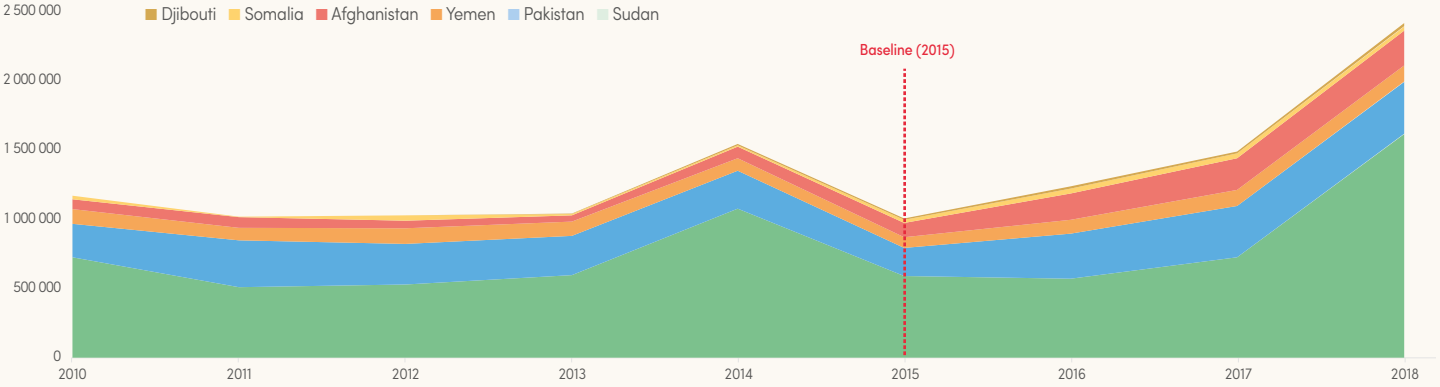
D. Share of estimated malaria cases, 2018



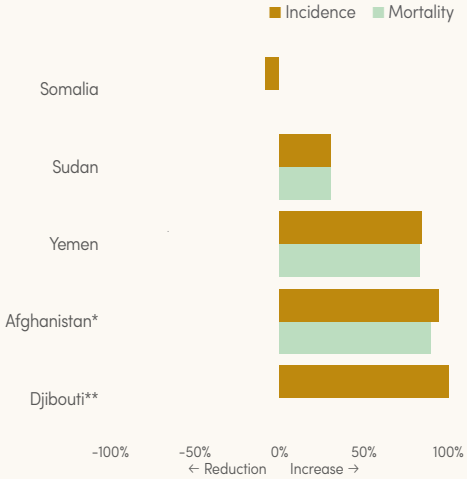
E. Percentage of *Plasmodium* species from indigenous cases, 2010 and 2018



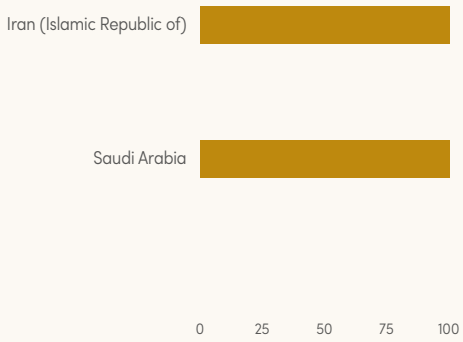
F. Countries with an increase in reported cases, 2015–2018



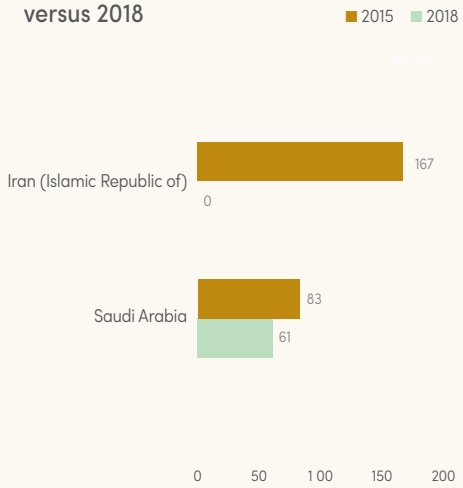
G. Change in estimated malaria incidence and mortality rates, 2015–2018*



H. Percentage of total confirmed cases investigated, 2018



I. Reported indigenous cases in countries with national elimination activities, 2015 versus 2018



* Estimates of change in Afghanistan may be exaggerated due to uncertainties in adjustments; estimates for Pakistan were excluded due to high uncertainties.

** Reported confirmed cases are used for Djibouti (as opposed to estimated cases). No mortality data was reported for Djibouti for 2017 or 2018.

KEY MESSAGES

- Fourteen countries in the WHO Eastern Mediterranean Region are free of indigenous malaria and are at the stage of prevention of re-establishment. There are eight malaria endemic countries in the region, and *P. falciparum* is responsible for 75% of all detected infections. Estimated malaria incidence in the region declined between 2010 and 2015, but increased over the past 3 years. Estimated malaria deaths also increased by 13% since 2010. Sudan accounted for 40% of reported cases. In 2018, the region reported more than 5 million cases (presumed and confirmed), of which only about 2 million (46%) were confirmed. The proportion of confirmed cases was 18% in 2010 but has improved since then. The reported number of deaths increased from 1140 in 2010 to just over 3300 in 2018.
- The Islamic Republic of Iran and Saudi Arabia are both targeting elimination by 2020. The Islamic Republic of Iran reported zero indigenous cases for the first time in 2018, and 20 introduced cases. In Saudi Arabia, the number of indigenous malaria cases declined from 272 in 2016 to 61 in 2018. Both the Islamic Republic of Iran and Saudi Arabia have reported zero indigenous deaths over the past 3 years. These countries undertake continued vigilance for malaria in the general health service, and provide free-of-charge diagnosis and treatment to all imported cases.
- Vector resistance to pyrethroids and organochlorines was confirmed in all countries except for Saudi Arabia. Resistance to organophosphates and carbamates was confirmed in most of the countries of the region.
- Challenges include low coverage of essential interventions (below universal target) in most malaria endemic countries, inadequate funding and dependence on external resources, difficult operational environments and population displacements, a shortage of skilled technical staff (particularly at subnational level), and weak surveillance and health information systems. These challenges may have led to an overall increase in cases during the period 2015–2018 in some countries of the region.

Annex 2 - D. WHO South-East Asia Region

EPIDEMIOLOGY

Population at risk: 1.61 billion

Parasites: *P. falciparum* and mixed (52%), *P. vivax* (48%) and other (<1%)

Vectors: *An. albimanus, An. annularis, An. balabacensis, An. barbirostris, An. culicifacies s.l., An. dirus s.l., An. farauti s.l., An. fluviatilis, An. leteri, An. maculatus s.l., An. minimus s.l., An. peditaeniatus, An. philippinensis, An. pseudowillmori, An. punctulatus s.l., An. sinensis s.l., An. stephensi s.l., An. subpictus s.l., An. sundaicus s.l., An. tessellatus, An. vagus, An. varuna* and *An. yatsushiroensis.*

FUNDING (US$), 2010–2018

246.6 million (2010), 198.4 million (2015), 151.0 million (2018); decrease 2010–2018: 39%

Proportion of domestic source* in 2018: 59%

Regional funding mechanisms: Malaria Elimination in the Greater Mekong Region (MME): Myanmar and Thailand

* Domestic source excludes patient service delivery costs and out-of-pocket expenditure.

INTERVENTIONS, 2018

Number of people protected by IRS: 76.4 million (2010), 57.2 million (2015), 35.4 million (2018)

Total LLINs distributed: 7.4 million (2010), 7.3 million (2015), 2.9 million (2018)

Number of RDTs distributed: 11.4 million (2010), 23.5 million (2015), 14.0 million (2018)

Number of ACT courses distributed: 3.5 million (2010), 2.8 million (2015), 1.8 million (2018)

Number of any first-line antimalarial treatment courses (incl. ACT) distributed: 2.9 million (2010), 2.9 million (2015), 2.2 million (2018)

REPORTED CASES AND DEATHS IN PUBLIC SECTOR*, 2010–2018

Total (presumed and confirmed) cases: 3.1 million (2010), 1.6 million (2015), 744 000 (2018)

Confirmed cases: 2.6 million (2010), 1.6 million (2015), 707 000 (2018)

Percentage of total cases confirmed: 84.8% (2010), 98.4% (2015), 95% (2018)

Deaths: 2421 (2010), 620 (2015), 165 (2018)

* In Bhutan, India, Indonesia, Myanmar, Thailand and Timor-Leste, cases from the private sector and/or community are included in 2018.

ESTIMATED CASES AND DEATHS, 2010–2018

Cases: 25.1 million (2010), 13.6 million (2015), 7.9 million (2018); decrease 2010–2018: 69%

Deaths: 39 100 (2010), 24 500 (2015), 11 600 (2018); decrease 2010–2018: 70%

ACCELERATION TO ELIMINATION

Countries with subnational/territorial elimination programme: Bangladesh, India, Indonesia, Myanmar and Thailand

Countries with nationwide elimination programme: Bhutan, Democratic People's Republic of Korea, Nepal and Timor-Leste

Zero indigenous cases in 2018: Timor-Leste

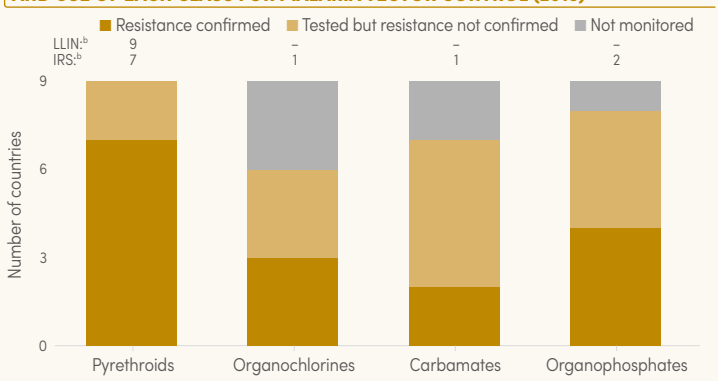
Certified as malaria free since 2010: Maldives (2015) and Sri Lanka (2016)

THERAPEUTIC EFFICACY TESTS (CLINICAL AND PARASITOLOGICAL FAILURE, %)

Medicine	Study years	No. of studies	Min.	Median	Max.	Percentile 25	Percentile 75
AL	2010–2018	72	0.0	0.0	14.3	0.0	2.0
AS-SP	2010–2017	55	0.0	0.0	21.4	0.0	1.5
AS-MQ	2010–2016	22	0.0	1.8	49.1	0.0	17.3
DHA-PPQ	2010–2017	29	0.0	0.0	92.9	0.0	2.2

AL: artemether-lumefantrine; AS-MQ: artesunate-mefloquine; AS-SP: artesunate-sulfadoxine-pyrimethamine; DHA-PPQ: dihydroartemisinin-piperaquine.

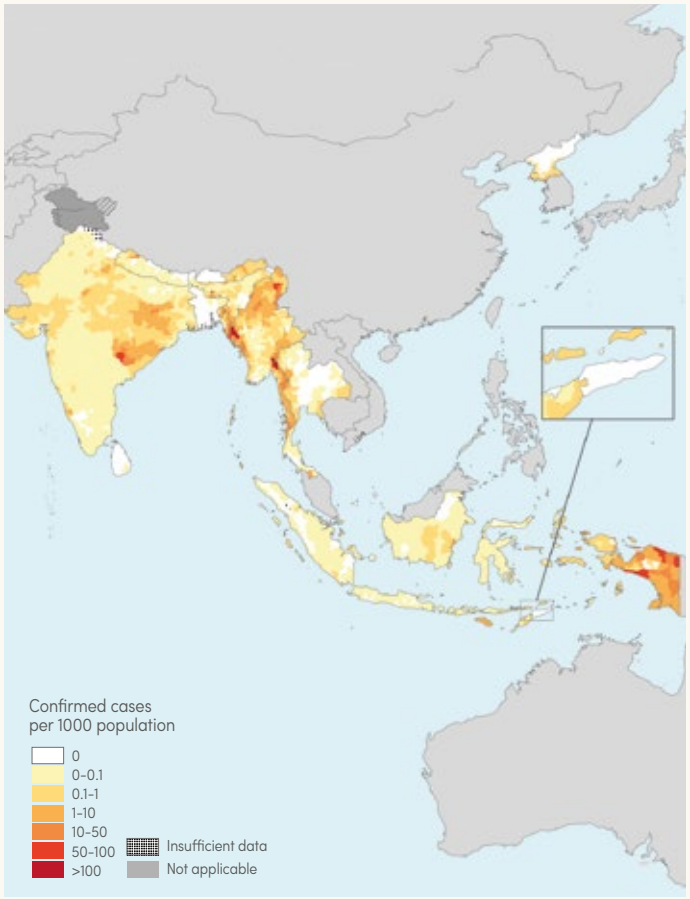
STATUS OF INSECTICIDE RESISTANCE[a] PER INSECTICIDE CLASS (2010–2018) AND USE OF EACH CLASS FOR MALARIA VECTOR CONTROL (2018)



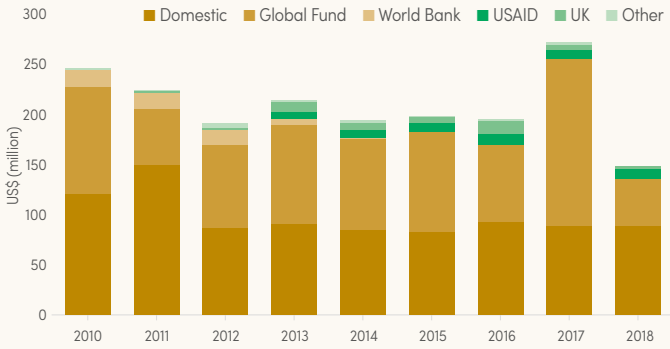
[a] Resistance is considered confirmed when it was detected to one insecticide in the class, in at least one malaria vector from one collection site.

[b] Number of countries that reported using the insecticide class for malaria vector control (2018).

A. Confirmed malaria cases per 1000 population, 2018



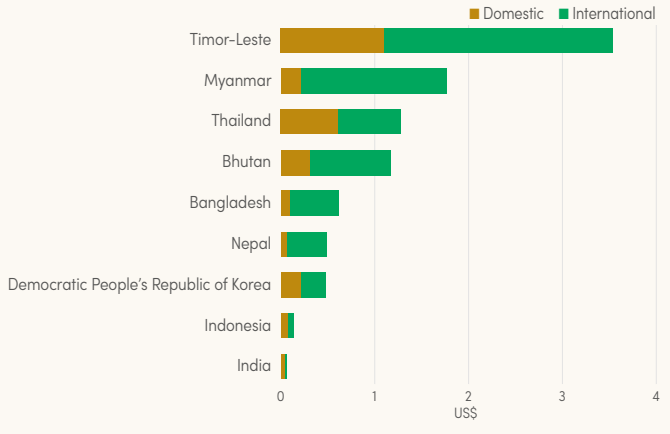
B. Malaria funding* by source, 2010–2018



Global Fund: Global Fund to Fight AIDS, Tuberculosis and Malaria; UK: United Kingdom of Great Britain and Northern Ireland; USAID: United States Agency for International Development.

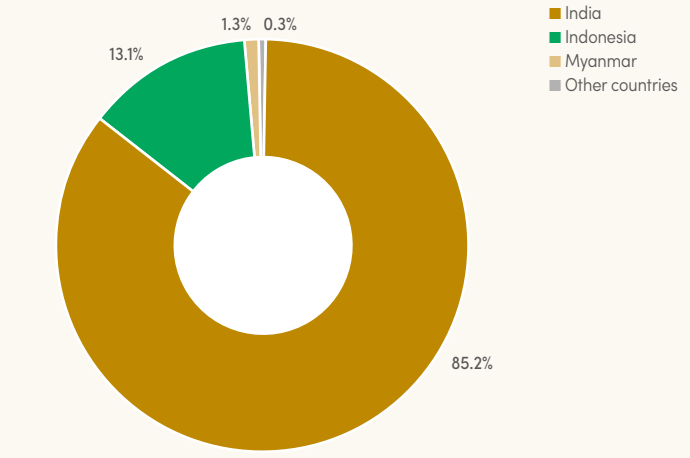
* Excludes patient service delivery costs and out-of-pocket expenditure.

C. Malaria funding* per person at risk, 2016–2018

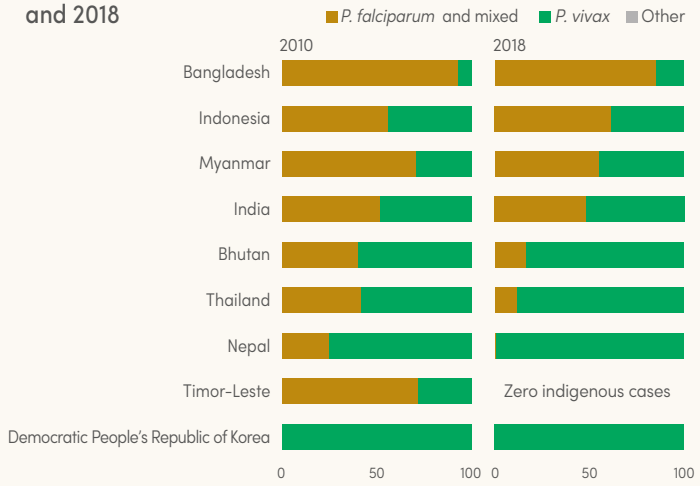


* Excludes costs related to health staff, costs at sub-national level and out-of-pocket expenditure.

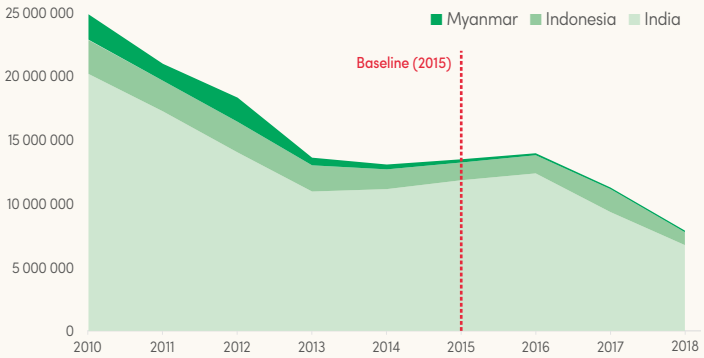
D. Share of estimated malaria cases, 2018

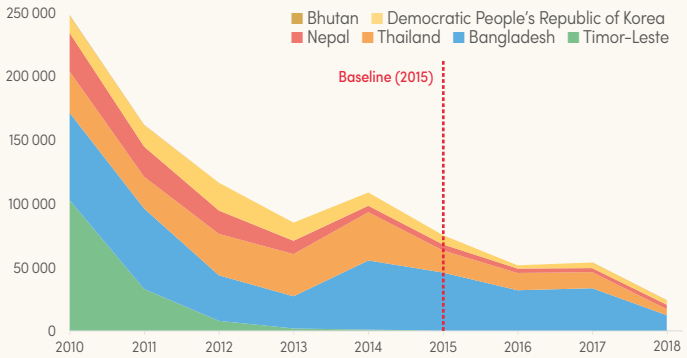


E. Percentage of *Plasmodium* species from indigenous cases, 2010 and 2018

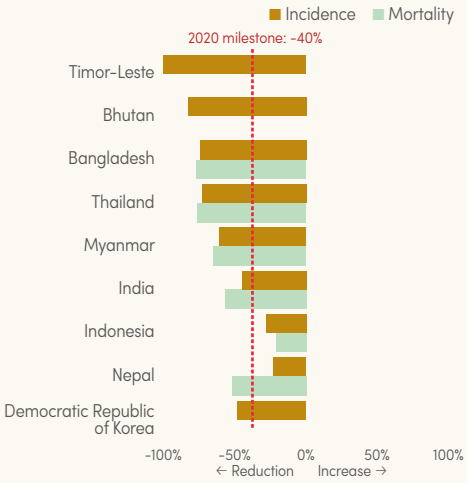


F. Countries on track to reduce case incidence by ≥40% by 2020





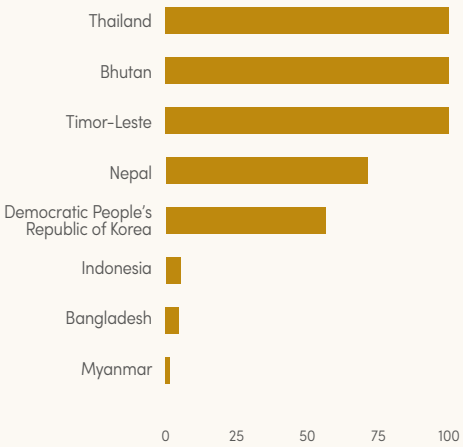
G. Change in estimated malaria incidence and mortality rates, 2015–2018



*Bhutan, Democratic People's Republic of Korea and Timor-Leste already achieved the 40% reduction in mortality rate in 2015; since then there has been no change.

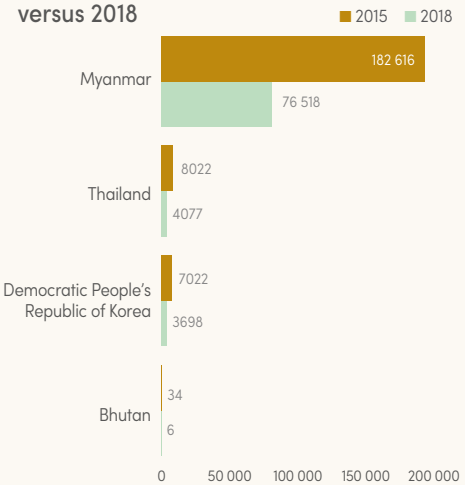
** Reported confirmed cases are used for Bhutan and Democratic People's Republic of Korea (as opposed to estimated cases).

H. Percentage of total confirmed cases investigated, 2018



* Countries with no reported case investigation: India.

I. Reported indigenous cases in countries with national elimination activities, 2015 versus 2018



KEY MESSAGES

- An estimated 1.61 billion people in the WHO South-East Asia Region are at risk of malaria. The disease is endemic in 9 out of 11 countries of the region, accounting for 50% of the burden outside the WHO African Region. In 2018, the region had almost 8 million estimated cases and about 11 600 estimated deaths – reductions of 69% and 70%, respectively, compared with 2010 – representing the largest decline among all regions. All countries are on target to achieve a more than 40% reduction in case incidence by 2020, and all have strategic plans that aim for malaria elimination by 2030 at the latest.
- Three countries accounted for 98% of the total reported cases in the region, the main contributor being India (58%), followed by Indonesia (30%) and Myanmar (10%). Despite being the highest burden country of the region, India showed a reduction in reported cases of 51% compared with 2017 and of 60% compared with 2016. Although cases continue to decrease in the public sector, estimates indicate that there are still gaps in reporting from the private sector and in treatment seeking in the three countries (estimated versus reported: India 6.7 million versus 400 000, Indonesia 1 million versus 200 000, Myanmar 100 000 versus 76 500). Two other countries in the region reported substantial decline in total reported cases between 2017 and 2018: by 62% in Bangladesh and by 21% in Thailand.
- Timor-Leste had no indigenous malaria cases in a year for the first time, while Bhutan had only six indigenous (and 14 introduced) cases. Maldives and Sri Lanka, certified as malaria free in 2015 and 2016, respectively, continue to maintain their malaria free status.
- Continuing the declining trend, reported malaria deaths in the region dropped to 165 in 2018, reductions of 93% and 45 compared with 2010 and 2017, respectively. India, Indonesia and Myanmar accounted for 58%, 21% and 12% of the total reported deaths in the region, respectively. Bhutan, Democratic People's Republic of Korea and Timor-Leste continue to record zero indigenous deaths.
- Vector resistance to pyrethroids was confirmed in one third of the countries. Resistance to organophosphates was confirmed in almost half of the countries, and resistance to organochlorines and carbamates was confirmed in less than one third of them. There are still significant gaps in standard resistance monitoring for these three classes of vector control agents.
- Challenges include decreased funding, multiple ACT treatment failures in the countries of the GMS and vector resistance to pyrethroids. Efforts are underway to strengthen surveillance and to enhance reporting from private sector and nongovernmental organizations (where relevant), and case-based surveillance and response to accelerate towards elimination.

Annex 2 - E. WHO Western Pacific Region

EPIDEMIOLOGY

Population at risk: 762 million

Parasites: *P. falciparum* and mixed (66%), *P. vivax* (33%) and other (<1%)

Vectors: *An. anthropophagus, An. balabacensis, An. barbirostris s.l., An. dirus s.l., An. donaldi, An. epirotivulus, An. farauti s.l., An. flavirostris, An. jeyporiensis, An. koliensis, An. litoralis, An. maculatus s.l., An. mangyanus, An. minimus s.l., An. punctulatus s.l., An. sinensis s.l.* and *An. sundaicus s.l.*

FUNDING (US$), 2010–2018

213.7 million (2010), 145.4 million (2015), 129.4 million (2018); decrease 2010–2018: 39%

Proportion of domestic source* in 2018: 60%

Regional funding mechanisms: Mekong Malaria Elimination (MME) Initiative in the Greater Mekong Subregion: Cambodia, China (Yunnan), Lao People's Democratic Republic and Viet Nam (supported by RAI2e Global Fund)

* Domestic source excludes patient service delivery costs and out-of-pocket expenditure.

INTERVENTIONS, 2018

Number of people protected by IRS: 27.9 million (2010), 3.3 million (2015), 1.5 million (2018)

Total LLINs distributed: 3.4 million (2010), 2.7 million (2015), 3.4 million (2018)

Number of RDTs distributed: 1.6 million (2010), 2.5 million (2015), 3.5 million (2018)

Number of ACT courses distributed: 591 000 (2010), 1.3 million (2015), 1.7 million (2018)

Number of any antimalarial treatment courses (incl. ACT) distributed: 963 000 (2010), 1.4 million (2015), 1.7 million (2018)

REPORTED CASES AND DEATHS IN PUBLIC SECTOR, 2010–2018

Total (presumed and confirmed) cases: 1.6 million (2010), 704 000 (2015), 1.1 million (2018)

Confirmed cases: 260 000 (2010), 411 000 (2015), 634 000 (2018)

Percentage of total cases confirmed: 15.8% (2010), 58.3% (2015), 58.9% (2018)

Deaths: 910 (2010), 234 (2015), 254 (2018)

ESTIMATED CASES AND DEATHS, 2010–2018

Cases: 1.8 million (2010), 1.4 million (2015), 2.0 million (2018); increase 2010–2018: 8%

Deaths: 3780 (2010), 2840 (2015), 3450 (2018); decrease 2010–2018: 9%

ACCELERATION TO ELIMINATION

Countries with subnational/territorial elimination programme: Philippines

Countries with nationwide elimination programme: Cambodia, China, Lao People's Democratic Republic, Malaysia, Republic of Korea and Viet Nam

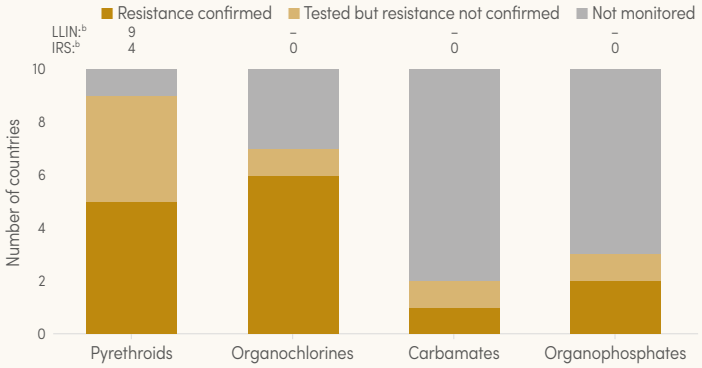
Zero indigenous cases in 2018: China and Malaysia

THERAPEUTIC EFFICACY TESTS (CLINICAL AND PARASITOLOGICAL FAILURE, %)

Medicine	Study years	No. of studies	Min.	Median	Max.	Percentile 25	Percentile 75
AL	2010–2018	30	0.0	0.0	17.2	0.0	5.2
AS-MQ	2010–2018	21	0.0	0.0	11.1	0.0	1.4
AS-PY	2014–2018	13	0.0	1.7	18.0	0.0	7.7
DHA-PPQ	2010–2017	75	0.0	0.8	62.5	0.0	12.3

AL: artemether-lumefantrine; AS-MQ: artesunate-mefloquine; AS-PY: artesunate-pyronaridine; DHA-PPQ: dihydroartemisinin-piperaquine.

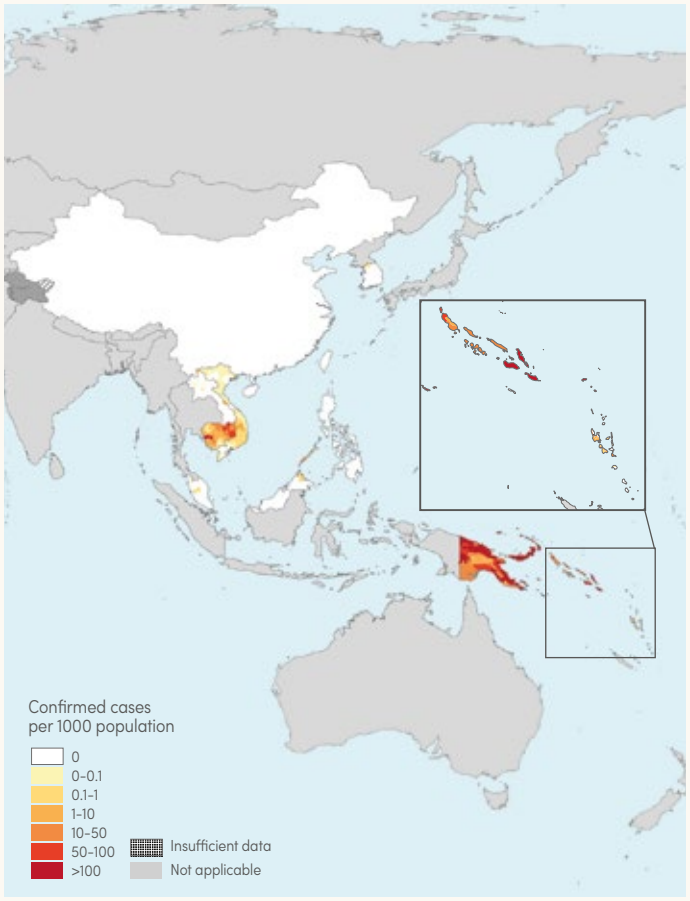
STATUS OF INSECTICIDE RESISTANCE[a] PER INSECTICIDE CLASS (2010–2018) AND USE OF EACH CLASS FOR MALARIA VECTOR CONTROL (2018)



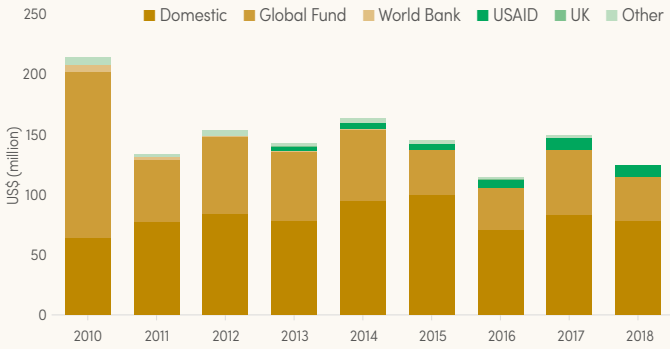
[a] Resistance is considered confirmed when it was detected to one insecticide in the class, in at least one malaria vector from one collection site.

[b] Number of countries that reported using the insecticide class for malaria vector control (2018).

A. Confirmed malaria cases per 1000 population, 2018



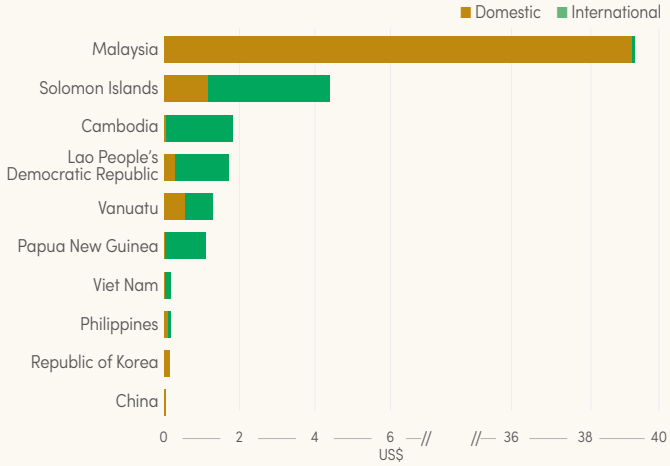
B. Malaria funding* by source, 2010–2018



Global Fund: Global Fund to Fight AIDS, Tuberculosis and Malaria; UK: United Kingdom of Great Britain and Northern Ireland; USAID: United States Agency for International Development.

* Excludes patient service delivery costs and out-of-pocket expenditure.

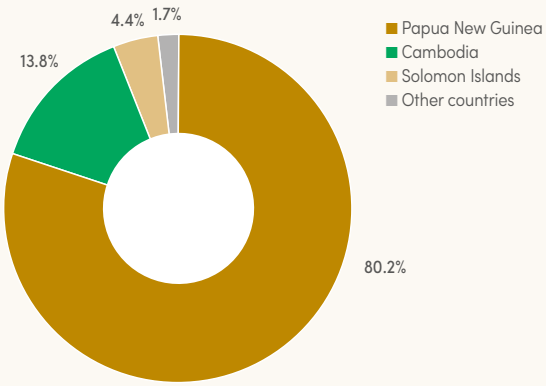
C. Malaria funding* per person at risk, 2016–2018



* Excludes costs related to health staff, costs at subnational level and out-of-pocket expenditure.

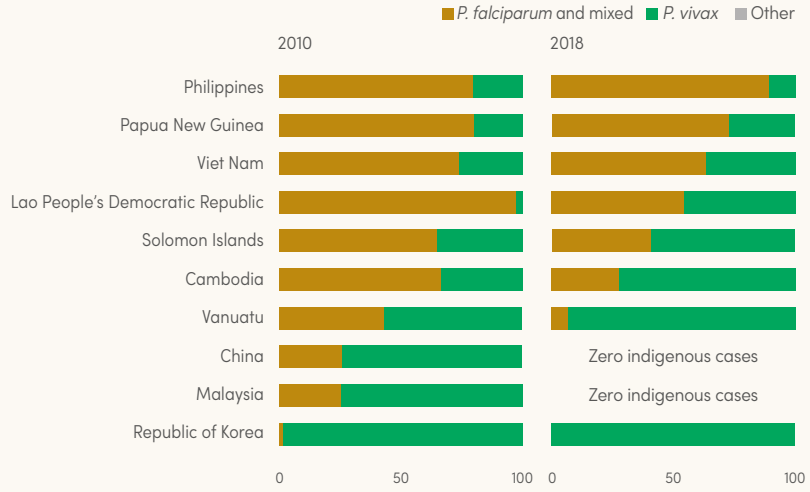
** Only domestic funding in China and the Republic of Korea.

D. Share of estimated malaria cases, 2018

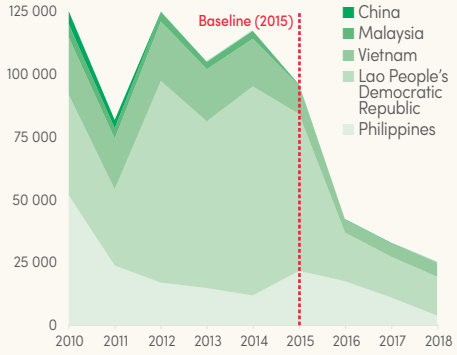


* Countries with zero cases: China and Malaysia.

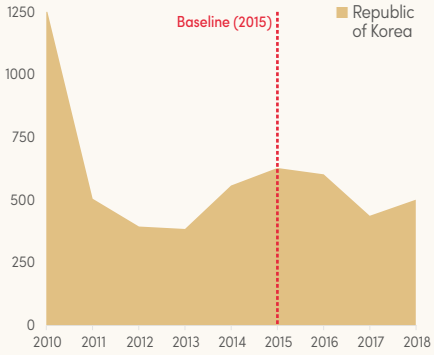
E. Percentage of *Plasmodium* species from indigenous cases, 2010 and 2018



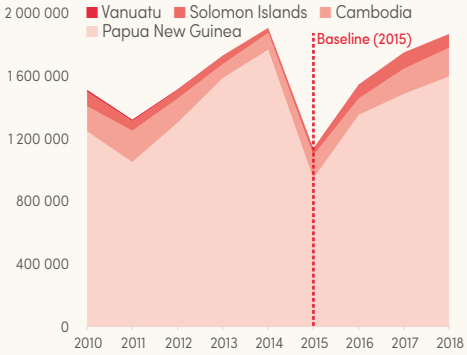
F. Countries on track to reduce case incidence by ≥40% by 2020



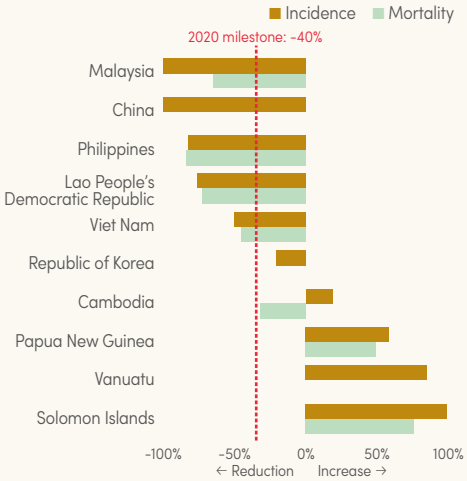
G. Countries likely to reduce case incidence by <40% by 2020



H. Countries with an increase in case incidence, 2015–2018

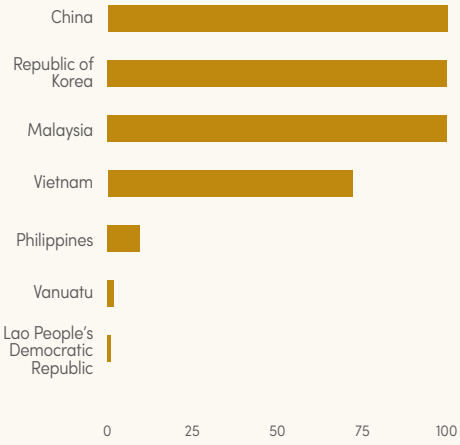


I. Change in estimated malaria incidence and mortality rates, 2015–2018



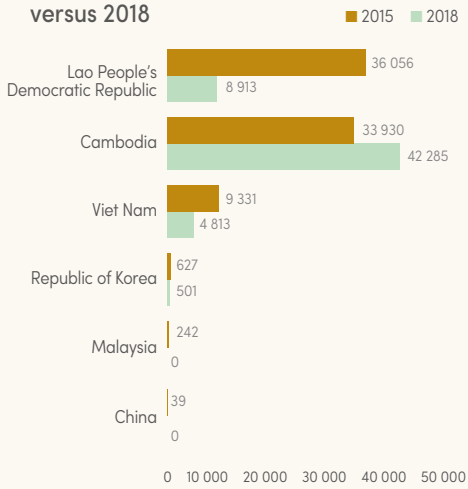
* China, Republic of Korea and Vanuatu already achieved the 40% reduction in mortality rate in 2015; since then there has been no change.

J. Percentage of total confirmed cases investigated, 2018



* Imported cases are included.

K. Reported indigenous cases in countries with national elimination activities, 2015 versus 2018



KEY MESSAGES

- About 762 million people in 10 countries are at risk of malaria; infections are predominantly caused by *P. falciparum*, with about one third due to *P. vivax*. In 2018, the region had almost 2 million malaria cases and about 3500 estimated deaths – an 8% increase and a 9% decrease compared with 2010, respectively. Most of the cases were in Papua New Guinea (80%); when taken together with Cambodia and Solomon Islands, the three countries comprise 98% of the estimated cases. In the public health sector, just over 1 million cases were reported, of which 59% were confirmed. The proportion of total cases that were confirmed improved substantially between 2010 and 2015, from 15.8% to 58.3%, but since 2015 there has been little improvement. There were only about 250 reported deaths due to malaria.
- Five out of the 10 malaria endemic countries in the region are on target to achieve more than a 40% reduction in case incidence by 2020, and the Republic of Korea is on track for a 20–40% reduction. Cambodia, Papua New Guinea, Solomon Islands and Vanuatu have seen an increase in estimated cases since 2015: 18.8%, 40.2%, 99.6% and 37.3%, respectively. All countries are on track to reduce the malaria mortality rate by at least 40% by 2020, except Papua New Guinea and Solomon Islands.
- China and Malaysia are on course for elimination by 2020. China has reported zero indigenous cases for 2 consecutive years, and Malaysia reported zero indigenous human malaria cases for the first time in 2018. However, Malaysia is facing increasing cases of the zoonotic malaria *P. knowlesi*, which increased from 1600 to over 4000 between 2016 and 2018, and resulted in 12 deaths this year. The Republic of Korea is facing the challenge of malaria transmission in military personnel along the northern border. Philippines has initiated subnational elimination, reporting zero indigenous cases in 78 out of 81 provinces in 2018.
- Three countries of the GMS (Cambodia, Lao People's Democratic Republic and Viet Nam) aim to eliminate *P. falciparum* by 2020 and all species of malaria by 2030, through support from a Global Fund financed regional artemisinin-resistance initiative. The percentage of cases in Cambodia due to *P. falciparum* has fallen significantly, from 61% in 2015 to 27% in 2018, owing to intensified efforts in community outreach and active case detection to reduce *P. falciparum*. Although the goal of *P. falciparum* elimination will not be met by 2020, much progress has been made. Reducing *P. falciparum* cases in Lao People's Democratic Republic and Viet Nam has been more challenging, and from 2015 to 2018 they saw increases of 12% and 14%, respectively, due to sporadic outbreaks in 2017 and 2018.
- Vector resistance to pyrethroids was confirmed in half of the countries. Resistance to organochlorines was confirmed in more than half of the countries, although there are significant gaps in standard resistance monitoring for this class. Almost no standard resistance monitoring was reported for carbamates or organophosphates, other than in China, Philippines and Solomon Islands.
- Challenges include decreased funding, multiple ACT treatment failures, vector resistance to pyrethroids (in Cambodia, Lao People's Democratic Republic, Philippines and Viet Nam), resurgence of malaria in Cambodia and Solomon Islands, and sustained high levels of malaria in Papua New Guinea due to health system strengthening challenges. Recent efforts are underway to improve access to services and case-based surveillance to accelerate elimination in Cambodia, Lao People's Democratic Republic, Malaysia, Philippines, Republic of Korea, Vanuatu and Viet Nam.

Annex 3 - A. Policy adoption, 2018

WHO region Country/area	Insecticide-treated mosquito nets				Indoor residual spraying		Chemoprevention	
	ITNs/LLINs are distributed free of charge	ITNs/LLINs are distributed through ANC	ITNs/LLINs distributed through EPI/well baby clinic	ITNs/LLINs distributed through mass campaigns	IRS is recommended by malaria control programme	DDT is used for IRS	IPTp is used to prevent malaria during pregnancy	Seasonal malaria chemo-prevention (SMC or IPTc) is used
AFRICAN								
Algeria	NA	NA	NA	NA	●	●	NA	NA
Angola	●	●	●	●	●	●	●	NA
Benin	●	●	●	●	●	●	●	●
Botswana	●	NA	NA	NA	●	●	●	NA
Burkina Faso	●	●	●	●	●	●	●	●
Burundi	●	●	●	●	●	●	●	NA
Cabo Verde	NA	NA	NA	NA	●	●	NA	NA
Cameroon	●	●	●	●	●	●	●	●
Central African Republic	●	●	●	●	●	●	●	NA
Chad	●	●	●	●	●	●	●	●
Comoros	●	●	●	●	●	●	●	NA
Congo	●	●	●	●	●	●	●	NA
Côte d'Ivoire	●	●	●	●	●	●	●	NA
Democratic Republic of the Congo	●	●	●	●	●	●	●	NA
Equatorial Guinea	●	●	●	●	●	●	●	NA
Eritrea	●	●	●	●	●	●	●	NA
Eswatini	●	NA	NA	●	●	●	NA	NA
Ethiopia	●	●	●	●	●	●	●	NA
Gabon	●	●	●	●	●	●	●	NA
Gambia	●	●	●	●	●	●	●	●
Ghana	●	●	●	●	●	●	●	●
Guinea	●	●	●	●	●	●	●	●
Guinea-Bissau	●	●	●	●	●	●	●	●
Kenya	●	●	●	●	●	●	●	NA
Liberia	●	●	●	●	●	●	●	NA
Madagascar	●	●	●	●	●	●	●	NA
Malawi	●	●	●	●	●	●	●	NA
Mali	●	●	●	●	●	●	●	●
Mauritania	●	●	●	●	●	●	●	●
Mayotte	●	–	–	–	–	●	NA	NA
Mozambique	●	●	●	●	●	●	●	NA
Namibia	●	NA	NA	●	●	●	●	NA
Niger	●	●	●	●	●	●	●	●
Nigeria	●	●	●	●	●	●	●	●
Rwanda	●	●	●	●	●	●	●	NA
Sao Tome and Principe	●	●	●	●	●	●	●	NA
Senegal	●	●	●	●	●	●	●	●
Sierra Leone	●	●	●	●	●	●	●	NA
South Africa	NA	●	●	●	●	●	●	NA
South Sudan[2]	●	●	●	●	●	●	●	NA
Togo	●	●	●	●	●	●	●	●
Uganda	●	●	●	●	●	●	●	NA
United Republic of Tanzania[3]								NA
Mainland	●	●	●	●	●	●	●	NA
Zanzibar	●	●	●	●	●	●	●	NA
Zambia	●	●	●	●	●	●	●	NA
Zimbabwe	●	●	●	●	●	●	●	NA
AMERICAS								
Argentina	NA	●	●	●	●	●	NA	NA
Belize	●	●	●	●	●	●	NA	NA
Bolivia (Plurinational State of)	●	●	●	●	●	●	NA	NA
Brazil	●	●	●	●	●	●	NA	NA
Colombia	●	●	●	●	●	●	NA	NA

Testing				Treatment				
Patients of all ages should get diagnostic test	Malaria diagnosis is free of charge in the public sector	RDTs are used at community level	G6PD test is recommended before treatment with primaquine is used for treatment of *P. vivax* cases	ACT for treatment of *P. falciparum*	Pre-referral treatment with quinine or artemether IM or artesunate suppositories	Single dose of primaquine is used as gametocidal medicine for *P. falciparum*[1]	Primaquine is used for radical treatment of *P. vivax* cases	Directly observed treatment with primaquine is undertaken
–	⚪	–	🔴	NA	–	⚪	⚫	⚪
⚪	⚪	⚫	⚪	⚫	⚪	🔴	⚪	🔴
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⚪	🔴	⚫	🔴	⚫	⚪	🔴	🔴	🔴
⚪	⚪	⚫	🔴	⚫	⚪	🔴	🔴	🔴
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–	⚪	–	⚪	⚫	–	⚪	⚪	⚪
⚪	⚪	⚫	🔴	⚫	⚪	🔴	🔴	🔴
⚪	⚪	🔴	🔴	⚫	⚪	⚪	⚫	⚪
⚪	⚪	⚫	🔴	⚫	⚪	🔴	🔴	🔴
⚪	🔴	⚫	🔴	⚫	⚪	🔴	🔴	🔴
⚪	🔴	⚫	🔴	⚫	⚪	🔴	🔴	🔴
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⚪	⚪	⚫	🔴	⚫	⚪	🔴	🔴	🔴
⚪	⚪	⚫	🔴	⚫	🔴	🔴	⚪	⚪
⚪	⚪	⚪	🔴	⚫	⚪	🔴	⚪	🔴
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⚪	⚪	⚫	🔴	⚫	⚪	⚪	⚪	⚪
⚪	⚪	🔴	🔴	⚫	🔴	⚪	⚫	⚪
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Annex 3 - A. Policy adoption, 2018

WHO region Country/area	Insecticide-treated mosquito nets				Indoor residual spraying		Chemoprevention	
	ITNs/LLINs are distributed free of charge	ITNs/LLINs are distributed through ANC	ITNs/LLINs distributed through EPI/well baby clinic	ITNs/LLINs distributed through mass campaigns	IRS is recommended by malaria control programme	DDT is used for IRS	IPTp is used to prevent malaria during pregnancy	Seasonal malaria chemo-prevention (SMC or IPTc) is used
AMERICAS								
Costa Rica	●	●	●	●	●	●	NA	NA
Dominican Republic	●	●	●	●	●	●	NA	NA
Ecuador	●	●	●	●	●	●	NA	NA
El Salvador	●	●	●	●	●	●	NA	NA
French Guiana	●	●	●	●	●	●	NA	NA
Guatemala	●	●	●	●	●	●	NA	NA
Guyana	●	●	●	●	●	●	NA	NA
Haiti	●	●	●	●	●	●	NA	NA
Honduras	●	●	●	●	●	●	NA	NA
Mexico	●	●	●	●	●	●	NA	NA
Nicaragua	●	●	●	●	●	●	NA	NA
Panama	●	●	●	●	●	●	NA	NA
Peru	●	●	●	●	●	●	NA	NA
Suriname	●	●	●	●	●	●	NA	NA
Venezuela (Bolivarian Republic of)	●	●	●	●	●	●	NA	NA
EASTERN MEDITERRANEAN								
Afghanistan	●	●	●	●	●	●	NA	NA
Djibouti	●	●	●	●	●	●	NA	NA
Iran (Islamic Republic of)	●	●	●	●	●	●	NA	NA
Pakistan	●	●	●	●	●	●	NA	NA
Saudi Arabia	●	●	●	●	●	●	NA	NA
Somalia	●	●	●	●	●	●	●	NA
Sudan	●	●	●	●	●	●	●	NA
Yemen	●	●	●	●	●	●	NA	NA
SOUTH-EAST ASIA								
Bangladesh	●	●	●	●	●	●	NA	NA
Bhutan	●	●	●	●	●	●	NA	NA
Democratic People's Republic of Korea	●	●	●	●	●	●	NA	NA
India	●	●	●	●	●	●	NA	NA
Indonesia	●	●	●	●	●	●	NA	NA
Myanmar	●	●	●	●	●	●	NA	NA
Nepal	●	●	●	●	●	●	NA	NA
Thailand	●	●	●	●	●	●	NA	NA
Timor-Leste	●	●	●	●	●	●	NA	NA
WESTERN PACIFIC								
Cambodia	●	●	●	●	●	●	NA	NA
China	●	●	●	●	●	●	NA	NA
Lao People's Democratic Republic	●	●	●	●	●	●	NA	NA
Malaysia	●	●	●	●	●	●	NA	NA
Papua New Guinea	●	●	●	●	●	●	●	NA
Philippines	●	●	●	●	●	●	NA	NA
Republic of Korea	●	●	●	●	●	●	NA	NA
Solomon Islands	●	●	●	●	●	●	NA	NA
Vanuatu	●	●	●	●	●	●	NA	NA
Viet Nam	●	●	●	●	●	●	NA	NA

ACT: artemisinin-based combination therapy; ANC: antenatal care; DDT: dichloro-diphenyl-trichloroethane; EPI: Expanded Programme on Immunization; G6PD: glucose-6-phosphate dehydrogenase; IM: intramuscular; IPTc: intermittent preventive treatment in children; IPTp: intermittent preventive treatment in pregnancy; IRS: indoor residual spraying; ITN: insecticide-treated mosquito net; LLIN: long-lasting insecticidal net; RDT: rapid diagnostic test; SMC: seasonal malaria chemoprevention; WHO: World Health Organization.

[1] Single dose of primaquine (0.75 mg base/kg) for countries in the WHO Region of the Americas.

[2] In May 2013, South Sudan was reassigned to the WHO African Region (WHA resolution 66.21, https://apps.who.int/gb/ebwha/pdf_files/WHA66/A66_R21-en.pdf).

[3] Where national data for the United Republic of Tanzania are unavailable, refer to Mainland and Zanzibar.

Testing				Treatment				
Patients of all ages should get diagnostic test	Malaria diagnosis is free of charge in the public sector	RDTs are used at community level	G6PD test is recommended before treatment with primaquine is used for treatment of *P. vivax* cases	ACT for treatment of *P. falciparum*	Pre-referral treatment with quinine or artemether IM or artesunate suppositories	Single dose of primaquine is used as gametocidal medicine for *P. falciparum*[1]	Primaquine is used for radical treatment of *P. vivax* cases	Directly observed treatment with primaquine is undertaken
●	●	●	●	●	●	●	●	●
●	●	●	●	●	●	●	●	●
●	●	●	●	●	●	●	●	●
●	●	●	●	●	●	●	●	●
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●	●	●	●	NA	●	●	●	●
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●	●	●	●	●	●	●	●	●
●	●	●	●	●	●	●	●	●

● = Policy adopted and implemented this year. Available data from the world malaria report data collection form provides evidence for implementation.

● = Policy adopted but not implemented this year (2018) or no supportive available data reported to WHO.

● = Policy not adopted.

NA = Question not applicable.

– = Question not answered and there is no information from previous years.

* Free for children and/or pregnant women only.

Annex 3 – B. Antimalarial drug policy, 2018

WHO region Country/area	*P. falciparum*				*P. vivax*
	Uncomplicated unconfirmed	Uncomplicated confirmed	Severe	Prevention during pregnancy	Treatment
AFRICAN					
Algeria	-	-	-	-	PQ
Angola	AL	AL	AS; QN	SP(IPT)	-
Benin	AL	AL	AS; QN	SP(IPT)	-
Botswana	AL	AL	QN	-	-
Burkina Faso	AL; AS+AQ	AL; AS+AQ	AS; QN	SP(IPT)	-
Burundi	AS+AQ	AS+AQ	AS; QN	SP(IPT)	-
Cabo Verde	AL	AL	QN	-	-
Cameroon	AS+AQ	AS+AQ	AS; AM; QN	SP(IPT)	-
Central African Republic	AL	AL	AS; AM; QN	SP(IPT)	-
Chad	AL; AS+AQ	AL; AS+AQ	AS; QN	SP(IPT)	-
Comoros	AL	AL	QN	SP(IPT)	-
Congo	AS+AQ	AS+AQ	QN	SP(IPT)	-
Côte d'Ivoire	AS+AQ	AS+AQ	QN	SP(IPT)	-
Democratic Republic of the Congo	AS+AQ	AS+AQ	AS; QN	SP(IPT)	-
Equatorial Guinea	AS+AQ	AS+AQ	AS	SP(IPT)	-
Eritrea	AS+AQ	AS+AQ	QN	-	AS+AQ+PQ
Eswatini	-	AL	AS	-	-
Ethiopia	AL	AL	AS; AM; QN	-	CQ
Gabon	AS+AQ	AS+AQ	AS; AM; QN	SP(IPT)	-
Gambia	AL	AL	QN	SP(IPT)	-
Ghana	AS+AQ	AL; AS+AQ	AS; AM; QN	SP(IPT)	-
Guinea	AS+AQ	AS+AQ	AS	SP(IPT)	-
Guinea-Bissau	AL	AL	AS; QN	SP(IPT)	-
Kenya	AL	AL	AS; AM; QN	SP(IPT)	-
Liberia	AS+AQ	AS+AQ	AS; AM; QN	SP(IPT)	-
Madagascar	AS+AQ	AS+AQ	QN	SP(IPT)	-
Malawi	AL	AL	AS; QN	SP(IPT)	-
Mali	AS+AQ	AL; AS+AQ	QN	SP(IPT)	-
Mauritania	AS+AQ	AL; AS+AQ	QN	-	-
Mayotte	-	AL	QN; AS; QN+AS; AS+D; QN+D	-	CQ+PQ
Mozambique	AL	AL	AS; QN	SP(IPT)	-
Namibia	AL	AL	QN	-	AL
Niger	AL	AL	AS; QN	SP(IPT)	-
Nigeria	AL; AS+AQ	AL; AS+AQ	AS; AM; QN	SP(IPT)	-
Rwanda	AL	AL	AS; QN	-	-
Sao Tome and Principe	AS+AQ	AS+AQ	QN	-	-
Senegal	AL; AS+AQ; DHA-PPQ	AL; AS+AQ; DHA-PPQ	AS; QN	SP(IPT)	-
Sierra Leone	AS+AQ	AL; AS+AQ	AS; AM; QN	SP(IPT)	-
South Africa	-	AL; QN+CL; QN+D	QN	-	AL+PQ; CQ+PQ
South Sudan[1]	AS+AQ	AS+AQ	AM; AS; QN	-	AS+AQ+PQ
Togo	AL; AS+AQ	AL; AS+AQ	AS; AM; QN	SP(IPT)	-
Uganda	AL	AL	AS; QN	SP(IPT)	-
United Republic of Tanzania	AL; AS+AQ	AL; AS+AQ	AS; AM; QN	-	-
Mainland	AL	AL	AS; AM; QN	SP(IPT)	-
Zanzibar	AS+AQ	AS+AQ	AS; QN	SP(IPT)	-
Zambia	AL	AL	AS; AM; QN	SP(IPT)	-
Zimbabwe	AL	AL	QN	SP(IPT)	-
AMERICAS					
Argentina	-	AL	AS; AL	-	CQ + PQ
Belize	-	CQ+PQ	QN; AL	-	CQ+PQ
Bolivia (Plurinational State of)	-	AL	AS	-	CQ+PQ
Brazil	-	AL+PQ; AS+MQ+PQ	AS	-	CQ+PQ
Colombia	-	AL+PQ	AS	-	CQ+PQ
Costa Rica	-	CQ+PQ	AL	-	CQ+PQ

WHO region Country/area	*P. falciparum*				*P. vivax*
	Uncomplicated unconfirmed	Uncomplicated confirmed	Severe	Prevention during pregnancy	Treatment
AMERICAS					
Dominican Republic	-	CQ+PQ	AS	-	CQ+PQ
Ecuador	-	AL+PQ	AS	-	CQ+PQ
El Salvador	-	CQ+PQ	AS	-	CQ+PQ
French Guiana	-	AL	AS	-	CQ+PQ
Guatemala	-	CQ+PQ	AS	-	CQ + PQ
Guyana	-	AL+PQ	AM	-	CQ+PQ
Haiti	-	CQ+PQ	QN	-	CQ+PQ
Honduras	-	CQ+PQ	QN; AS	-	CQ+PQ
Mexico	-	AL+PQ	AM; AL	-	CQ+PQ
Nicaragua	-	CQ+PQ	QN	-	CQ+PQ
Panama	-	AL+PQ	-	-	CQ+PQ
Paraguay	-	AL+PQ	AS	-	CQ+PQ
Peru	-	AS+MQ+PQ	AS+MQ	-	CQ+PQ
Suriname	-	AL+PQ	AS	-	CQ+PQ
Venezuela (Bolivarian Republic of)	-	AL+PQ	AS	-	CQ+PQ
EASTERN MEDITERRANEAN					
Afghanistan	CQ	AL+PQ	AS; AM; QN	-	CQ+PQ
Djibouti	AL	AL+PQ	AS	-	AL+PQ
Iran (Islamic Republic of)	-	AS+SP+PQ	AS; QN	-	CQ+PQ
Pakistan	CQ	AL+PQ	AS; QN	-	CQ+PQ
Saudi Arabia	-	AS+SP+PQ	AS; AM; QN	-	CQ+PQ
Somalia	AL	AL+PQ	AS; AM; QN	SP(IPT)	AL+PQ
Sudan	-	AL	AS; QN	-	AL+PQ
Yemen	AS+SP	AS+SP	AS, QN	-	CQ+PQ
SOUTH-EAST ASIA					
Bangladesh	-	AL	AS+AL; QN	-	CQ+PQ
Bhutan	-	AL	AM; QN	-	CQ+PQ
Democratic People's Republic of Korea	-	-	-	-	CQ+PQ
India	CQ	AS+SP+PQ; AL+PQ	AM; AS; QN	-	CQ+PQ
Indonesia	-	DHA-PPQ+PQ	AS; QN	-	DHA-PPQ+PQ
Myanmar	-	AL; AS+MQ; DHA-PPQ; PQ	AM; AS; QN	-	CQ+PQ
Nepal	-	AL+PQ	AS	-	CQ+PQ
Sri Lanka	-	AL+PQ	AS	-	CQ+PQ
Thailand	-	DHA-PPQ	AS	-	CQ+PQ
Timor-Leste	-	AL+PQ	AS; QN	-	AL+PQ
WESTERN PACIFIC					
Cambodia	-	AS+MQ	AM; AS; QN	-	AS+MQ+PQ
China	-	ART-PPQ; AS+AQ; DHA-PPQ; PYR	AM; AS; PYR	-	CQ+PQ; PQ+PPQ; ACTs+PQ; PYR
Lao People's Democratic Republic	AL+PQ	AL+PQ	AS+AL+PQ	-	AL+PQ; CQ+PQ
Malaysia	-	AS+MQ	AS+D; QN	-	ACT+PQ
Papua New Guinea	-	AL	AM; AS	SP(IPT)	AL+PQ
Philippines	AL	AL+PQ	QN+T; QN+D; QN+CL	SP(IPT)	CQ+PQ
Republic of Korea	CQ	-	QN	-	CQ+PQ
Solomon Islands	AL	AL	AS+AL; QN	CQ	AL+PQ
Vanuatu	-	AL	AS	CQ	AL+PQ
Viet Nam	DHA-PPQ	DHA-PPQ	AS; QN	-	CQ+PQ

ACT: artemisinin-based combination therapy; AL: artemether-lumefantrine; AM: artemether; AQ: amodiaquine; ART: artemisinin; AS: artesunate; AT: atovaquone; CL: clindamycline; CQ: chloroquine; D: doxycycline; DHA: dihydroartemisinin; IPT: intermittent preventive treatment; MQ: mefloquine; NQ: naphroquine; PG: proguanil; PPQ: piperaquine; PQ: primaquine; PYR: pyronaridine; QN: quinine; SP: sulfadoxine-pyrimethamine; T: tetracycline; WHO: World Health Organization.

[1] In May 2013, South Sudan was reassigned to the WHO African Region (WHA resolution 66.21, http://apps.who.int/gb/ebwha/pdf_files/WHA66/A66_R21-en.pdf).

Annex 3 - C. Funding for malaria control, 2016–2018

WHO region Country/area	Year	Contributions reported by donors			
		Global Fund[1]	PMI/USAID[2]	World Bank[3]	UK[4]
AFRICAN					
Algeria	2016	0	0	0	0
	2017	0	0	0	0
	2018	0	0	0	0
Angola	2016	2 725 165	28 133 718	0	0
	2017	15 453 275	22 496 168	0	0
	2018	12 123 750	22 000 000	0	0
Benin	2016	2 476 172	17 192 827	0	0
	2017	25 699 563	16 360 849	0	0
	2018	4 743 095	16 000 000	0	0
Botswana	2016	0	0	0	0
	2017	1 654 745	0	0	0
	2018	1 475 705	0	0	0
Burkina Faso	2016	29 722 841	14 587 854	5 420 843	58 501
	2017	9 680 365	25 563 827	10 570 944	1 375 065
	2018	32 552 591	25 000 000	10 570 944	991 422
Burundi	2016	7 877 578	9 898 901	0	0
	2017	28 433 018	9 202 978	0	0
	2018	1 805 521	9 000 000	0	0
Cabo Verde	2016	32 723	0	0	0
	2017	237 164	0	0	0
	2018	-19 013	0	0	0
Cameroon	2016	11 081 109	0	0	0
	2017	23 218 072	20 451 062	0	0
	2018	17 076 812	22 500 000	0	0
Central African Republic	2016	2 221 630	0	0	0
	2017	13 524 488	0	0	0
	2018	17 167 200	0	0	0
Chad	2016	34 361 246	0	0	0
	2017	14 272 836	0	0	0
	2018	18 323 111	0	0	0
Comoros	2016	3 017 257	0	0	0
	2017	860 330	0	0	0
	2018	2 298 799	0	0	0
Congo	2016	0	0	0	0
	2017	0	0	0	0
	2018	1 186 414	0	0	0
Côte d'Ivoire	2016	62 118 732	0	0	0
	2017	31 403 441	25 563 827	0	0
	2018	27 474 941	25 000 000	0	0
Democratic Republic of the Congo	2016	120 394 350	52 099 477	0	7 437 989
	2017	128 846 868	51 127 654	0	6 084 289
	2018	77 617 223	50 000 000	0	4 386 772
Equatorial Guinea	2016	0	0	0	0
	2017	0	0	0	0
	2018	0	0	0	0
Eritrea	2016	6 905 539	0	0	0
	2017	13 301 118	0	0	0
	2018	4 791 899	0	0	0
Eswatini	2016	897 122	0	0	0
	2017	1 686 517	0	0	0
	2018	579 780	0	0	0

Contributions reported by countries							
Government (NMP)	Global Fund	World Bank	PMI/USAID	Other bilaterals	WHO	UNICEF	Other contributions[7]
1 743 483	0	0	0	0		0	0
1 748 498	0	0	0	0	43 809	0	0
1 812 462	0	0	0	0	9 214	0	0
50 874 556 [6]	16 852 909		27 000 000				
9 020 546	12 023 625		18 000 000		139 995		
46 457 232 [5]	9 578 147		22 000 000		88 217		
17 540 458 [5]	13 424 427	230 534	3 387 786		148 346	179 879	
4 395 380	33 122 938	0	9 642 332	3 140	158 723	5 400	
611 841	2 235 811	0	1 419 738	0	21 292	75 628	0
1 310 536	2 019 079	0	0	0		0	0
1 092 695	1 079 069	0	0	0		0	0
2 124 880	2 087 088	0	0	0		0	0
805 813	41 106 186	2 522 884	5 849 900		20 367	179 278	3 638 120
15 573 795	9 474 402	5 608 893	13 053 101		164 363	163 431	5 570 878
123 337	14 880 669	5 321 114	16 646 476		431 795	228 084	2 900 368
3 050 306	4 759 452		9 500 000		18 579	786 133	
3 070 872	21 228 086		9 000 000		37 832	4 967 372	869 962
1 157 984	4 734 738		9 000 000		68 488	433 441	4 664 286
1 229 033 [5]	315 038				59 219		
4 627 843	466 244				29 000		
621 612	221 609				25 641		
1 989 500	14 478 500				747 500		2 024 000
2 288 193 [5]	28 008 486				882 650	1 105 377	9 477
10 607 209 [5]	47 200 683		29 913 228				
530 000	4 724 918				150 000		
530 000	443 466				70 419		
675 455	8 399 445				50 000	306 968	
1 000 000 [5]	504 853			73 721	1 000	263 754	
641 141 [6]	34 927 891				416	540 870	867 119
534 407 [6]							
114 684	2 154 616				15 000		
114 684	852 996	0	0	0	54 000		0
114 684		0	0	0	60 000		0
118 498	0	0	0	0	24 727	2 863	0
122 182	0	0	0	0	15 000	0	10 000
50 509	9 090 909	0	0	0	0	0	9 090
4 688 040	60 352 423	0	0	0	13 627	35 933	0
5 380 263	95 971 000	0	0	0	18 218	76 943	10 319
7 493 797 991	6 619 727 462	0	25 000 000	0	0	874 070 529	0
7 327 062	143 685 771	0	49 325 000	8 063 499	3 677 567	4 771 747	0
683 314	75 183 622	0	46 738 755	4 694 136	2 265 298	82 857	0
1 948 241	92 444 112	0	49 075 000	0	636 951	0	0
3 122 871 [6]							
3 153 487 [6]							
3 153 487 [6]							
397 657 [6]	16 685 629	0	0	0	200 000	0	0
401 555 [6]	9 150 700	0	0	0	80 450	0	
401 555 [6]	2 748 778	0	0	0	82 500	0	0
1 112 523	1 719 139	0	0	0		0	
10 019 754	20 910 608	0	0	0	620 000	0	0
989 110	1 376 660	0	0	0		0	0

Annex 3 - C. Funding for malaria control, 2016–2018

WHO region Country/area	Year	Contributions reported by donors			
		Global Fund[1]	PMI/USAID[2]	World Bank[3]	UK[4]
AFRICAN					
Ethiopia	2016	26 310 036	41 679 582	0	0
	2017	73 672 826	37 834 464	0	0
	2018	36 485 376	36 000 000	0	0
Gabon	2016	-574	0	0	0
	2017	0	0	0	0
	2018	0	0	0	0
Gambia	2016	3 171 117	0	0	336 595
	2017	10 403 537	0	0	0
	2018	7 988 886	0	0	0
Ghana	2016	39 257 572	29 175 707	0	5 224 120
	2017	40 834 747	28 631 486	0	1 136 043
	2018	44 164 622	28 000 000	0	819 087
Guinea	2016	29 160 172	15 629 843	255 449	0
	2017	14 405 410	15 338 296	535 378	0
	2018	12 534 176	15 000 000	535 378	0
Guinea-Bissau	2016	9 113 073	0	0	0
	2017	6 739 432	0	0	0
	2018	7 686 968	0	0	0
Kenya	2016	11 362 945	36 469 634	0	6 776 489
	2017	60 499 518	35 789 358	0	990 329
	2018	12 442 150	35 000 000	0	714 027
Liberia	2016	6 373 170	14 587 854	0	0
	2017	14 115 769	14 315 743	0	0
	2018	20 155 173	14 000 000	0	0
Madagascar	2016	12 460 235	27 091 728	0	0
	2017	14 309 923	26 586 380	0	0
	2018	40 366 061	26 000 000	0	0
Malawi	2016	16 538 845	22 923 770	0	3 783 827
	2017	11 926 740	22 496 168	0	0
	2018	30 542 662	24 000 000	0	0
Mali	2016	9 714 772	26 049 738	4 888 374	125 410
	2017	23 204 310	25 563 827	5 578 034	0
	2018	30 478 473	25 000 000	5 578 034	0
Mauritania	2016	1 861 629	0	0	0
	2017	4 592 194	0	0	0
	2018	4 020 544	0	0	0
Mozambique	2016	61 708 435	30 217 697	1 431 916	0
	2017	63 584 965	29 654 039	1 995 892	7 668 217
	2018	35 773 022	29 000 000	1 995 892	5 528 785
Namibia	2016	2 212 537	0	0	0
	2017	2 707 554	0	0	0
	2018	742 672	0	0	0
Niger	2016	9 226 298	0	3 837 140	0
	2017	24 712 609	18 405 955	6 472 782	0
	2018	28 316 962	18 000 000	6 472 782	0
Nigeria	2016	106 477 832	78 149 215	13 526 155	2 946 514
	2017	121 497 648	76 691 481	0	0
	2018	66 607 410	70 000 000	0	0
Rwanda	2016	22 669 934	18 755 812	0	0
	2017	17 066 738	18 405 955	0	0
	2018	9 931 433	18 000 000	0	0

Contributions reported by countries							
Government (NMP)	Global Fund	World Bank	PMI/USAID	Other bilaterals	WHO	UNICEF	Other contributions[7]
18 947 911	49 500 000		10 600 000		0	30 000	13 500 000
19 401 447	31 604 918		7 150 000		0	30 000	13 500 000
20 758 465	44 800 000		26 358 971				14 000 000
1 410 426 [6]	0	0	0	0		0	
142 296	0	0	0	0	12 616	0	0
0	0	0	0	0	128 016	0	49 674
604 456 [6]	9 352 149				0	0	1 031 868
610 382 [6]	9 557 650				14 400	33 839	117 749
1 327 049	8 376 620				39 000	50 414	176 987
9 856 505	36 596 848	0	28 000 000	9 883 185	300 000	0	0
683 179	40 951 105	0	22 445 306		140 000	0	0
140 392 544	47 579 039	0	30 634 694	7 560 000	300 000	0	0
4 229 893	36 810 868		15 000 000	2 235 000	91 500	5 001	636 998
14 796 [5]	9 251 505	125 000	12 500 000		65 000		
6 438 381	12 000 000	156 000	14 000 000		45 000		
241 163	8 972 945	0	0	0		0	269 981
1 655 769	9 086 476	0	0	0		0	256 659
651 820	3 199 732	0	0	0		0	0
1 633 148 [6]							
1 649 159 [6]							
1 649 159 [6]							
305 428 [6]							
308 423 [6]	18 526 566		14 000 000				
308 423 [6]							
32 100	6 395 563	0	26 000 000	0	486 635		
37 214	43 205 989	0	26 000 000	0	220 000	0	0
13 007	33 200 289	0	26 000 000		46 000		
347 710 [5]			22 000 000				
291 194 [5]	16 282 087		22 000 000				
282 401	33 049 389		20 000 000				
3 263 366	16 374 449		25 500 000		4 983	2 203 890	
4 382 069	19 288 748	3 226 759	25 500 000	0	140 713	854 199	
14 329 420	54 053 651	6 406 499	25 000 000			337 884	
2 450 845		3 500 400			220	384 900	
605 079 [5]	6 957 945				47 950		13 944
2 191 549	164 778						
1 237 214	190 374 239		29 000 000		325 000	1 250 640	
76 074	58 222 077		29 000 000		240 000	3 848 028	10 995
2 136 147	45 915 417		29 000 000			1 590 000	4 361 414
5 218 841	4 227 559	0	0	0	100 000	0	878 882
5 166 667	1 096 657	0	0	0	100 000	0	789 566
11 216 160	908 515	0	0	0	100 000	100 000	1 148 515
2 672 787	14 911 144	641 402	106 000	0	75 586	39 712	39 712
4 454 320	22 404 758	2 177 698	220 000	0	328 594	805 598	476 444
7 363 777	20 159 800	4 490 567	18 000 000	0	220 356	674 811	0
476 077 607	372 939 170		75 000 000	2 967 421			
107 005 355	198 176 039		75 000 000				
2 232 700 [6]	43 206 463		70 000 000				
16 853 782	30 497 401		18 000 000		72 000		
13 704 611	11 440 292		18 000 000		270 000		
13 460 220	27 505 974		18 000 000				

Annex 3 - C. Funding for malaria control, 2016–2018

WHO region Country/area	Year	Contributions reported by donors			
		Global Fund[1]	PMI/USAID[2]	World Bank[3]	UK[4]
AFRICAN					
Sao Tome and Principe	2016	2 945 763	0	0	0
	2017	2 978 337	0	0	0
	2018	0	0	0	0
Senegal	2016	10 227 184	25 007 749	0	0
	2017	5 941 567	25 563 827	0	0
	2018	12 400 978	24 000 000	0	0
Sierra Leone	2016	5 776 307	0	0	7 657 486
	2017	1 521 619	15 338 296	0	1 264 107
	2018	1 442 219	15 000 000	0	911 421
South Africa	2016	0	0	0	48 271
	2017	0	0	0	0
	2018	0	0	0	0
South Sudan[8]	2016	6 625 486	6 251 937	0	21 105 454
	2017	23 225 030	0	0	13 351 190
	2018	11 119 479	0	0	9 626 208
Togo	2016	4 909 746	0	1 868 045	0
	2017	18 204 847	0	2 334 730	0
	2018	6 564 615	0	2 334 730	0
Uganda	2016	76 258 031	35 427 644	0	30 424 581
	2017	54 107 401	33 744 252	0	7 293 653
	2018	64 750 030	33 000 000	0	5 258 724
United Republic of Tanzania[9]	2016	62 681 243	0	0	0
	2017	72 183 435	0	0	0
	2018	0	0	0	0
Mainland	2016	61 652 875	0	0	0
	2017	69 674 305	0	0	0
	2018	0	0	0	0
Zanzibar	2016	1 028 368	0	0	0
	2017	2 509 129	0	0	0
	2018	0	0	0	0
Zambia	2016	27 622 155	26 049 738	286 668	28 080
	2017	40 378 684	30 676 592	606 731	0
	2018	22 106 638	30 000 000	606 731	0
Zimbabwe	2016	17 000 019	15 629 843	0	0
	2017	17 503 053	15 338 296	0	0
	2018	12 952 709	15 000 000	0	0
AMERICAS					
Belize	2016	0	0	0	0
	2017	0	0	0	0
	2018	0	0	0	0
Bolivia (Plurinational State of)	2016	4 324 861	0	0	0
	2017	2 805 373	0	0	0
	2018	3 347 788	0	0	0
Brazil	2016	0	0	0	0
	2017	0	0	0	0
	2018	0	0	0	0
Colombia	2016	0	0	0	0
	2017	0	0	0	0
	2018	0	0	0	0

Contributions reported by countries							
Government (NMP)	Global Fund	World Bank	PMI/USAID	Other bilaterals	WHO	UNICEF	Other contributions[7]
1 745 437	2 261 202	0	0	1 000 000	52 985	2 826	4 584
2 044 439	3 296 207	0	0	0	89 244	0	0
0 [6]							
4 816 000	1 865 570	0	24 000 000	0	7 828	28 795	24 167
4 931 741	3 039 725	0	24 000 000	0	0	0	4 500 000
4 931 741	11 602 821	0	24 000 000	11 602 821	0	0	0
346 772 [5]	5 389 748				36 569	55 295	
807 592 [6]	19 300 000				72 812	3 464 362	
65 189 [5]	8 728 599		15 000 000		70 000	148 214	2 742
15 428 406	0	0	0	0	0	0	75 061
10 656 029	27 226 495	0	0	0	20 000	0	0
16 954 533	4 197 290	0	0	0	50 000	0	
8 919 615 [5]	20 288 506	7 000 000	6 000 000	6 000 808	4 779 900	12 812 860	6 758 505
2 603 242 [5]	16 478 112	0	6 000 000	6 654 000	200 000		5 249 000
2 658 638 [6]							
68 213	2 973 548	943 022	0	0	7 158	169 496	10 650
1 847 898	24 435 381	1 014 708	0	0	7 765	556 712	5 238 461
64 103	23 830 061	440 567	0	0	4 715	553 567	0
7 585 730	31 501 450	0	33 000 000	29 246 018		743 791	3 772 657
7 280 412	150 649 446	0	34 000 000	8 974 881		743 791	4 335 860
7 243 128	47 530 743	0	33 000 000	14 073 138		743 791	0
5 873 258 [6]	104 603 541	37 578 250	2 888 539	5 466 569	0	0	0
70 283 449 [6]	73 235 141	0	978 962		52 000		
145 338 516 [6]	146 767 363	0	16 104 693	0	14 574	0	12 168
5 858 187	103 964 466	37 578 250	2 025 000	4 982 394	0	0	0
70 274 555	70 274 555				42 000		
145 258 808	145 258 808		713 228				12 168
15 071	639 075	0	863 539	484 175	0	0	0
8 894	2 960 586	0	978 962		10 000		
79 708	1 508 555	0	15 391 465	0	14 574	0	0
25 500 000	20 134 623		24 000 000		200 000		
27 928 587	45 468 736		25 000 000		200 000		
18 159 340	24 605 077		3 000 000		200 000		3 692 991
675 000	21 823 373		12 000 000		46 698		
782 250	17 407 287		15 120 000				224 970
2 786 540	16 973 379	0	11 000 000	0	118 000	0	0
248 000	0	0	1 419	0	0	0	0
250 000	0	0	9 778	0	0	0	0
252 000	11 122	0	3 234	0	5 609	0	0
425 405	2 846 786	0	0	0		0	
451 993		0	0	0		0	0
416 666							
44 240 812 [5]	0	0		0		0	
54 904 744 [5]	0	0		0		0	
61 816 864 [5]	0	0	82 861	0		0	
10 159 785	0	0	147 210	0	14 660	0	0
10 897 170	0	0	2 872	0	0	0	0
3 237 708	0	0	70 647				

Annex 3 - C. Funding for malaria control, 2016–2018

WHO region Country/area	Year	Contributions reported by donors			
		Global Fund[1]	PMI/USAID[2]	World Bank[3]	UK[4]
AMERICAS					
Costa Rica	2016	0	0	0	0
	2017	0	0	0	0
	2018	0	0	0	0
Dominican Republic	2016	0	0	0	0
	2017	0	0	0	0
	2018	0	0	0	0
Ecuador	2016	0	0	0	0
	2017	-598 176	0	0	0
	2018	0	0	0	0
El Salvador	2016	0	0	0	0
	2017	0	0	0	0
	2018	636 619	0	0	0
French Guiana	2016	0	0	0	0
	2017	0	0	0	0
	2018	0	0	0	0
Guatemala	2016	1 859 389	0	0	0
	2017	2 296 407	0	0	0
	2018	2 190 728	0	0	0
Guyana	2016	-61 194	0	0	0
	2017	761 382	0	0	0
	2018	58 421	0	0	0
Haiti	2016	6 410 459	0	0	0
	2017	10 667 044	0	0	0
	2018	5 481 055	0	0	0
Honduras	2016	1 227 533	0	0	0
	2017	1 231 343	0	0	0
	2018	1 115 139	0	0	0
Mexico	2016	0	0	0	0
	2017	0	0	0	0
	2018	0	0	0	0
Nicaragua	2016	5 281 217	0	0	0
	2017	2 491 441	0	0	0
	2018	2 289 236	0	0	0
Panama	2016	0	0	0	0
	2017	0	0	0	0
	2018	0	0	0	0
Paraguay	2016	1 547 843	0	0	0
	2017	334 089	0	0	0
	2018	0	0	0	0
Peru	2016	0	0	0	0
	2017	0	0	0	0
	2018	0	0	0	0
Suriname	2016	170 752	0	0	0
	2017	1 168 802	0	0	0
	2018	819 904	0	0	0
Venezuela (Bolivarian Republic of)[10]	2016	0	0	0	0
	2017	0	0	0	0
	2018	0	0	0	0

Contributions reported by countries							
Government (NMP)	Global Fund	World Bank	PMI/USAID	Other bilaterals	WHO	UNICEF	Other contributions[7]
5 090 000 [5]	14 000	0	1 624	0	3 000	0	0
4 980 000 [5]	0	0	0	0	9 770	0	0
5 000 000 [5]	0	0	0	0	12 155	0	0
3 525 868	0	0	0	0	0	0	334 363
1 149 368	125 543	0	0	0	824	0	27 987
367 647	9 949 957	0	0	0	143 176	0	48 938
20 000 000 [5]	0	0		0	69 279	0	0
5 835 716 [5]	0	0		0	69 039	0	0
6 898 763 [5]	0	0	0	0	85 733	0	
2 662 869	166 311	0	1 089	0	4 733	0	65 789
2 662 869	538 732	0	0	0	73 758	0	0
3 950 441	707 436	0	0	0	15 156	0	0
0 [6]	0	0	0	0	0	0	0
0 [6]	0	0	0	0	0	0	0
0 [6]							
2 639 249	10 669 242	0		0		0	
3 374 612	2 231 020		75 981				
3 492 749	1 724 076	0	138 643	0		0	580 000
521 018	338 772	0	98 000	0	50 000	0	0
1 473 101	1 009 615	0	8 015	0	9 793	0	0
1 503 535	340 471	0	211 698	0	0	0	0
362 174 [5]	4 926 108	0	0	500 000	227 455		330 566
381 452 [6]	12 540 295	0	17 956	500 000	227 455		196 777
408 174 [5]	7 384 832	0	0	0	275 872		514 271
543 312	3 413 845		7 840	0	0	0	
543 312	2 594 856	0	54 475	0	0	0	554 378
543 312	1 929 881	0	46 855	0	36 961	0	714 145
43 376 321	0	0	0	0		0	0
40 661 276	0	0	0	0		0	0
37 544 836	0	0	0	0		0	0
3 544 313	3 727 737	0		0	8 250	0	
3 984 944	1 826 934		23 971		98 131		
3 263 970	1 986 357		13 254		83 000		401 133
3 822 596		0	23 247	0	9 665	0	
3 671 002			49 705		7 087		
8 000 000 [5]	0	0	59 277	0	18 823	0	
2 264 399	1 517 493	0	0	0	0	0	0
2 883 082	593 059	0	0	0	0	0	0
-							
180 563	0	0	183 809	0		0	0
2 074 113 [6]			39 886		168 737		
1 774 350			90 000				
106 372 [6]	945 713	0	16 151	0	60 176	0	0
61 800	1 041 205	0	52 213	0	12 920	0	0
63 194 [6]		0	22 037	0		0	
2 200 925	945 713	0	0	0	21 411	0	0
29 452 393 982 [5]			0		85 193		
573 136 589			0		435 366		

Annex 3 - C. Funding for malaria control, 2016–2018

WHO region Country/area	Year	Contributions reported by donors			
		Global Fund[1]	PMI/USAID[2]	World Bank[3]	UK[4]
EASTERN MEDITERRANEAN					
Afghanistan	2016	5 945 750	0	0	0
	2017	7 043 533	0	0	0
	2018	9 556 500	0	0	0
Djibouti	2016	4 738 086	0	138 717	0
	2017	2 617 141	0	230 220	0
	2018	652 220	0	230 220	0
Iran (Islamic Republic of)	2016	1 798 772	0	0	0
	2017	1 113 357	0	0	0
	2018	0	0	0	0
Pakistan	2016	11 332 383	0	0	0
	2017	16 609 001	0	0	0
	2018	13 590 722	0	0	0
Saudi Arabia	2016	0	0	0	0
	2017	0	0	0	0
	2018	0	0	0	0
Somalia	2016	9 829 626	0	0	0
	2017	16 327 923	0	0	0
	2018	7 501 955	0	0	0
Sudan	2016	55 654 840	0	0	0
	2017	10 485 931	0	0	0
	2018	34 723 839	0	0	0
Yemen	2016	4 706 687	0	0	0
	2017	3 664 258	0	1 553 074	0
	2018	-7 248	0	0	0
SOUTH-EAST ASIA					
Bangladesh	2016	6 658 153	0	0	0
	2017	12 956 676	0	0	0
	2018	6 940 221	0	0	0
Bhutan	2016	455 891	0	0	0
	2017	572 637	0	0	0
	2018	326 974	0	0	0
Democratic People's Republic of Korea	2016	3 781 468	0	0	0
	2017	1 523 252	0	0	0
	2018	2 314 541	0	0	0
India	2016	4 248 221	0	0	0
	2017	67 799 731	0	0	0
	2018	270 626	0	0	0
Indonesia	2016	11 275 924	0	0	49 453
	2017	23 553 669	0	0	0
	2018	9 987 790	0	0	0
Myanmar	2016	35 058 903	10 419 895	0	12 914 507
	2017	40 780 480	10 225 531	0	3 913 209
	2018	17 007 953	10 000 000	0	2 821 423
Nepal	2016	3 101 226	0	0	0
	2017	5 165 221	0	0	0
	2018	1 408 576	0	0	0
Thailand	2016	9 107 668	0	0	0
	2017	10 956 433	0	0	0
	2018	6 040 728	0	0	0
Timor-Leste	2016	3 233 190	0	0	0
	2017	2 688 860	0	0	0
	2018	2 427 241	0	0	0

Contributions reported by countries							
Government (NMP)	Global Fund	World Bank	PMI/USAID	Other bilaterals	WHO	UNICEF	Other contributions[7]
944 566 [6]	9 762 977				12 905		
921 528 [6]	1 053 356				85 814		
200 000 [6]	10 556 626				26 571		
4 547 153 [5]	4 547 153	0		1 000 000	25 000	25 000	
3 222 506 [5]		0		0	51 000	0	
3 295 183 [6]	871 414			0	30 000	0	
2 500 000	1 364 857						
2 700 000					48 000		
3 300 000	0	0	0		38 286		
16 400 000	11 536 047				300 000		
18 344 729 [6]	22 635 097				130 000		
3 774 306	9 615 605				196 378		
30 000 000	0	0	0	0	7 500	0	0
30 000 000	0	0	0	0	100 000	0	0
30 000 000	0	0	0	0	10 000	0	0
81 200	9 946 059	0	0	0	135 000		0
85 350	20 986 170	0	0	0	147 000		0
90 726	5 534 919	0	0	0	56 000		0
24 209 740	61 304 230	0	0	0	93 302	1 200 574	0
19 087 941	31 496 505	0	0	0	3 084	0	0
16 726 945	21 485 294	0	0	0	60 000	203 000	9 619
0	1 140 758	0	0	0	105 000	0	
0	7 933 620				2 080 000	473 627	
0 [5]	1 890 037				1 427 948		
1 162 970	9 734 466	0	0	0	188 000	0	0
1 493 690	8 821 888	0	0	0	210 000	0	0
2 496 429	6 835 307	0	0	0	250 000	0	0
163 046	550 197	0	0	0	40 273	0	72 424
179 470	586 015	0	0	0	35 212	0	121 212
176 791	577 403	0	0	0	34 687	0	0
2 080 000	3 775 232	0	0	0	35 000	0	
2 151 000	3 426 508	0	0	0	35 000	0	0
2 181 000	3 219 957	0	0	0		0	
48 364 518	15 892 221	0	0	0		0	
145 564 257	94 474 099	0	0	0		0	
46 783 323	34 958 663	0	0	0		0	
20 307 710 [5]	10 821 533	0	0	0	228 000	1 938 220	0
17 686 075 [5]	30 336 061				147 033	1 385 855	
21 683 909 [5]	12 272 515				260 738	115 242	
6 437 430 [5]	55 302 769		9 000 000	6 607 886	25 000		
6 780 092 [6]	53 056 520	0	10 000 000	6 532 464	25 000	0	3 462 068
6 780 092 [6]	29 581 578		9 000 000	6 607 886	25 000		
966 200 [5]	10 228 041	0	69 334	0	23 000		
263 262	102 424				24 509		
613 873	1 107 196	0	120 482	0	31 214	0	0
8 502 036	13 984 633	0	0	0	103 514	0	61 463
7 664 899	15 622 625	0			188 686		49 859
7 131 736	8 337 877	0	1 308 800	0	78 056	0	93 546
1 523 993	3 261 859	0	0	0	45 868	0	20 000
1 115 484	4 039 622	0	0	0	42 456	0	20 000
1 121 287	1 573 936	0	0	0	26 600	0	5 000

Annex 3 - C. Funding for malaria control, 2016–2018

WHO region Country/area	Year	Contributions reported by donors			
		Global Fund[1]	PMI/USAID[2]	World Bank[3]	UK[4]
WESTERN PACIFIC					
Cambodia	2016	8 383 140	6 251 937	0	0
	2017	14 368 640	10 225 531	0	0
	2018	10 380 499	10 000 000	0	0
China	2016	-317 097	0	0	0
	2017	0	0	0	0
	2018	0	0	0	0
Lao People's Democratic Republic	2016	5 920 486	0	0	0
	2017	3 667 214	0	0	0
	2018	3 901 819	0	0	0
Malaysia	2016	0	0	0	779 447
	2017	0	0	0	0
	2018	0	0	0	0
Papua New Guinea	2016	7 880 106	0	0	135 199
	2017	10 563 330	0	0	0
	2018	7 276 337	0	0	0
Philippines	2016	3 531 540	0	0	0
	2017	7 342 397	0	0	0
	2018	3 195 184	0	0	0
Republic of Korea	2016	0	0	0	0
	2017	0	0	0	0
	2018	0	0	0	0
Solomon Islands	2016	2 540 226	0	0	0
	2017	1 025 914	0	0	0
	2018	1 729 636	0	0	0
Vanuatu	2016	0	0	0	0
	2017	0	0	0	0
	2018	0	0	0	0
Viet Nam	2016	6 091 536	0	0	0
	2017	15 802 793	0	0	0
	2018	9 296 596	0	0	0

NMP: National Malaria Programme; PMI: United States President's Malaria Initiative; UK: United Kingdom of Great Britain and Northern Ireland government; UNICEF: United Nations Children's Fund; USAID: United States Agency for International Development; WHO: World Health Organization.

"–" refers to data not available.

[1] Source: Global Fund to Fight AIDS, Tuberculosis and Malaria.

[2] Source: www.foreignassistance.gov.

[3] Source: Organisation for Economic Co-operation and Development (OECD) creditor reporting system (CRS) database.

[4] Source: OECD CRS database.

[5] Budget not expediture.

Contributions reported by countries							
Government (NMP)	Global Fund	World Bank	PMI/USAID	Other bilaterals	WHO	UNICEF	Other contributions[7]
22 297	2 002 435	0	6 000 000	0	304 651	0	
663 526	8 045 144	0	6 000 000	0	579 738	0	
83 636	3 181 783	0	10 000 000	0	628 297	0	
18 929 499 [6]							
19 115 082 [6]							
19 602 589 [6]							
260 975	5 050 407	0	340 021	184 632	75 000	0	45 199
1 008 060	1 728 818	0	604 000	0	256 734	0	1 066 089
1 914 750	3 725 427	0	500 000	0	288 108	0	1 783 267
39 703 616	0	0	0	0	0	0	0
48 365 863	0	0	0	0	0	0	0
49 561 180	0	0	0	0	0	0	0
181 200	5 900 000	0	0	0	56 000	0	0
753 771	10 330 449	0	0	0	95 000	0	911 770
108 100	7 407 034	0	0	0	86 500	0	1 083 168
6 720 000 [5]	3 944 923	0	0	0	0	0	0
7 012 009	6 471 549	0	0	0	0	0	0
3 548 266	4 190 984	0	0	0	0	0	0
526 499	0	0	0	0	0	0	0
475 173	0	0	0	0	0	0	0
433 726	0	0	0	0	0	0	0
327 032	1 309 126	0	0	448 718	358 000	0	0
858 256	977 025	0	0	0	736 892	0	0
979 891	1 494 080				79 770		
196 760	927 486	0	0	249 071	148 217	0	0
139 254	285 333	0	0	206 575	21 918	0	0
128 194	131 786	0	0	92 363	9 367	0	0
801 554	11 088 506				200 764		200 000
3 022 523	9 324 657	0	0	0	200 000	0	500 000
1 813 863	7 901 624	0	0	0	105 045	0	315 396

[6] WHO NMP funding estimates.

[7] Other contributions as reported by countries: NGOs, foundations, etc.

[8] South Sudan became an independent State on 9 July 2011 and a Member State of WHO on 27 September 2011. South Sudan and Sudan have distinct epidemiological profiles comprising high-transmission and low-transmission areas, respectively. For this reason data up to June 2011 from the high-transmission areas of Sudan (10 southern states which correspond to contemporary South Sudan) and low-transmission areas (15 northern states which correspond to contemporary Sudan) are reported separately.

[9] Where national totals for the United Republic of Tanzania are unavailable, refer to the sum of Mainland and Zanzibar.

[10] Government contributions for 2016, 2017 and 2018 are indicated in local currency during that period.

Note: Negative disbursements reflect recovery of funds on behalf of the financing organization.

Annex 3 - D. Commodities distribution and coverage, 2016–2018

WHO region Country/area	Year	No. of LLINs sold or delivered	Modelled percentage of population with access to an ITN	No. of people protected by IRS	No of RDTs distributed	Any first-line treatment courses delivered (including ACT)	ACT treatment courses delivered
AFRICAN							
Algeria	2016	0	-	-	0	432	-
	2017	0	-	-	36	453	-
	2018	0	-	-	0	1 242	-
Angola	2016	3 507 740	21	-	3 000 000	4 000 000	4 000 000
	2017	2 924 769	32	-	397 882	3 090 761	3 090 761
	2018	3 863 521	38	-	2 000 350	1 950 000	1 950 000
Benin	2016	720 706	36	853 221	1 500 047	1 199 055	1 199 055
	2017	6 771 009	44	853 221	2 171 867	1 530 617	1 530 617
	2018	0	59	1 321 758	2 016 745	1 815 236	1 815 236
Botswana	2016	116 048	-	115 973	2 196	1 634	1 634
	2017	3 000	-	139 244	2 645	4 429	4 429
	2018	-	-	83 488	3 141	1 954	1 954
Burkina Faso	2016	10 924 031	62	-	11 974 810	9 519 568	9 519 568
	2017	986 164	68	-	12 853 861	10 457 752	10 457 752
	2018	1 946 047	48	766 374	13 026 870	11 968 368	11 968 368
Burundi	2016	755 182	49	-	8 077 703	8 277 026	8 031 773
	2017	6 717 994	58	848 441	10 046 047	7 978 264	7 613 646
	2018	986 025	81	1 754 679	7 012 203	5 149 436	5 032 209
Cabo Verde	2016	0	-	349 126	8 906	71	71
	2017	80	-	495 313	16 573	420	420
	2018	21	-	-	9 588	21	21
Cameroon	2016	9 588 733	56	-	1 380 725	1 093 036	1 093 036
	2017	362 629	67	-	1 589 218	879 039	785 765
	2018	573 843	55	-	1 739 286	1 064 668	918 505
Central African Republic	2016	57 110	59	-	1 651 645	1 714 647	1 714 647
	2017	857 198	59	-	806 218	947 205	947 205
	2018	753 889	63	-	1 189 881	1 773 072	1 773 072
Chad	2016	384 606	15	-	882 617	-	-
	2017	6 886 534	45	-	1 287 405	1 486 086	1 486 086
	2018	-	65	-	-	-	-
Comoros	2016	451 358	73	-	61 600	1 373	1 373
	2017	34 590	89	-	21 988	2 794	2 794
	2018	31 012	77	-	-	-	-
Congo	2016	1 291	39	-	45 000	0	0
	2017	2 223	27	-	0	0	0
	2018	4 641	29	-	0	0	0
Côte d'Ivoire	2016	1 177 906	69	-	5 351 325	4 964 065	4 964 065
	2017	13 216 468	70	-	6 986 825	5 373 545	5 373 545
	2018	15 875 381	80	-	6 069 250	6 799 565	6 799 565
Democratic Republic of the Congo	2016	31 439 920	70	916 524	18 630 636	17 258 290	17 258 290
	2017	8 412 959	75	232 181	18 994 861	17 250 728	17 250 728
	2018	16 919 441	71	111 735	18 549 327	16 917 207	16 917 207
Equatorial Guinea	2016	66 232	34	82 749	62 133	18 072	18 072
	2017	42 317	34	64 617	60 798	15 341	15 341
	2018	120 376	34	74 416	78 695	15 633	15 633
Eritrea	2016	156 553	46	364 007	0	177 525	177 525
	2017	1 724 972	50	375 696	481 600	296 399	296 399
	2018	60 083	58	376 143	400 900	301 525	301 525
Eswatini	2016	4 758	-	24 179	56 780	600	600
	2017	0	-	21 316	59 760	900	861
	2018	0	-	39 144	61 974	631	579
Ethiopia	2016	13 266 926	62	15 050 413	9 742 450	6 530 973	5 239 080
	2017	2 755 700	55	17 628 133	6 400 000	8 470 000	7 300 000
	2018	11 100 000	39	10 486 854	4 053 200	3 773 179	3 036 690

WHO region Country/area	Year	No. of LLINs sold or delivered	Modelled percentage of population with access to an ITN	No. of people protected by IRS	No of RDTs distributed	Any first-line treatment courses delivered (including ACT)	ACT treatment courses delivered
AFRICAN							
Gabon	2016	9 660	9	0	0	0	0
	2017	–	8	–	0	0	0
	2018	4 582	7	–	71 787	–	208 953
Gambia	2016	113 385	55	399 176	1 017 889	272 895	272 895
	2017	1 051 391	64	396 546	767 984	174 556	174 166
	2018	115 801	77	426 788	678 621	113 563	113 563
Ghana	2016	5 962 179	68	1 409 967	4 823 250	2 289 145	2 289 145
	2017	3 059 363	66	1 868 861	7 051 875	4 522 410	4 522 410
	2018	16 839 135	75	1 855 326	13 119 275	5 253 298	5 253 298
Guinea	2016	8 236 154	65	–	2 138 494	3 362 668	3 362 668
	2017	523 328	68	–	2 920 298	2 673 947	2 673 947
	2018	645 980	59	–	2 741 607	1 886 685	1 886 685
Guinea-Bissau	2016	71 500	77	–	238 412	133 647	115 361
	2017	1 222 428	73	–	303 651	136 507	110 508
	2018	93 859	72	–	320 217	162 773	147 927
Kenya	2016	2 005 477	68	0	8 352 950	11 327 340	11 327 340
	2017	15 621 773	70	906 388	11 337 850	10 696 827	10 696 827
	2018	2 673 730	74	1 833 860	–	–	–
Liberia	2016	–	59	–	–	–	–
	2017	157 954	30	–	–	–	–
	2018	2 500 796	34	–	–	994 008	994 008
Madagascar	2016	464 407	63	2 856 873	1 352 225	757 613	757 613
	2017	764 022	41	2 008 963	2 465 600	1 620 050	1 620 050
	2018	184 859	31	–	4 731 125	2 165 450	2 165 450
Malawi	2016	9 093 657	61	–	8 746 750	6 799 354	6 440 490
	2017	994 136	60	–	15 060 625	10 177 530	10 177 530
	2018	11 805 392	60	–	13 003 518	8 948 286	9 186 040
Mali	2016	2 189 027	69	788 711	3 250 000	3 511 970	3 511 970
	2017	4 148 911	66	823 201	4 164 041	3 746 616	3 746 616
	2018	4 993 868	68	665 581	6 105 500	3 558 964	3 558 964
Mauritania	2016	51 000	11	–	208 650	174 420	84 000
	2017	921 245	37	–	234 520	101 450	–
	2018	478 230	65	–	117 000	25 890	25 890
Mayotte	2016	–	–	–	–	–	–
	2017	–	–	–	–	–	–
	2018	–	–	–	–	44	44
Mozambique	2016	4 527 936	53	4 375 512	19 822 825	14 136 250	14 136 250
	2017	15 482 093	62	5 349 948	19 662 975	15 996 892	15 996 892
	2018	1 337 905	60	4 211 138	21 180 223	16 293 318	16 293 318
Namibia	2016	0	–	485 730	379 625	21 519	21 519
	2017	0	–	753 281	914 175	79 316	79 316
	2018	15 000	–	549 243	49 852	35 355	1 721
Niger	2016	746 469	64	0	4 622 433	3 257 506	3 257 506
	2017	981 423	56	0	3 909 600	2 697 115	2 161 440
	2018	4 015 529	58	–	5 149 981	3 536 000	3 536 000
Nigeria	2016	9 896 250	56	130 061	11 178 434	9 177 309	9 177 309
	2017	21 978 907	53	–	9 701 771	7 752 372	7 752 372
	2018	27 004 605	49	–	18 662 105	32 707 785	32 707 785
Rwanda	2016	2 882 445	66	2 484 672	6 013 020	7 639 177	7 603 560
	2017	2 816 586	73	1 753 230	4 960 020	6 300 445	6 265 890
	2018	974 847	70	1 621 955	5 364 990	5 233 680	5 214 330
Sao Tome and Principe	2016	11 922	–	149 930	117 676	2 121	2 121
	2017	15 151	–	138 000	96 826	2 410	2 410
	2018	142 894	–	–	–	–	–

Annex 3 - D. Commodities distribution and coverage, 2016–2018

WHO region Country/area	Year	No. of LLINs sold or delivered	Modelled percentage of population with access to an ITN	No. of people protected by IRS	No of RDTs distributed	Any first-line treatment courses delivered (including ACT)	ACT treatment courses delivered
AFRICAN							
Senegal	2016	8 960 663	66	496 728	1 823 405	709 394	709 394
	2017	448 305	71	619 578	2 391 311	958 473	958 473
	2018	617 470	50	0	2 646 144	1 606 813	1 490 147
Sierra Leone	2016	452 608	42	-	3 093 725	4 714 900	4 714 900
	2017	4 611 638	53	-	2 611 550	2 504 960	2 504 960
	2018	502 834	73	-	4 316 420	3 415 480	3 415 480
South Africa	2016	0	-	1 165 955	227 325	12 677	12 677
	2017	0	-	1 550 235	865 050	72 439	72 439
	2018	0	-	1 600 747	887 300	51 142	51 142
South Sudan[1]	2016	2 759 527	65	281 998	5 147 954	13 617 422	13 617 422
	2017	1 902 020	75	153 285	1 945 875	12 188 601	12 188 601
	2018	-	73	-	-	2 680 776	2 680 776
Togo	2016	155 660	64	-	1 428 696	1 064 876	1 049 903
	2017	4 706 417	68	-	1 613 393	1 355 640	1 196 518
	2018	224 265	80	-	2 485 086	1 988 845	2 055 831
Uganda	2016	899 823	65	3 811 484	27 230 375	29 667 150	29 667 150
	2017	23 797 483	76	3 223 800	24 620 100	27 396 300	27 396 300
	2018	11 220 492	88	4 436 156	28 200 125	25 606 514	25 606 514
United Republic of Tanzania[2]	2016	-	59	-	-	-	-
	2017	5 335 910	60	2 568 522	-	-	-
	2018	-	59	-	-	-	-
Mainland	2016	11 731 272	59	2 377 403	23 223 400	13 786 620	13 786 620
	2017	5 335 910	60	2 377 403	34 649 050	20 895 180	20 895 180
	2018	6 200 375	59	2 507 920	29 906 950	16 420 560	16 420 560
Zanzibar	2016	756 445	-	27 664	24 026	11 100	10 020
	2017	0	-	191 119	459 957	8 506	8 506
	2018	177 794	-	334 715	356 775	5 050	4 650
Zambia	2016	1 292 400	58	6 737 918	15 286 570	19 084 818	19 084 818
	2017	10 759 947	64	7 717 767	18 884 600	17 460 232	17 460 232
	2018	-	79	6 436 719	17 868 550	27 071 994	27 071 994
Zimbabwe	2016	1 752 855	43	3 674 932	3 154 200	934 580	934 580
	2017	513 300	44	3 673 311	875 713	549 083	553 953
	2018	171 038	32	3 020 032	1 484 134	607 379	615 359
AMERICAS							
Argentina	2016	0	-	0	0	30	0
	2017	0	-	4 208	0	39	9
	2018	0	-	155	0	213	92
Belize	2016	4 000	-	35 264	0	5	0
	2017	0	-	37 466	0	9	1
	2018	2 619	-	36 688	0	7	0
Bolivia (Plurinational State of)	2016	84 000	-	12 689	-	5 553	5 553
	2017	23 500	-	20 000	3 500	0	0
	2018	23 500	-	2 000	-	-	-
Brazil	2016	0	-	98 593	68 650	567 842	103 428
	2017	0	-	83 990	72 200	651 274	69 960
	2018	300 000	-	99 321	114 775	634 935	79 200
Colombia	2016	306 498	-	1 180 400	21 575	202 175	94 494
	2017	295 250	-	153 690	265 250	95 570	56 030
	2018	0	-	60 000	13 252	46 217	26 507
Costa Rica	2016	206	-	430	0	13	3
	2017	104	-	8 479	0	25	7
	2018	3 100	-	4 095	700	108	5

WHO region Country/area	Year	No. of LLINs sold or delivered	Modelled percentage of population with access to an ITN	No. of people protected by IRS	No of RDTs distributed	Any first-line treatment courses delivered (including ACT)	ACT treatment courses delivered
AMERICAS							
Dominican Republic	2016	1 483	–	40 510	89 800	755	40
	2017	0	–	30 361	48 850	398	–
	2018	5 052	–	36 891	42 425	484	9
Ecuador	2016	51 795	–	–	–	1 191	403
	2017	72 015	–	667 111	–	1 380	371
	2018	50 000	–	775 884	51 200	1 806	191
El Salvador	2016	2 578	–	27 338	0	14	0
	2017	2 925	–	19 167	0	4	0
	2018	4 817	–	32 691	0	2	1
French Guiana	2016	4 455	–	–	–	–	–
	2017	–	–	–	–	–	–
	2018	–	–	–	–	–	–
Guatemala	2016	485 010	–	–	92 100	0	0
	2017	83 258	–	6 245	170 325	9 995	0
	2018	310 218	–	15 358	75 300	3 246	–
Guyana	2016	8 320	–	0	8 268	10 979	3 759
	2017	5 534	–	–	–	13 936	5 141
	2018	43 181	–	–	–	11 767	3 073
Haiti	2016	10 000	–	–	274 404	19 702	–
	2017	709 720	–	–	261 600	18 772	–
	2018	1 919	–	42 130	207 800	8 083	–
Honduras	2016	81 470	–	360 553	27 300	43 097	45
	2017	24 092	–	225 027	29 710	–	–
	2018	53 944	–	338 730	15 000	–	45
Mexico	2016	61 000	–	112 184	0	596	13
	2017	5 695	–	–	0	765	14
	2018	17 891	–	48 608	0	803	10
Nicaragua	2016	191 178	–	147 801	20 840	6 284	–
	2017	103 676	–	182 602	46 500	49 085	50
	2018	47 301	–	183 098	117 350	86 195	–
Panama	2016	0	–	9 675	0	811	0
	2017	–	–	3 921	16 000	689	144
	2018	0	–	19 500	20 000	715	3
Paraguay	2016	0	–	217	0	10	7
	2017	0	–	631	5 000	2 498	408
	2018	–	–	–	–	–	–
Peru	2016	430	–	30 499	150 000	74 554	6 500
	2017	–	–	62 804	–	–	–
	2018	83 220	–	23 420	180 000	65 000	14 500
Suriname	2016	37 000	–	–	13 825	–	–
	2017	6 022	–	–	14 325	–	–
	2018	15 000	–	–	13 575	–	–
Venezuela (Bolivarian Republic of)	2016	30 000	–	29 232	80 000	240 613	61 034
	2017	5 000	–	3 900	–	–	–
	2018	81 402	–	–	48 117	404 924	97 293
EASTERN MEDITERRANEAN							
Afghanistan	2016	992 319	–	–	758 675	93 335	89 500
	2017	2 372 354	–	–	514 875	27 850	27 850
	2018	649 383	–	–	28 915	–	47 665
Djibouti	2016	33 851	10	–	–	–	–
	2017	134 701	27	–	63 488	14 212	–
	2018	109 500	53	–	91 416	46 380	98 380

Annex 3 - D. Commodities distribution and coverage, 2016–2018

WHO region Country/area	Year	No. of LLINs sold or delivered	Modelled percentage of population with access to an ITN	No. of people protected by IRS	No of RDTs distributed	Any first-line treatment courses delivered (including ACT)	ACT treatment courses delivered
EASTERN MEDITERRANEAN							
Iran (Islamic Republic of)	2016	6 393	-	172 666	120 000	-	-
	2017	4 218	-	126 111	-	-	-
	2018	4 500	-	117 174	128 650	-	-
Pakistan	2016	1 304 305	-	552 500	13 446 268	850 000	62 000
	2017	1 048 037	-	776 650	1 826 221	800 000	63 566
	2018	2 762 975	-	2 937 767	2 584 675	1 000 000	65 000
Saudi Arabia	2016	0	-	307 927	-	3 922	3 922
	2017	127 800	-	253 222	-	1 915	1 915
	2018	127 801	-	242 009	-	1 908	1 908
Somalia	2016	655 798	13	11 015	593 310	351 755	351 755
	2017	2 571 923	19	1 267 526	468 750	322 260	322 260
	2018	357 569	21	2 038 381	755 750	260 580	260 580
Sudan	2016	5 370 774	52	3 678 400	2 375 275	3 847 768	3 847 768
	2017	5 741 449	56	3 683 031	3 498 425	4 507 838	4 507 838
	2018	3 454 519	51	3 830 195	4 117 300	4 195 600	4 195 600
Yemen	2016	1 482 982	-	548 436	442 570	283 408	283 408
	2017	433 266	-	1 338 585	148 935	138 494	77 115
	2018	1 461 760	-	995 328	571 175	440 265	38 420
SOUTH-EAST ASIA							
Bangladesh	2016	41 255	-	-	420 049	28 407	24 431
	2017	2 242 527	-	-	373 138	29 916	24 790
	2018	1 559 423	-	72 000	500 440	10 762	8 609
Bhutan	2016	22 322	-	66 675	12 600	216	216
	2017	137 000	-	71 690	21 650	132	132
	2018	29 770	-	76 809	12 300	293	293
Democratic People's Republic of Korea	2016	0	-	1 152 402	182 980	23 231	0
	2017	0	-	1 147 548	176 612	17 038	0
	2018	500 815	-	169 841	657 050	3 698	0
India	2016	5 000 000	-	43 477 154	21 082 000	2 123 760	300 000
	2017	16 340 000	-	39 341 409	1 064 000	104 110	62 650
	2018	9 648 400	-	34 290 886	10 500 000	1 400 000	1 100 000
Indonesia	2016	2 977 539	-	6 240	1 382 208	438 178	438 178
	2017	4 376 636	-	3 320	1 783 498	607 965	607 965
	2018	340 074	-	305 493	255 300	670 603	670 603
Myanmar	2016	3 965 187	-	44 484	1 596 525	126 585	126 585
	2017	5 835 192	-	-	2 053 525	108 364	108 364
	2018	775 251	-	14 017	1 761 775	57 144	57 144
Nepal	2016	290 647	-	286 865	61 000	4 500	274
	2017	324 156	-	300 000	100 000	3 070	238
	2018	319 046	-	230 000	132 065	3 949	120
Sri Lanka	2016	16 465	-	57 111	31 950	41	19
	2017	18 019	-	10 317	27 500	57	27
	2018	21 759	-	15 707	11 150	48	15
Thailand	2016	465 600	-	237 398	68 500	40 801	14 321
	2017	358 400	-	207 250	173 425	21 540	7 540
	2018	131 425	-	165 580	30 550	25 292	9 892
Timor-Leste	2016	309 067	-	166 426	114 263	84	84
	2017	334 471	-	102 891	115 115	30	30
	2018	35 367	-	154 410	144 061	8	8

WHO region Country/area	Year	No. of LLINs sold or delivered	Modelled percentage of population with access to an ITN	No. of people protected by IRS	No of RDTs distributed	Any first-line treatment courses delivered (including ACT)	ACT treatment courses delivered
WESTERN PACIFIC							
Cambodia	2016	4 089 321	–	–	400 350	98 990	88 990
	2017	1 994 150	–	–	503 250	145 518	145 518
	2018	1 624 507	–	–	–	–	–
China	2016	26 562	–	272 108	–	6 290	4 130
	2017	11 349	–	352 731	–	–	–
	2018	5 987	–	161 224	–	–	–
Lao People's Democratic Republic	2016	1 213 755	–	–	270 950	63 889	62 994
	2017	242 405	–	–	333 675	42 972	39 272
	2018	50 403	–	2 052	34 387	8 931	34 765
Malaysia	2016	284 031	–	513 076	0	2 302	2 197
	2017	278 104	–	539 029	0	4 114	3 443
	2018	213 073	–	–	0	4 630	3 891
Papua New Guinea	2016	944 847	–	–	1 733 500	540 400	540 400
	2017	1 694 315	–	–	1 135 577	832 532	832 532
	2018	1 480 705	–	–	2 268 750	1 385 940	1 385 940
Philippines	2016	806 603	–	1 025 096	256 875	6 810	6 810
	2017	814 984	–	490 640	145 325	23 400	23 400
	2018	1 156 837	–	1 015 672	168 300	4 318	4 318
Republic of Korea	2016	0	–	–	4 625	673	–
	2017	0	–	–	0	515	–
	2018	0	–	–	0	576	–
Solomon Islands	2016	291 339	–	16 179	542 975	237 492	237 492
	2017	85 976	–	0	374 850	238 665	238 665
	2018	150 248	–	–	386 975	233 917	233 917
Vanuatu	2016	110 215	–	–	39 525	11 729	11 729
	2017	91 028	–	–	56 150	27 409	20 853
	2018	27 151	–	–	50 850	0	0
Viet Nam	2016	200 000	–	417 142	408 055	71 853	2 358
	2017	752 000	–	151 153	921 897	87 225	40 000
	2018	1 193 024	–	319 866	576 930	45 040	40 000

ACT: artemisinin-based combination therapy; IRS: indoor residual spraying; ITN: insecticide-treated mosquito net; LLIN: long-lasting insecticidal net; RDT: rapid diagnostic test; WHO: World Health Organization.

"–" refers to data not available.

[1] In May 2013, South Sudan was reassigned to the WHO African Region (WHA resolution 66.21, http://apps.who.int/gb/ebwha/pdf_files/WHA66/A66_R21-en.pdf).

[2] Where national data for the United Republic of Tanzania are unavailable, refer to Mainland and Zanzibar.

Annex 3 - Ea. Household survey results, 2015–2018, compiled through STATcompiler

WHO region Country/area	Source	% of households					% of population	
		with at least one ITN	with at least one ITN for every two persons who stayed in the household the previous night	with IRS in last 12 months	with at least one ITN and/or IRS in the past 12 months	with at least one ITN for every two persons and/or IRS in the past 12 months	with access to an ITN	who slept under an ITN last night
AFRICAN								
Angola	2015–16 DHS	30.9	11.3	1.6	31.8	12.5	19.7	17.6
Benin	2017–18 DHS	91.5	60.5	8.7	92.0	63.8	77.2	71.1
Burkina Faso	2017–18 MIS	75.3	32.8	–	–	–	54.5	44.1
Burundi	2016–17 DHS	46.2	17.1	1.0	46.8	17.9	32.3	34.7
Chad	2014–15 DHS	77.3	42.4	0.6	77.3	42.4	61.2	33.3
Ethiopia	2016 DHS	–	–	–	–	–	–	–
Ghana	2016 MIS	73.0	50.9	8.1	74.1	53.6	65.8	41.7
Kenya	2015 MIS	62.5	40.0	–	62.5	39.7	52.5	47.6
Liberia	2016 MIS	61.5	25.2	1.2	62.1	25.9	41.5	39.3
Madagascar	2016 MIS	79.5	44.4	6.9	80.9	47.9	62.1	68.2
Malawi	2015–16 DHS	56.9	23.5	4.9	58.6	27.0	38.8	33.9
Malawi	2017 MIS	82.1	41.7	–	–	–	63.1	55.4
Mali	2015 MIS	93.0	39.3	4.0	93.6	41.8	69.5	63.9
Mali	2018 DHS	89.8	54.8	–	–	–	75.2	72.9
Mozambique	2015 AIS	66.0	38.9	11.2	68.7	45.3	53.8	45.4
Mozambique	2018 MIS	82.2	51.2	–	–	–	68.5	68.4
Nigeria	2015 MIS	68.8	34.9	1.3	69.0	35.5	54.7	37.3
Rwanda	2014–15 DHS	80.6	42.6	–	80.6	42.5	63.8	61.4
Rwanda	2017 MIS	84.1	55.1	19.6	89.2	66.9	71.9	63.9
Senegal	2015 DHS	76.8	40.5	4.8	77.1	43.0	66.0	51.0
Senegal	2016 DHS	82.4	56.4	5.3	82.9	58.0	75.7	63.1
Senegal	2017 DHS	84.2	50.4	4.2	84.5	52.3	72.8	56.9
Sierra Leone	2016 MIS	60.3	16.2	1.7	61.1	17.7	37.1	38.6
Togo	2017 MIS	85.2	71.4	–	–	–	82.3	62.5
Uganda	2014–15 MIS	90.2	62.3	4.9	90.5	64.0	78.8	68.6
Uganda	2016 DHS	78.4	51.1	–	–	–	64.6	55.0
United Republic of Tanzania	2015–16 DHS	65.6	38.8	5.5	66.2	41.0	55.9	49.0
United Republic of Tanzania	2017 MIS	77.9	45.4	–	–	–	62.5	52.2
Zimbabwe	2015 DHS	47.9	26.4	21.3	54.9	39.4	37.2	8.5
AMERICAS								
Haiti	2016–17 DHS	30.7	12.3	2.2	32.0	14.1	19.9	13.0
EASTERN MEDITERRANEAN								
Afghanistan	2015 DHS	26.0	2.9				13.2	3.9
Pakistan	2017–18 DHS	3.6	0.6	5.1	8.4	5.7	2.0	0.2
SOUTH-EAST ASIA								
India	2015–16 DHS	0.9	0.4	–	–	–	0.6	4.1
Myanmar	2015–16 DHS	26.8	14.1	–	–	–	21.2	15.6
Timor-Leste	2016 DHS	63.6	32.7	–	–	–	48.1	47.3

ACT: artemisinin-based combination therapy; AIS: AIDS indicator survey; DHS: demographic and health survey; IPTp: intermittent preventive treatment in pregnancy; IRS: indoor residual spraying; ITN: insecticide-treated mosquito net; MIS: malaria indicator survey.

"–" refers to not applicable or data not available.

Sources: Nationally representative household survey data from DHS and MIS, compiled through STATcompiler – https://www.statcompiler.com/.

% of ITNs	% of pregnant women		% of children <5 years				% of children <5 years with fever in last 2 weeks			
that were used last night	who slept under an ITN	who took 3+ doses of IPTp	who slept under an ITN	with moderate or severe anaemia	with a positive RDT	with a positive microscopy blood smear	for whom advice or treatment was sought	who had blood taken from a finger or heel for testing	who took antimalarial drugs	who took an ACT among those who received any antimalarial
71.0	23.0	20.0	21.7	34.0	13.5	–	50.8	34.3	18.1	76.7
73.4	79.3	13.7	76.3	43.8	36.3	39.1	53.1	17.7	17.5	37.0
76.0	58.2	57.7	54.4	50.1	20.2	16.9	73.5	48.8	51.1	79.4
86.9	43.9	12.9	39.9	36.3	37.9	26.8	69.6	66.4	47.0	11.3
48.6	34.7	8.5	36.4	–	–	–	36.9	12.9	26.9	10.0
–	–	–	–	32.0	–	–	35.3		7.7	11.5
47.7	50.0	59.6	52.2	35.2	27.9	20.6	71.8	30.3	50.1	58.8
75.2	57.8	22.9	56.1	16.2	9.1	5.0	71.9	39.2	27.1	91.6
71.2	39.5	23.1	43.7	49.2	44.9	–	78.2	49.8	65.5	81.1
78.7	68.5	10.6	73.4	20.5	5.1	6.9	55.5	15.5	10.1	17.0
73.3	43.9	30.4	42.7	36.1	–	–	67.0	52.0	37.6	91.8
76.8	62.5	41.1	67.5	37.1	36.0	24.3	54.4	37.6	29.4	96.4
90.7	77.9	21.0	71.2	63.0	32.4	35.7	49.2	14.2	28.7	28.9
88.7	83.7	28.3	79.1	56.7	18.9	–	52.8	16.4	18.7	31.0
70.9	52.1	23.3	47.9	36.7	40.2	–	62.7	39.6	38.4	92.6
85.4	76.4	40.6	72.7	55.2	38.9	–	68.6	47.9	32.7	98.6
60.8	49.0	21.4	43.6	43.1	45.1	27.4	66.1	12.6	41.2	37.6
77.4	72.9	–	67.7	15.7	7.8	2.2	56.7	36.1	11.4	98.7
71.0	68.5	–	68.0	–	11.8	7.2	55.6	38.1	19.6	98.7
70.0	51.8	11.2	55.4	38.0	0.6	0.3	49.3	9.5	3.4	12.5
68.2	69.0	22.1	66.6	36.7	0.9	0.9	49.5	13.0	1.7	85.0
68.6	61.8	22	60.7	41.8	0.9	0.4	51.4	16.1	4.7	65.5
89.0	44.0	31.1	44.1	49.2	52.7	40.1	71.4	51.1	57.0	96.0
52.3	69.0	41.7	69.7	47.8	43.9	28.3	55.9	29.3	31.1	76.3
74.4	75.4	27.5	74.3	28.8	31.7	20.0	82.0	35.8	76.9	86.7
74.0	64.1	17.2	62.0	29.2	30.4	–	81.2	49.0	71.5	87.8
69.4	53.9	8.0	54.4	31.2	14.4	5.6	80.1	35.9	51.1	84.9
66.7	51.4	25.8	54.6	30.5	7.3	–	75.4	43.1	36.2	89.4
18.8	6.1	–	9.0	14.9	–	–	50.5	12.7	1.0	–
62.3	16.0	–	18.2	37.5	–	–	40.3	15.8	1.1	–
21.4	4.1	–	4.6	–	–	–	63.7	7.9	11.8	4.4
11.6	0.4	–	0.4	–	–	–	81.4	–	9.2	3.3
68.9	4.3	–	4.6	30.8	–	–	73.2	10.8	20.1	8.5
58.3	18.4	–	18.6	26.7	–	–	65.0	3.0	0.8	–
79.8	60.1	–	55.4	12.6	–	–	57.6	24.5	10.0	11.1

Annex 3 - Eb. Household survey results, 2015–2018, compiled through WHO calculations

WHO region Country/area	Survey	Fever prevalence	Health sector where treatment was sought							Diagnostic testing coverage in each health sector	
		Overall	Public excluding community health workers	Community health workers	Formal medical private excluding pharmacies	Pharmacies or accredited drug stores	Informal private	No treatment seeking	Trained provider	Public excluding community health workers	Community health workers
AFRICAN											
Angola	2015–16 DHS	15%	47%	–	5%	1%	2%	45%	53%	59%	–
Benin	2017–18 DHS	20%	22%	–	9%	9%	14%	46%	40%	52%	–
Burkina Faso	2017–18 MIS	20%	71%	1%	1%	0%	2%	26%	73%	66%	–
Burundi	2016–17 DHS	40%	54%	3%	10%	5%	1%	30%	69%	87%	95%
Ethiopia	2016 DHS	14%	26%	–	8%	0%	2%	63%	34%	–	–
Ghana	2016 MIS	31%	34%	–	15%	10%	12%	28%	60%	59%	–
Kenya	2015 MIS	36%	51%	–	15%	5%	3%	27%	70%	52%	–
Liberia	2016 MIS	39%	46%	–	13%	14%	8%	22%	71%	77%	–
Madagascar	2016 MIS	16%	36%	7%	10%	1%	7%	40%	53%	31%	37%
Malawi	2017 MIS	40%	38%	3%	6%	2%	7%	46%	48%	76%	–
Mali	2018 DHS	16%	24%	3%	2%	7%	23%	42%	36%	46%	37%
Mozambique	2018 MIS	31%	64%	4%	0%	0%	1%	31%	68%	72%	41%
Nigeria	2015 MIS	41%	20%	1%	6%	39%	3%	32%	65%	32%	–
Rwanda	2017 MIS	31%	33%	18%	3%	5%	1%	44%	55%	73%	74%
Senegal	2017 DHS	21%	39%	1%	4%	6%	3%	48%	49%	32%	–
Sierra Leone	2016 MIS	27%	63%	–	4%	4%	2%	28%	70%	74%	–
Togo	2017 MIS	24%	26%	5%	7%	3%	16%	43%	42%	78%	76%
Uganda	2016 DHS	34%	34%	3%	34%	12%	1%	18%	80%	77%	58%
United Republic of Tanzania	2017 MIS	21%	46%	–	13%	17%	1%	25%	75%	66%	–
Zimbabwe	2015 DHS	14%	35%	1%	9%	0%	6%	49%	45%	26%	–

ACT: artemisinin-based combination therapy; DHS: demographic and health survey; MIS: malaria indicator survey; WHO: World Health Organization.
"–" refers to not applicable or data not available.
Note: Figures with fewer than 30 children in the denominator were removed.
Sources: Nationally representative household survey data from DHS and MIS, compiled through WHO calculations.

Diagnostic testing coverage in each health sector				Antimalarial treatment coverage in each health sector							ACT use among antimalarial treatment in each health sector		
Formal medical private excluding pharmacies	Pharmacies or accredited drug stores	Informal private	Trained provider	Public excluding community health workers	Community health workers	Formal medical private excluding pharmacies	Pharmacies or accredited drug stores	Self-treatment	No treatment seeking	Trained provider	Public	Private	Informal private
82%	27%	23%	60%	27%	–	40%	23%	10%	7%	28%	74%	88%	–
30%	9%	8%	37%	38%	–	34%	23%	12%	7%	34%	44%	28%	40%
–	–	–	66%	69%	–	–	–	–	10%	68%	80%	–	–
86%	36%	54%	84%	69%	93%	55%	32%	–	9%	66%	12%	10%	–
–	–	–	–	16%	–	19%	–	–	4%	17%	14%	–	–
60%	11%	0%	50%	64%	–	49%	56%	61%	29%	59%	57%	63%	40%
57%	9%	25%	49%	31%	–	30%	44%	29%	19%	31%	93%	91%	–
82%	35%	14%	70%	84%	–	75%	76%	62%	21%	81%	87%	71%	80%
7%	–	3%	27%	13%	19%	13%	–	18%	5%	14%	9%	–	–
76%	–	4%	73%	55%	–	55%	–	21%	7%	54%	98%	–	–
–	8%	5%	36%	61%	56%	–	17%	5%	4%	50%	35%	–	–
–	–	–	70%	47%	57%	–	–	–	10%	47%	98%	–	–
29%	6%	7%	16%	48%	47%	56%	48%	20%	28%	48%	46%	37%	–
70%	14%	–	67%	30%	60%	13%	31%	–	2%	37%	99%	–	–
23%	6%	20%	28%	9%	–	11%	3%	8%	1%	8%	68%	–	–
72%	13%	–	71%	77%	–	77%	41%	–	19%	75%	98%	92%	–
45%	–	4%	66%	70%	83%	54%	–	10%	7%	66%	82%	–	–
49%	22%	36%	57%	82%	87%	79%	78%	67%	43%	80%	91%	84%	96%
76%	13%	–	55%	34%	–	49%	57%	–	24%	42%	96%	83%	–
13%	–	9%	23%	2%	–	1%	–	0%	1%	1%	–	–	–

Annex 3 - F. Population at risk and estimated malaria cases and deaths, 2010–2018

WHO region Country/area	Year	Population at risk	Cases			Deaths		
			Lower	Point	Upper	Lower	Point	Upper
AFRICAN								
Algeria[1,2,3]	2010	2 113 135	–	1	–	–	1	–
	2011	2 153 309	–	1	–	–	0	–
	2012	2 195 743	–	55	–	–	0	–
	2013	2 240 160	–	8	–	–	0	–
	2014	2 286 182	–	0	–	–	0	–
	2015	2 333 425	–	0	–	–	0	–
	2016	2 381 786	–	0	–	–	0	–
	2017	2 431 200	–	0	–	–	0	–
	2018	2 480 497	–	0	–	–	0	–
Angola	2010	23 356 247	3 209 000	4 332 945	5 712 000	11 000	13 387	16 500
	2011	24 220 660	3 171 000	4 262 568	5 614 000	10 400	12 803	16 100
	2012	25 107 925	3 241 000	4 379 690	5 807 000	9 930	12 408	15 900
	2013	26 015 786	3 464 000	4 706 326	6 229 000	9 700	12 229	15 900
	2014	26 941 773	3 762 000	5 063 524	6 625 000	9 780	12 484	16 600
	2015	27 884 380	4 238 000	5 576 653	7 193 000	10 100	13 118	17 800
	2016	28 842 482	4 852 000	6 345 114	8 177 000	10 100	13 252	18 200
	2017	29 816 769	5 109 000	6 825 325	8 998 000	10 100	13 345	18 500
	2018	30 809 787	5 261 000	7 052 636	9 225 000	10 200	13 425	18 800
Benin	2010	9 199 254	2 734 000	3 567 057	4 589 000	7 530	8 048	8 610
	2011	9 460 829	2 707 000	3 501 513	4 472 000	6 830	7 303	7 830
	2012	9 729 254	2 894 000	3 677 978	4 636 000	6 270	6 720	7 210
	2013	10 004 594	3 123 000	3 951 788	4 930 000	5 930	6 362	6 840
	2014	10 286 839	3 233 000	4 106 892	5 127 000	5 950	6 404	6 910
	2015	10 575 962	3 467 000	4 355 431	5 386 000	6 140	6 655	7 220
	2016	10 872 072	3 692 000	4 583 409	5 611 000	6 340	6 915	7 530
	2017	11 175 192	3 571 000	4 465 137	5 509 000	6 480	7 115	7 810
	2018	11 485 035	3 489 000	4 435 318	5 556 000	6 370	7 081	7 870
Botswana	2010	1 317 417	1 300	2 229	3 900	0	5	13
	2011	1 336 179	520	682	1 000	0	1	3
	2012	1 352 187	230	304	410	0	0	1
	2013	1 367 436	570	729	980	0	1	3
	2014	1 384 718	1 600	2 075	2 800	0	5	10
	2015	1 405 998	400	521	700	0	1	2
	2016	1 431 993	890	1 154	1 500	0	2	5
	2017	1 461 921	2 300	2 999	4 000	0	7	14
	2018	1 494 401	680	879	1 200	0	2	4
Burkina Faso	2010	15 605 211	6 884 000	8 602 187	10 590 000	28 000	30 750	33 800
	2011	16 081 915	6 968 000	8 677 204	10 710 000	25 200	27 994	31 200
	2012	16 571 252	7 043 000	8 742 005	10 760 000	18 500	20 916	23 700
	2013	17 072 791	6 694 000	8 323 401	10 230 000	17 200	19 930	23 100
	2014	17 586 029	6 151 000	7 668 618	9 439 000	15 300	18 144	21 500
	2015	18 110 616	5 741 000	7 245 827	9 025 000	13 100	15 940	19 300
	2016	18 646 350	5 249 000	7 490 818	10 340 000	11 400	14 072	17 500
	2017	19 193 236	5 406 000	7 676 215	10 590 000	10 300	12 955	16 600
	2018	19 751 466	5 551 000	7 875 575	10 960 000	9 860	12 725	16 700
Burundi	2010	8 675 606	1 321 000	1 823 594	2 488 000	4 390	4 720	5 090
	2011	8 958 406	1 193 000	1 649 646	2 226 000	4 300	4 636	5 020
	2012	9 245 992	1 037 000	1 423 214	1 903 000	4 390	4 776	5 230
	2013	9 540 302	936 000	1 341 256	1 858 000	4 330	4 754	5 260
	2014	9 844 301	967 000	1 393 043	1 969 000	4 370	4 850	5 480
	2015	10 160 034	1 167 000	1 681 495	2 322 000	4 380	4 917	5 640
	2016	10 488 002	1 739 000	2 367 597	3 150 000	4 410	5 020	5 870
	2017	10 827 010	2 009 000	2 709 703	3 557 000	4 420	5 097	6 060
	2018	11 175 379	2 079 000	2 796 890	3 682 000	4 410	5 118	6 170
Cabo Verde[1,2]	2010	128 087	–	47	–	–	1	–
	2011	129 703	–	7	–	–	1	–
	2012	131 362	–	1	–	–	0	–
	2013	133 052	–	22	–	–	0	–
	2014	134 751	–	26	–	–	1	–
	2015	136 432	–	7	–	–	0	–
	2016	138 096	–	48	–	–	1	–
	2017	139 749	–	423	–	–	1	–
	2018	141 378	–	2	–	–	0	–
Cameroon	2010	20 341 236	4 436 000	6 011 372	7 914 000	11 400	12 409	13 600
	2011	20 906 392	4 204 000	5 542 323	7 153 000	10 900	11 903	13 100
	2012	21 485 267	3 993 000	5 266 733	6 827 000	11 200	12 317	13 600
	2013	22 077 300	3 839 000	5 365 639	7 162 000	11 300	12 481	13 800
	2014	22 681 853	3 808 000	5 536 236	7 750 000	11 300	12 547	14 000
	2015	23 298 376	4 059 000	5 929 407	8 411 000	10 900	12 276	13 900
	2016	23 926 549	4 011 000	6 324 089	9 433 000	10 300	11 886	13 700
	2017	24 566 070	3 807 000	6 441 846	10 160 000	9 700	11 371	13 400
	2018	25 216 261	3 644 000	6 228 154	9 831 000	9 360	11 192	13 500

WHO region Country/area	Year	Population at risk	Cases			Deaths		
			Lower	Point	Upper	Lower	Point	Upper
AFRICAN								
Central African Republic	2010	4 386 765	1 393 000	1 906 095	2 567 000	5 890	7 378	9 320
	2011	4 418 639	1 304 000	1 852 888	2 559 000	5 020	6 389	8 270
	2012	4 436 411	1 289 000	1 832 621	2 527 000	4 490	5 845	7 750
	2013	4 447 945	1 265 000	1 809 535	2 499 000	3 770	5 053	6 880
	2014	4 464 171	1 218 000	1 754 603	2 434 000	3 420	4 721	6 620
	2015	4 493 171	1 183 000	1 707 013	2 394 000	3 060	4 302	6 200
	2016	4 537 683	1 094 000	1 642 736	2 373 000	2 730	3 949	5 860
	2017	4 596 023	1 050 000	1 596 323	2 318 000	2 530	3 739	5 700
	2018	4 666 375	1 078 000	1 620 758	2 361 000	2 410	3 654	5 730
Chad	2010	11 821 305	1 610 000	2 670 920	4 135 000	12 600	13 692	14 900
	2011	12 225 682	1 584 000	2 573 306	3 958 000	11 600	12 672	13 800
	2012	12 644 806	1 514 000	2 469 991	3 805 000	10 400	11 499	12 600
	2013	13 075 722	1 297 000	2 345 147	3 920 000	9 580	10 607	11 700
	2014	13 514 000	1 242 000	2 301 093	3 969 000	8 680	9 685	10 800
	2015	13 956 512	1 268 000	2 334 698	3 924 000	8 160	9 190	10 300
	2016	14 402 266	1 288 000	2 447 429	4 300 000	7 780	8 862	10 100
	2017	14 852 327	1 248 000	2 559 078	4 687 000	7 510	8 693	10 000
	2018	15 308 245	1 253 000	2 523 288	4 594 000	7 370	8 693	10 300
Comoros[1]	2010	689 696	–	36 538	–	3	89	140
	2011	706 578	–	24 856	–	2	61	95
	2012	723 865	–	49 840	–	4	125	200
	2013	741 511	–	53 156	–	5	134	210
	2014	759 390	–	2 203	–	0	5	8
	2015	777 435	–	1 300	–	0	3	5
	2016	795 597	–	1 143	–	0	2	4
	2017	813 890	–	3 230	–	0	8	12
	2018	832 322	–	15 613	–	1	39	62
Congo	2010	4 273 738	593 000	944 174	1 442 000	1 800	1 894	2 000
	2011	4 394 842	628 000	986 118	1 500 000	1 770	1 883	2 000
	2012	4 510 197	650 000	1 013 105	1 499 000	1 770	1 899	2 040
	2013	4 622 757	694 000	1 068 018	1 580 000	1 790	1 955	2 150
	2014	4 736 965	724 000	1 098 243	1 597 000	1 790	1 972	2 220
	2015	4 856 093	703 000	1 100 944	1 635 000	1 730	1 907	2 160
	2016	4 980 996	679 000	1 162 467	1 855 000	1 760	1 948	2 250
	2017	5 110 701	697 000	1 229 822	2 053 000	1 750	1 938	2 260
	2018	5 244 363	703 000	1 232 815	2 017 000	1 760	1 961	2 310
Côte d'Ivoire	2010	20 532 944	7 829 000	9 635 484	11 700 000	15 400	16 488	17 700
	2011	21 028 652	7 612 000	9 296 942	11 240 000	13 500	14 492	15 600
	2012	21 547 188	6 845 000	8 538 623	10 460 000	11 300	12 157	13 100
	2013	22 087 506	5 714 000	7 484 764	9 688 000	9 830	10 548	11 400
	2014	22 647 672	5 354 000	7 135 696	9 284 000	8 840	9 486	10 200
	2015	23 226 148	5 561 000	7 433 189	9 805 000	8 800	9 501	10 300
	2016	23 822 726	6 048 000	8 448 875	11 500 000	8 530	9 275	10 100
	2017	24 437 475	6 128 000	8 855 281	12 340 000	8 460	9 263	10 200
	2018	25 069 226	5 381 000	8 287 840	12 270 000	8 410	9 297	10 300
Democratic Republic of the Congo	2010	64 563 853	22 370 000	27 653 200	33 780 000	54 100	63 385	74 000
	2011	66 755 151	21 440 000	26 674 386	32 590 000	40 900	48 721	57 500
	2012	69 020 749	19 980 000	25 054 526	30 890 000	38 500	46 851	56 100
	2013	71 358 804	18 320 000	23 378 784	29 300 000	35 500	43 955	53 500
	2014	73 767 445	17 600 000	22 748 873	28 730 000	36 600	46 394	57 900
	2015	76 244 532	17 940 000	23 546 242	30 470 000	34 700	44 994	57 300
	2016	78 789 130	18 860 000	25 430 848	33 900 000	30 800	40 491	53 100
	2017	81 398 765	19 410 000	26 790 666	35 990 000	33 100	44 991	60 700
	2018	84 068 092	19 600 000	26 888 424	35 910 000	32 200	44 615	62 000
Equatorial Guinea	2010	943 640	207 000	320 824	481 000	860	1 058	1 290
	2011	986 861	224 000	337 903	489 000	860	1 078	1 340
	2012	1 031 191	276 000	368 909	488 000	810	1 054	1 340
	2013	1 076 412	306 000	393 693	495 000	760	1 012	1 320
	2014	1 122 273	313 000	405 084	514 000	660	906	1 210
	2015	1 168 575	288 000	396 704	537 000	540	760	1 040
	2016	1 215 181	216 000	373 026	604 000	470	662	930
	2017	1 262 008	180 000	360 585	652 000	460	662	950
	2018	1 308 966	183 000	352 124	623 000	440	659	970
Eritrea	2010	3 170 437	53 000	83 471	118 000	8	161	320
	2011	3 213 969	49 000	76 678	107 000	8	141	280
	2012	3 250 104	33 000	52 483	76 000	6	85	170
	2013	3 281 453	31 000	49 309	70 000	5	88	180
	2014	3 311 444	70 000	109 689	153 000	11	227	460
	2015	3 342 818	41 000	64 176	90 000	6	128	260
	2016	3 376 558	47 000	86 561	137 000	6	198	440
	2017	3 412 894	74 000	115 928	161 000	12	221	450
	2018	3 452 797	64 000	99 716	139 000	10	196	390

Annex 3 - F. Population at risk and estimated malaria cases and deaths, 2010–2018

WHO region Country/area	Year	Population at risk	Cases			Deaths		
			Lower	Point	Upper	Lower	Point	Upper
AFRICAN								
Eswatini[1]	2010	298 155	–	268	–	0	0	1
	2011	300 168	–	549	–	0	1	2
	2012	302 199	–	562	–	0	1	2
	2013	304 316	–	962	–	0	2	3
	2014	306 606	–	711	–	0	1	2
	2015	309 130	–	157	–	–	0	–
	2016	311 918	–	350	–	0	0	1
	2017	314 946	–	724	–	0	1	2
	2018	318 156	–	268	–	0	0	1
Ethiopia	2010	59 595 174	470 000	7 652 137	26 680 000	63	14 424	62 900
	2011	61 295 151	415 000	7 118 302	24 110 000	55	11 571	47 600
	2012	63 054 347	431 000	7 326 062	24 490 000	58	12 042	49 800
	2013	64 862 339	431 000	7 238 627	22 650 000	56	13 081	52 700
	2014	66 704 099	432 000	3 809 119	10 240 000	57	6 665	23 600
	2015	68 568 108	513 000	3 618 580	9 267 000	80	6 769	22 600
	2016	70 450 353	515 000	2 917 544	7 035 000	80	5 687	17 900
	2017	72 351 949	537 000	2 658 314	6 225 000	78	5 352	16 400
	2018	74 272 598	474 000	2 362 979	5 553 000	74	4 757	14 700
Gabon	2010	1 624 146	122 000	288 810	597 000	400	424	450
	2011	1 684 629	167 000	358 358	686 000	420	448	490
	2012	1 749 677	231 000	429 606	730 000	430	469	520
	2013	1 817 070	285 000	495 758	799 000	450	497	550
	2014	1 883 801	317 000	538 273	864 000	460	514	580
	2015	1 947 690	316 000	553 999	902 000	470	523	600
	2016	2 007 882	284 000	543 480	933 000	460	510	590
	2017	2 064 812	264 000	524 958	937 000	460	521	610
	2018	2 119 275	276 000	526 060	922 000	470	528	620
Gambia	2010	1 793 199	402 000	518 727	651 000	560	618	690
	2011	1 848 142	384 000	475 455	575 000	570	629	710
	2012	1 905 020	420 000	523 533	637 000	580	637	720
	2013	1 963 708	366 000	465 386	575 000	580	645	740
	2014	2 024 037	228 000	287 463	354 000	590	654	760
	2015	2 085 860	321 000	406 835	499 000	590	661	770
	2016	2 149 134	199 000	250 439	308 000	600	668	780
	2017	2 213 900	93 000	117 383	144 000	600	677	800
	2018	2 280 092	119 000	150 480	184 000	610	688	820
Ghana	2010	24 779 614	7 354 000	9 023 507	10 910 000	14 300	14 866	15 500
	2011	25 387 713	7 904 000	9 635 269	11 650 000	14 100	14 626	15 200
	2012	25 996 454	8 005 000	9 730 304	11 800 000	13 500	14 092	14 700
	2013	26 607 641	7 532 000	9 293 452	11 290 000	12 900	13 469	14 000
	2014	27 224 480	6 872 000	8 596 537	10 630 000	12 100	12 558	13 100
	2015	27 849 203	6 040 000	7 719 431	9 709 000	11 300	11 757	12 300
	2016	28 481 947	5 190 000	6 721 686	8 620 000	10 800	11 277	11 800
	2017	29 121 464	4 570 000	6 190 041	8 182 000	10 600	11 003	11 500
	2018	29 767 108	4 187 000	6 678 000	10 100 000	10 600	11 070	11 700
Guinea	2010	10 192 168	3 284 000	4 226 309	5 365 000	12 300	13 400	14 700
	2011	10 420 459	3 599 000	4 448 442	5 435 000	11 800	13 003	14 300
	2012	10 652 032	3 751 000	4 556 901	5 474 000	10 900	12 084	13 500
	2013	10 892 821	3 534 000	4 445 128	5 537 000	9 800	11 017	12 400
	2014	11 150 970	3 216 000	4 249 538	5 529 000	8 840	10 017	11 500
	2015	11 432 096	2 945 000	4 077 155	5 512 000	8 050	9 223	10 700
	2016	11 738 434	2 614 000	3 890 993	5 570 000	7 400	8 573	10 200
	2017	12 067 516	2 312 000	3 759 396	5 708 000	7 020	8 234	9 900
	2018	12 414 292	2 055 000	3 524 261	5 625 000	6 880	8 203	10 100
Guinea-Bissau	2010	1 522 603	133 000	204 588	303 000	610	651	710
	2011	1 562 996	135 000	219 683	337 000	600	651	710
	2012	1 604 981	114 000	206 635	343 000	600	646	710
	2013	1 648 259	86 000	186 899	355 000	590	646	710
	2014	1 692 433	64 000	158 919	331 000	590	647	720
	2015	1 737 207	57 000	138 573	290 000	580	637	710
	2016	1 782 434	44 000	127 177	292 000	600	671	760
	2017	1 828 146	41 000	143 200	377 000	610	674	770
	2018	1 874 304	66 000	231 124	593 000	610	680	780
Kenya	2010	42 030 684	1 658 000	2 845 913	4 638 000	11 100	11 456	11 800
	2011	43 178 270	1 696 000	2 930 265	4 795 000	11 500	11 874	12 300
	2012	44 343 469	1 866 000	3 252 855	5 394 000	11 600	12 007	12 400
	2013	45 519 986	2 112 000	3 754 660	6 340 000	11 700	12 106	12 600
	2014	46 700 063	2 201 000	3 916 556	6 580 000	11 700	12 195	12 700
	2015	47 878 339	1 922 000	3 455 175	5 783 000	11 800	12 241	12 900
	2016	49 051 531	1 921 000	3 452 117	5 758 000	11 800	12 280	13 000
	2017	50 221 146	1 964 000	3 520 384	5 866 000	11 800	12 307	13 100
	2018	51 392 570	2 017 000	3 602 498	5 997 000	11 800	12 416	13 200

WHO region Country/area	Year	Population at risk	Cases			Deaths		
			Lower	Point	Upper	Lower	Point	Upper
AFRICAN								
Liberia	2010	3 891 357	1 025 000	1 345 523	1 736 000	2 410	2 583	2 780
	2011	4 017 446	1 009 000	1 327 415	1 718 000	2 260	2 437	2 640
	2012	4 135 662	918 000	1 273 383	1 726 000	2 120	2 310	2 530
	2013	4 248 337	916 000	1 347 912	1 924 000	1 970	2 157	2 390
	2014	4 359 508	1 011 000	1 471 653	2 094 000	1 900	2 110	2 380
	2015	4 472 229	1 140 000	1 551 740	2 039 000	1 730	1 928	2 190
	2016	4 586 788	1 422 000	1 771 898	2 180 000	1 770	2 001	2 330
	2017	4 702 224	1 465 000	1 886 107	2 378 000	1 750	2 004	2 380
	2018	4 818 976	1 182 000	1 742 079	2 447 000	1 730	2 006	2 420
Madagascar	2010	21 151 640	523 000	893 540	1 425 000	68	2 208	5 000
	2011	21 743 970	486 000	794 810	1 161 000	61	1 964	4 140
	2012	22 346 641	967 000	1 594 592	2 516 000	130	3 941	8 730
	2013	22 961 259	966 000	1 497 292	2 298 000	120	3 701	8 010
	2014	23 589 897	768 000	1 079 845	1 448 000	93	2 669	5 200
	2015	24 234 080	1 705 000	2 358 382	3 106 000	200	5 830	11 200
	2016	24 894 370	1 034 000	1 408 502	1 857 000	120	3 482	6 650
	2017	25 570 511	1 442 000	1 934 794	2 488 000	170	4 783	9 020
	2018	26 262 313	1 618 000	2 163 930	2 775 000	190	5 350	10 100
Malawi	2010	14 539 609	4 482 000	5 612 558	6 919 000	8 650	9 139	9 680
	2011	14 962 118	4 282 000	5 427 890	6 785 000	8 220	8 674	9 170
	2012	15 396 010	3 741 000	4 834 579	6 111 000	7 960	8 420	8 940
	2013	15 839 287	3 273 000	4 242 633	5 435 000	7 240	7 682	8 210
	2014	16 289 550	2 937 000	3 860 686	4 953 000	6 700	7 192	7 770
	2015	16 745 305	2 752 000	3 634 338	4 682 000	6 310	6 846	7 520
	2016	17 205 253	2 694 000	3 624 533	4 730 000	6 020	6 614	7 370
	2017	17 670 193	2 880 000	3 821 420	4 982 000	5 850	6 495	7 340
	2018	18 143 215	2 678 000	3 876 121	5 471 000	5 780	6 478	7 460
Mali	2010	15 049 352	4 132 000	5 772 983	7 951 000	15 700	16 884	18 200
	2011	15 514 593	4 471 000	6 279 267	8 582 000	17 300	18 737	20 300
	2012	15 979 492	4 942 000	6 961 475	9 455 000	17 700	19 306	21 000
	2013	16 449 854	5 334 000	7 448 756	10 240 000	17 400	19 142	21 000
	2014	16 934 213	5 365 000	7 468 113	10 370 000	15 800	17 513	19 400
	2015	17 438 772	4 827 000	6 833 022	9 671 000	13 800	15 478	17 400
	2016	17 965 448	4 860 000	6 902 717	9 818 000	12 000	13 602	15 500
	2017	18 512 429	5 057 000	7 160 192	10 190 000	10 400	12 017	13 800
	2018	19 077 755	5 200 000	7 378 847	10 480 000	10 100	11 848	13 800
Mauritania	2010	3 494 200	21 000	135 686	297 000	1 030	1 155	1 350
	2011	3 598 646	40 000	171 207	359 000	1 060	1 199	1 420
	2012	3 706 555	24 000	105 342	233 000	1 080	1 241	1 490
	2013	3 817 497	39 000	126 803	264 000	1 100	1 260	1 530
	2014	3 930 894	67 000	193 411	380 000	1 130	1 315	1 630
	2015	4 046 304	98 000	249 288	468 000	1 160	1 350	1 700
	2016	4 163 532	132 000	297 695	546 000	1 170	1 365	1 740
	2017	4 282 582	94 000	237 631	453 000	1 180	1 380	1 770
	2018	4 403 312	81 000	173 555	298 000	1 190	1 397	1 800
Mozambique	2010	23 531 567	7 707 000	9 375 217	11 280 000	15 500	16 896	18 500
	2011	24 187 500	7 749 000	9 431 228	11 370 000	15 400	16 935	18 800
	2012	24 862 673	7 716 000	9 492 059	11 490 000	15 200	16 940	19 100
	2013	25 560 752	7 710 000	9 635 885	11 850 000	14 900	16 919	19 600
	2014	26 286 192	7 778 000	9 590 106	11 670 000	14 300	16 451	19 400
	2015	27 042 001	7 905 000	9 623 584	11 580 000	13 400	15 644	18 800
	2016	27 829 930	7 844 000	9 596 334	11 620 000	12 700	14 951	18 300
	2017	28 649 007	7 505 000	9 350 958	11 590 000	12 100	14 412	18 000
	2018	29 496 009	7 159 000	9 006 864	11 160 000	11 900	14 426	18 400
Namibia	2010	1 681 850	800	2 590	6 200	0	6	20
	2011	1 711 870	2 600	3 654	5 400	0	9	19
	2012	1 742 095	2 700	5 861	9 700	0	15	36
	2013	1 772 836	6 400	8 068	9 800	0	20	37
	2014	1 804 522	21 000	26 144	32 000	2	66	120
	2015	1 837 443	16 000	19 990	24 000	1	51	93
	2016	1 871 687	33 000	41 397	51 000	3	105	190
	2017	1 907 082	71 000	89 155	109 000	7	228	420
	2018	1 943 338	41 000	51 898	64 000	4	132	240
Niger	2010	16 464 025	3 841 000	7 007 707	10 720 000	18 900	21 543	24 600
	2011	17 114 770	4 112 000	7 323 097	11 180 000	18 800	21 975	25 600
	2012	17 795 209	4 442 000	7 660 985	11 850 000	18 100	21 678	25 900
	2013	18 504 287	4 425 000	7 780 901	12 250 000	17 000	20 907	25 700
	2014	19 240 182	4 185 000	7 700 900	12 430 000	15 700	19 775	25 000
	2015	20 001 663	3 920 000	7 397 212	12 220 000	14 200	18 392	24 000
	2016	20 788 789	3 908 000	7 457 829	12 450 000	13 700	18 164	24 400
	2017	21 602 388	4 050 000	7 702 777	12 850 000	12 700	17 120	23 700
	2018	22 442 831	4 215 000	8 002 454	13 360 000	12 300	17 084	24 200

Annex 3 - F. Population at risk and estimated malaria cases and deaths, 2010–2018

WHO region Country/area	Year	Population at risk	Cases			Deaths		
			Lower	Point	Upper	Lower	Point	Upper
AFRICAN								
Nigeria	2010	158 503 203	51 570 000	63 227 343	77 010 000	142 000	153 437	166 000
	2011	162 805 080	49 400 000	60 654 202	73 960 000	132 000	143 660	157 000
	2012	167 228 803	46 370 000	58 151 864	72 090 000	124 000	136 386	150 000
	2013	171 765 819	44 150 000	56 451 623	70 980 000	112 000	123 585	137 000
	2014	176 404 931	43 450 000	55 462 568	69 290 000	108 000	121 382	137 000
	2015	181 137 454	42 460 000	53 631 431	66 830 000	98 300	111 554	128 000
	2016	185 960 244	38 610 000	52 324 868	68 990 000	90 600	104 403	122 000
	2017	190 873 247	37 020 000	54 029 359	76 150 000	82 100	95 916	115 000
	2018	195 874 685	38 940 000	57 184 148	81 230 000	80 800	95 844	117 000
Rwanda	2010	10 039 338	852 000	1 268 118	1 751 000	3 020	3 132	3 260
	2011	10 293 333	301 000	404 386	514 000	2 970	3 098	3 260
	2012	10 549 668	595 000	753 855	916 000	2 940	3 092	3 290
	2013	10 811 538	1 095 000	1 313 059	1 550 000	2 920	3 088	3 320
	2014	11 083 629	1 827 000	2 436 249	3 069 000	2 920	3 100	3 370
	2015	11 369 066	2 892 000	3 887 798	4 907 000	2 920	3 123	3 420
	2016	11 668 829	5 035 000	6 832 535	8 707 000	2 950	3 153	3 480
	2017	11 980 960	4 706 000	6 449 821	8 267 000	2 980	3 194	3 550
	2018	12 301 969	4 369 000	5 984 752	7 678 000	3 020	3 244	3 630
Sao Tome and Principe[1,2]	2010	180 372	-	2 740	-	-	14	-
	2011	184 521	-	8 442	-	-	19	-
	2012	188 394	-	10 701	-	-	7	-
	2013	192 076	-	9 243	-	-	11	-
	2014	195 727	-	1 754	-	-	0	-
	2015	199 439	-	2 058	-	-	0	-
	2016	203 221	-	2 238	-	-	1	-
	2017	207 086	-	2 239	-	-	1	-
	2018	211 032	-	2 937	-	-	0	-
Senegal	2010	12 678 143	526 000	751 511	1 001 000	4 090	4 194	4 310
	2011	13 033 814	455 000	650 480	867 000	4 080	4 187	4 310
	2012	13 401 990	522 000	762 806	1 032 000	4 060	4 166	4 290
	2013	13 782 429	659 000	935 859	1 238 000	4 050	4 159	4 290
	2014	14 174 740	410 000	560 097	732 000	4 140	4 279	4 450
	2015	14 578 450	692 000	1 017 535	1 381 000	4 170	4 331	4 530
	2016	14 993 514	468 000	684 544	920 000	4 190	4 373	4 600
	2017	15 419 354	561 000	807 277	1 072 000	4 220	4 418	4 680
	2018	15 854 324	618 000	883 919	1 163 000	4 260	4 480	4 780
Sierra Leone	2010	6 415 636	2 295 000	2 943 081	3 698 000	13 100	14 100	15 100
	2011	6 563 238	2 319 000	2 977 428	3 753 000	11 800	12 757	13 700
	2012	6 712 586	2 390 000	3 003 669	3 738 000	10 000	10 831	11 700
	2013	6 863 975	2 304 000	2 970 027	3 765 000	8 390	9 151	9 990
	2014	7 017 153	2 187 000	2 872 180	3 698 000	7 220	7 975	8 820
	2015	7 171 909	2 255 000	2 895 435	3 672 000	6 530	7 329	8 210
	2016	7 328 846	2 311 000	2 868 006	3 530 000	6 110	6 983	7 940
	2017	7 488 427	2 000 000	2 726 766	3 625 000	5 830	6 786	7 860
	2018	7 650 149	1 433 000	2 451 110	3 979 000	5 520	6 564	7 770
South Africa[1,2]	2010	5 121 696	-	8 060	-	-	83	-
	2011	5 200 375	-	9 866	-	-	54	-
	2012	5 283 265	-	6 621	-	-	72	-
	2013	5 368 712	-	8 645	-	-	105	-
	2014	5 454 418	-	11 705	-	-	174	-
	2015	5 538 636	-	1 157	-	-	110	-
	2016	5 620 764	-	4 323	-	-	34	-
	2017	5 700 975	-	22 517	-	-	301	-
	2018	5 779 252	-	9 540	-	-	69	-
South Sudan[4]	2010	9 508 372	1 464 000	2 319 793	3 495 000	4 360	5 010	5 810
	2011	9 830 695	1 428 000	2 318 780	3 552 000	4 180	4 841	5 660
	2012	10 113 648	1 449 000	2 353 290	3 599 000	4 020	4 678	5 520
	2013	10 355 030	1 485 000	2 427 031	3 747 000	3 980	4 695	5 620
	2014	10 554 882	1 531 000	2 492 468	3 867 000	4 080	4 910	6 080
	2015	10 715 657	1 576 000	2 575 568	3 926 000	4 100	5 056	6 440
	2016	10 832 520	1 598 000	2 649 109	4 068 000	4 120	5 188	6 800
	2017	10 910 774	1 627 000	2 681 845	4 161 000	4 130	5 328	7 230
	2018	10 975 924	1 578 000	2 589 443	4 048 000	4 080	5 356	7 490
Togo	2010	6 421 674	1 489 000	1 983 506	2 596 000	4 520	4 947	5 420
	2011	6 595 939	1 570 000	2 067 173	2 686 000	4 280	4 715	5 200
	2012	6 773 807	1 855 000	2 368 811	2 987 000	4 100	4 554	5 050
	2013	6 954 721	2 182 000	2 680 257	3 253 000	4 040	4 532	5 080
	2014	7 137 997	2 247 000	2 745 866	3 324 000	4 240	4 812	5 470
	2015	7 323 162	2 170 000	2 667 930	3 237 000	4 430	5 129	5 950
	2016	7 509 952	1 953 000	2 439 684	3 008 000	4 440	5 244	6 220
	2017	7 698 476	1 678 000	2 141 714	2 694 000	4 310	5 199	6 320
	2018	7 889 095	1 508 000	2 108 823	2 901 000	4 170	5 132	6 410

WHO region Country/area	Year	Population at risk	Cases			Deaths		
			Lower	Point	Upper	Lower	Point	Upper
AFRICAN								
Uganda	2010	32 428 164	10 870 000	13 533 746	16 620 000	19 300	20 412	21 700
	2011	33 476 772	10 210 000	12 912 102	16 120 000	16 400	17 358	18 500
	2012	34 558 700	8 748 000	11 465 552	14 640 000	14 000	14 920	15 900
	2013	35 694 519	6 542 000	9 074 826	12 200 000	12 600	13 402	14 300
	2014	36 911 530	5 749 000	8 143 369	11 020 000	12 100	13 029	14 000
	2015	38 225 447	6 554 000	9 025 492	12 200 000	11 800	12 800	14 000
	2016	39 649 173	9 342 000	12 069 689	15 300 000	11 800	13 036	14 500
	2017	41 166 588	10 840 000	13 863 230	17 470 000	11 800	13 272	15 000
	2018	42 729 032	7 623 000	12 356 577	18 970 000	11 700	13 203	15 200
United Republic of Tanzania	2010	44 346 532	4 688 000	6 450 494	8 725 000	18 600	19 241	20 000
	2011	45 673 520	4 389 000	6 050 835	8 096 000	18 500	19 107	19 800
	2012	47 053 033	3 992 000	5 469 691	7 351 000	18 400	19 127	19 900
	2013	48 483 132	3 944 000	5 419 407	7 268 000	19 100	19 946	20 900
	2014	49 960 563	4 368 000	5 942 515	7 966 000	19 300	20 253	21 300
	2015	51 482 638	4 569 000	6 267 687	8 287 000	19 600	20 624	21 900
	2016	53 049 231	4 818 000	6 555 045	8 675 000	19 800	20 922	22 400
	2017	54 660 345	5 025 000	6 775 567	8 955 000	19 900	21 163	22 900
	2018	56 313 444	4 677 000	6 997 809	10 090 000	20 100	21 550	23 500
Zambia	2010	13 605 986	1 885 000	2 408 568	3 042 000	6 080	6 286	6 520
	2011	14 023 199	2 067 000	2 618 128	3 274 000	6 250	6 479	6 740
	2012	14 465 148	2 270 000	2 937 598	3 724 000	6 480	6 739	7 030
	2013	14 926 551	2 599 000	3 369 958	4 296 000	6 640	6 935	7 270
	2014	15 399 793	2 632 000	3 433 829	4 420 000	6 930	7 303	7 720
	2015	15 879 370	2 410 000	3 216 354	4 211 000	6 960	7 389	7 890
	2016	16 363 449	2 042 000	2 968 175	4 180 000	6 930	7 417	8 030
	2017	16 853 608	1 730 000	2 697 352	3 997 000	6 860	7 419	8 140
	2018	17 351 714	1 709 000	2 719 036	4 096 000	6 890	7 519	8 390
Zimbabwe	2010	9 998 533	606 000	1 094 108	1 709 000	73	2 800	6 220
	2011	10 153 338	468 000	717 620	989 000	52	1 837	3 690
	2012	10 327 222	402 000	590 910	793 000	44	1 512	3 010
	2013	10 512 448	613 000	861 512	1 122 000	66	2 205	4 280
	2014	10 698 542	805 000	1 090 113	1 397 000	86	2 790	5 320
	2015	10 878 022	717 000	1 062 200	1 448 000	80	2 719	5 430
	2016	11 047 866	489 000	726 722	995 000	54	1 860	3 740
	2017	11 210 282	805 000	1 216 876	1 710 000	90	3 115	6 410
	2018	11 369 510	393 000	579 888	789 000	43	1 484	2 960
AMERICAS								
Argentina[1,2,3]	2010	204 478	–	14	–	–	0	–
	2011	206 602	–	0	–	–	0	–
	2012	208 775	–	0	–	–	0	–
	2013	210 980	–	0	–	–	0	–
	2014	213 187	–	0	–	–	0	–
	2015	215 377	–	0	–	–	0	–
	2016	217 542	–	0	–	–	0	–
	2017	219 685	–	0	–	–	0	–
	2018	221 805	–	0	–	–	0	–
Belize[1,2]	2010	222 500	–	150	–	–	0	–
	2011	227 862	–	72	–	–	0	–
	2012	233 220	–	33	–	–	0	–
	2013	238 537	–	20	–	–	0	–
	2014	243 822	–	19	–	–	0	–
	2015	249 038	–	9	–	–	0	–
	2016	254 195	–	4	–	–	0	–
	2017	259 284	–	7	–	–	0	–
	2018	264 318	–	3	–	–	0	–
Bolivia (Plurinational State of)	2010	4 558 757	15 000	18 659	23 000	2	10	18
	2011	4 633 319	7 600	9 680	12 000	1	4	8
	2012	4 708 051	8 600	10 972	13 000	1	4	8
	2013	4 782 769	8 500	10 804	13 000	1	6	11
	2014	4 857 236	8 500	10 952	13 000	1	4	8
	2015	4 931 282	7 300	9 315	11 000	1	3	6
	2016	5 004 817	5 900	7 510	9 200	0	2	5
	2017	5 077 861	4 800	6 195	7 600	0	2	4
	2018	5 150 579	5 700	7 239	8 900	0	2	4
Brazil[2]	2010	39 729 868	349 000	389 809	422 000	–	76	–
	2011	40 095 451	273 000	284 024	303 000	–	70	–
	2012	40 455 320	248 000	258 095	275 000	–	60	–
	2013	40 810 288	176 000	196 793	213 000	–	40	–
	2014	41 161 040	142 000	148 071	158 000	–	36	–
	2015	41 507 767	144 000	161 093	174 000	–	35	–
	2016	41 851 100	129 000	134 862	144 000	–	35	–
	2017	42 190 266	197 000	220 848	239 000	–	34	–
	2018	42 522 271	207 000	217 900	232 000	–	44	–

Annex 3 - F. Population at risk and estimated malaria cases and deaths, 2010–2018

WHO region Country/area	Year	Population at risk	Cases			Deaths		
			Lower	Point	Upper	Lower	Point	Upper
AMERICAS								
Colombia[2]	2010	10 011 898	125 000	164 479	206 000	–	42	–
	2011	10 109 321	64 000	84 072	105 000	–	23	–
	2012	10 200 749	64 000	84 176	105 000	–	24	–
	2013	10 293 683	55 000	72 310	91 000	–	10	–
	2014	10 398 227	43 000	57 024	71 000	–	17	–
	2015	10 520 647	54 000	73 007	94 000	–	18	–
	2016	10 665 522	88 000	115 550	145 000	–	36	–
	2017	10 828 150	60 000	80 963	104 000	–	19	–
	2018	10 994 461	71 000	93 468	117 000	–	9	–
Costa Rica[1,2]	2010	1 602 079	–	110	–	–	0	–
	2011	1 621 580	–	10	–	–	0	–
	2012	1 640 801	–	6	–	–	0	–
	2013	1 659 738	–	0	–	–	0	–
	2014	1 678 386	–	0	–	–	0	–
	2015	1 696 731	–	0	–	–	0	–
	2016	1 714 767	–	4	–	–	0	–
	2017	1 732 484	–	12	–	–	0	–
	2018	1 749 805	–	70	–	–	0	–
Dominican Republic	2010	5 340 225	2 600	3 202	3 800	0	8	14
	2011	5 405 278	1 700	2 088	2 500	0	5	9
	2012	5 470 107	1 000	1 232	1 500	0	3	5
	2013	5 534 723	610	751	900	0	1	3
	2014	5 599 144	480	566	660	0	1	2
	2015	5 663 311	660	779	910	0	1	3
	2016	5 727 240	760	933	1 100	0	2	4
	2017	5 790 831	300	349	400	0	0	1
	2018	5 853 645	600	704	820	0	1	3
Ecuador[1,2]	2010	437 453	–	1 871	–	–	0	–
	2011	444 237	–	1 219	–	–	0	–
	2012	450 946	–	544	–	–	0	–
	2013	457 747	–	368	–	–	0	–
	2014	464 868	–	242	–	–	0	–
	2015	472 450	–	618	–	–	0	–
	2016	480 584	–	1 191	–	–	0	–
	2017	489 125	–	1 275	–	–	0	–
	2018	497 838	–	1 653	–	–	0	–
El Salvador[1,2]	2010	1 255 327	–	19	–	–	0	–
	2011	1 260 745	–	10	–	–	0	–
	2012	1 266 298	–	13	–	–	0	–
	2013	1 272 013	–	6	–	–	0	–
	2014	1 277 910	–	6	–	–	0	–
	2015	1 283 999	–	2	–	–	0	–
	2016	1 290 295	–	12	–	–	0	–
	2017	1 296 789	–	0	–	–	0	–
	2018	1 303 410	–	0	–	–	0	–
French Guiana	2010	128 915	1 800	2 260	2 900	0	4	8
	2011	131 893	1 300	1 412	1 600	0	2	4
	2012	134 816	940	1 052	1 200	0	2	3
	2013	137 797	960	1 123	1 300	0	2	3
	2014	140 961	480	541	620	0	0	1
	2015	144 406	410	460	530	–	0	–
	2016	148 180	240	267	310	–	0	–
	2017	152 257	610	681	780	–	0	–
	2018	156 543	230	444	710	–	0	–
Guatemala	2010	11 044 796	7 900	9 657	12 000	1	3	6
	2011	11 285 142	7 100	7 961	9 200	1	2	5
	2012	11 528 212	5 600	6 251	7 200	0	2	3
	2013	11 773 597	6 500	7 263	8 400	0	2	4
	2014	12 020 770	5 900	6 625	7 600	0	2	4
	2015	12 269 280	7 100	7 967	9 200	1	2	5
	2016	12 518 897	5 100	5 656	6 500	0	2	3
	2017	12 769 455	3 900	4 380	5 000	0	1	2
	2018	13 020 750	3 100	3 521	4 000	0	1	2
Guyana	2010	749 430	26 000	32 823	41 000	3	56	100
	2011	752 029	34 000	41 096	49 000	4	76	130
	2012	755 388	36 000	43 584	52 000	5	76	130
	2013	759 281	43 000	57 459	79 000	7	90	170
	2014	763 371	17 000	22 310	31 000	2	27	53
	2015	767 433	14 000	18 030	25 000	1	22	41
	2016	771 363	14 000	19 269	26 000	2	24	46
	2017	775 218	19 000	25 235	35 000	3	33	63
	2018	779 007	26 000	34 565	47 000	4	43	83

WHO region Country/area	Year	Population at risk	Cases			Deaths		
			Lower	Point	Upper	Lower	Point	Upper
AMERICAS								
Haiti	2010	8 888 919	44 000	77 638	125 000	5	198	450
	2011	9 023 827	50 000	81 483	127 000	5	208	460
	2012	9 158 378	36 000	59 798	92 000	4	153	340
	2013	9 292 168	30 000	49 387	77 000	3	126	280
	2014	9 424 693	22 000	32 932	45 000	2	84	170
	2015	9 555 609	22 000	32 829	44 000	2	84	170
	2016	9 684 651	24 000	36 765	50 000	2	94	190
	2017	9 811 866	23 000	34 878	47 000	2	89	180
	2018	9 937 674	11 000	16 000	22 000	1	40	81
Honduras	2010	7 533 978	10 000	13 306	16 000	2	7	13
	2011	7 681 807	8 000	10 124	12 000	1	5	8
	2012	7 826 756	6 800	8 677	11 000	1	4	7
	2013	7 969 720	5 700	7 317	8 900	1	5	10
	2014	8 111 981	3 600	4 553	5 600	0	3	5
	2015	8 254 486	3 800	4 849	5 900	0	4	7
	2016	8 397 503	4 800	6 230	7 800	0	6	11
	2017	8 540 802	1 500	1 876	2 300	0	0	1
	2018	8 684 378	900	1 154	1 400	–	0	–
Mexico[1,2]	2010	2 419 227	–	1 226	–	–	0	–
	2011	2 453 206	–	1 124	–	–	0	–
	2012	2 486 681	–	833	–	–	0	–
	2013	2 519 611	–	495	–	–	0	–
	2014	2 552 010	–	656	–	–	0	–
	2015	2 583 882	–	517	–	–	0	–
	2016	2 615 160	–	551	–	–	0	–
	2017	2 645 279	–	736	–	–	0	–
	2018	2 675 244	–	803	–	–	0	–
Nicaragua	2010	2 542 195	730	876	1 000	–	0	–
	2011	2 576 668	970	1 171	1 400	–	0	–
	2012	2 611 368	1 300	1 564	1 800	0	0	1
	2013	2 646 258	1 200	1 471	1 700	0	0	1
	2014	2 681 297	1 200	1 446	1 700	–	0	–
	2015	2 716 435	2 400	2 886	3 400	0	1	2
	2016	2 751 676	6 600	7 943	9 400	1	6	10
	2017	2 786 983	12 000	13 866	16 000	2	10	16
	2018	2 822 191	17 000	20 158	24 000	3	10	18
Panama[2]	2010	3 524 055	420	440	470	–	1	–
	2011	3 585 766	360	372	400	–	0	–
	2012	3 647 832	860	888	950	–	1	–
	2013	3 710 534	720	751	800	–	0	–
	2014	3 774 253	960	1 007	1 100	–	0	–
	2015	3 839 244	550	575	610	–	0	–
	2016	3 905 593	780	809	860	–	0	–
	2017	3 973 006	760	801	860	–	0	–
	2018	4 040 827	750	786	840	–	0	–
Paraguay[1,2,3]	2010	224 928	–	18	–	–	0	–
	2011	228 023	–	1	–	–	0	–
	2012	231 174	–	0	–	–	0	–
	2013	234 369	–	0	–	–	0	–
	2014	237 582	–	0	–	–	0	–
	2015	240 794	–	0	–	–	0	–
	2016	244 003	–	0	–	–	0	–
	2017	247 214	–	0	–	–	0	–
	2018	250 418	–	0	–	–	0	–
Peru[2]	2010	11 400 969	33 000	37 849	43 000	–	0	–
	2011	11 493 910	26 000	30 924	36 000	–	1	–
	2012	11 589 145	33 000	40 437	48 000	–	7	–
	2013	11 694 090	51 000	62 669	75 000	–	4	–
	2014	11 818 354	69 000	83 936	100 000	–	4	–
	2015	11 967 748	76 000	93 936	113 000	–	5	–
	2016	12 146 571	60 000	72 836	87 000	–	7	–
	2017	12 350 062	59 000	72 518	86 000	–	10	–
	2018	12 564 103	48 000	58 455	70 000	–	4	–
Suriname[1,2]	2010	78 151	–	1 823	–	–	1	–
	2011	79 045	–	771	–	–	1	–
	2012	79 942	–	554	–	–	0	–
	2013	80 835	–	729	–	–	1	–
	2014	81 719	–	401	–	–	1	–
	2015	82 584	–	81	–	–	0	–
	2016	83 433	–	76	–	–	0	–
	2017	84 262	–	40	–	–	1	–
	2018	85 073	–	29	–	–	0	–

Annex 3 - F. Population at risk and estimated malaria cases and deaths, 2010–2018

WHO region Country/area	Year	Population at risk	Cases			Deaths		
			Lower	Point	Upper	Lower	Point	Upper
AMERICAS								
Venezuela (Bolivarian Republic of)	2010	14 219 971	48 000	57 926	74 000	8	53	91
	2011	14 443 936	48 000	53 539	62 000	8	47	77
	2012	14 680 413	55 000	61 768	71 000	9	56	92
	2013	14 890 523	82 000	91 924	106 000	13	104	170
	2014	15 021 486	94 000	105 721	122 000	15	110	180
	2015	15 040 913	142 000	158 987	182 000	25	149	240
	2016	14 925 624	251 000	280 468	321 000	44	260	420
	2017	14 701 240	428 000	479 761	549 000	78	421	680
	2018	14 443 558	422 000	471 995	541 000	75	423	680
EASTERN MEDITERRANEAN								
Afghanistan	2010	22 496 454	171 000	339 820	571 000	54	192	400
	2011	23 214 771	204 000	438 076	736 000	65	232	480
	2012	24 019 470	126 000	267 829	467 000	33	113	240
	2013	24 873 691	126 000	224 236	370 000	34	103	210
	2014	25 722 516	220 000	325 811	461 000	54	156	290
	2015	26 526 314	263 000	395 552	561 000	66	187	340
	2016	27 273 556	506 000	712 132	975 000	120	341	610
	2017	27 977 405	573 000	757 412	982 000	140	353	620
	2018	28 652 489	633 000	831 091	1 068 000	140	383	670
Djibouti[1,2]	2010	630 077	–	1 010	–	–	0	–
	2011	640 184	1 700	2 189	2 700	–	0	–
	2012	651 032	1 700	2 153	2 600	–	0	–
	2013	662 401	–	1 684	–	–	17	–
	2014	673 958	–	9 439	–	–	28	–
	2015	685 425	–	9 473	–	–	23	–
	2016	696 763	–	13 804	–	–	5	–
	2017	707 999	–	14 671	–	–	0	–
	2018	719 115	–	25 319	–	–	0	–
Egypt[1,2]	2010	82 761 244	–	0	–	–	0	–
	2011	84 529 251	–	0	–	–	0	–
	2012	86 422 240	–	0	–	–	0	–
	2013	88 404 652	–	0	–	–	0	–
	2014	90 424 668	–	0	–	–	0	–
	2015	92 442 549	–	0	–	–	0	–
	2016	94 447 071	–	0	–	–	0	–
	2017	96 442 590	–	0	–	–	0	–
	2018	98 423 602	–	0	–	–	0	–
Iran (Islamic Republic of)[1,2]	2010	753 410	–	1 847	–	–	0	–
	2011	762 321	–	1 632	–	–	0	–
	2012	771 564	–	756	–	–	0	–
	2013	781 186	–	479	–	–	0	–
	2014	791 235	–	358	–	–	0	–
	2015	801 719	–	167	–	–	0	–
	2016	812 666	–	81	–	–	0	–
	2017	823 680	–	60	–	–	0	–
	2018	835 180	–	0	–	–	0	–
Morocco[1,2,3]	2010	32 343 384	–	0	–	–	0	–
	2011	32 781 860	–	0	–	–	0	–
	2012	33 241 898	–	0	–	–	0	–
	2013	33 715 705	–	0	–	–	0	–
	2014	34 192 358	–	0	–	–	0	–
	2015	34 663 608	–	0	–	–	0	–
	2016	35 126 274	–	0	–	–	0	–
	2017	35 581 257	–	0	–	–	0	–
	2018	36 029 089	–	0	–	–	0	–
Oman[1,2]	2010	3 041 435	–	7	–	–	0	–
	2011	3 251 102	–	0	–	–	0	–
	2012	3 498 031	–	0	–	–	0	–
	2013	3 764 805	–	0	–	–	0	–
	2014	4 027 255	–	0	–	–	0	–
	2015	4 267 341	–	0	–	–	0	–
	2016	4 479 217	–	0	–	–	0	–
	2017	4 665 926	–	0	–	–	0	–
	2018	4 829 476	–	0	–	–	0	–
Pakistan	2010	176 393 981	640 000	1 445 704	3 037 000	190	1 616	4 280
	2011	180 243 369	918 000	1 905 938	3 739 000	280	1 814	4 360
	2012	184 116 776	774 000	1 652 576	3 284 000	220	1 703	4 270
	2013	188 030 212	750 000	1 419 225	2 716 000	220	1 047	2 420
	2014	192 006 115	724 000	1 373 305	2 723 000	220	897	2 100
	2015	196 058 432	526 000	992 598	2 028 000	160	716	1 780
	2016	200 191 818	800 000	1 202 476	1 996 000	200	1 012	2 110
	2017	204 394 674	707 000	970 992	1 468 000	160	756	1 430
	2018	208 643 752	545 000	705 532	987 000	120	495	880

WHO region Country/area	Year	Population at risk	Cases			Deaths		
			Lower	Point	Upper	Lower	Point	Upper
EASTERN MEDITERRANEAN								
Saudi Arabia[1,2]	2010	2 196 624	–	29	–	–	0	–
	2011	2 264 403	–	69	–	–	0	–
	2012	2 335 482	–	82	–	–	0	–
	2013	2 407 350	–	34	–	–	0	–
	2014	2 476 605	–	30	–	–	0	–
	2015	2 540 776	–	83	–	–	0	–
	2016	2 598 914	–	272	–	–	0	–
	2017	2 651 735	–	177	–	–	0	–
	2018	2 699 927	–	61	–	–	0	–
Somalia	2010	12 043 886	214 000	356 323	526 000	24	912	2 000
	2011	12 376 305	181 000	301 405	441 000	20	771	1 680
	2012	12 715 487	188 000	310 864	454 000	21	795	1 730
	2013	13 063 711	223 000	366 378	546 000	26	937	2 070
	2014	13 423 571	265 000	430 886	640 000	30	1 103	2 440
	2015	13 797 204	304 000	514 253	769 000	35	1 316	2 920
	2016	14 185 635	311 000	528 591	795 000	35	1 353	3 020
	2017	14 589 165	320 000	541 768	813 000	37	1 386	3 100
	2018	15 008 225	305 000	514 396	772 000	35	1 316	2 960
Sudan	2010	34 545 014	779 000	1 059 304	1 405 000	87	2 711	5 160
	2011	35 349 676	781 000	1 059 374	1 400 000	88	2 711	5 090
	2012	36 193 781	797 000	1 091 647	1 457 000	90	2 794	5 400
	2013	37 072 555	812 000	1 166 089	1 645 000	92	2 985	5 900
	2014	37 977 657	827 000	1 267 868	1 843 000	97	3 245	6 680
	2015	38 902 948	847 000	1 395 818	2 202 000	100	3 573	7 710
	2016	39 847 433	842 000	1 662 933	2 933 000	110	4 257	10 100
	2017	40 813 398	871 000	1 908 105	3 652 000	120	4 884	12 100
	2018	41 801 532	904 000	1 954 302	3 686 000	120	5 003	12 300
Syrian Arab Republic[1,2]	2010	21 362 541	–	0	–	–	0	–
	2011	21 081 814	–	0	–	–	0	–
	2012	20 438 861	–	0	–	–	0	–
	2013	19 578 466	–	0	–	–	0	–
	2014	18 710 711	–	0	–	–	0	–
	2015	17 997 411	–	0	–	–	0	–
	2016	17 465 567	–	0	–	–	0	–
	2017	17 095 669	–	0	–	–	0	–
	2018	16 945 062	–	0	–	–	0	–
United Arab Emirates[1,2,3]	2010	8 549 998	–	0	–	–	0	–
	2011	8 946 778	–	0	–	–	0	–
	2012	9 141 598	–	0	–	–	0	–
	2013	9 197 908	–	0	–	–	0	–
	2014	9 214 182	–	0	–	–	0	–
	2015	9 262 896	–	0	–	–	0	–
	2016	9 360 975	–	0	–	–	0	–
	2017	9 487 206	–	0	–	–	0	–
	2018	9 630 966	–	0	–	–	0	–
Yemen	2010	18 035 338	649 000	1 131 912	2 191 000	82	2 866	7 350
	2011	18 543 752	492 000	792 413	1 326 000	60	2 013	4 620
	2012	19 062 181	577 000	859 569	1 302 000	67	2 193	4 690
	2013	19 587 110	494 000	700 432	1 006 000	56	1 786	3 670
	2014	20 113 940	412 000	585 987	850 000	46	1 495	3 080
	2015	20 639 226	362 000	513 816	737 000	40	1 309	2 700
	2016	17 515 888	464 000	661 252	949 000	54	1 668	3 420
	2017	17 945 659	525 000	747 173	1 073 000	64	1 853	3 800
	2018	18 373 670	587 000	842 226	1 233 000	68	2 138	4 400
EUROPEAN								
Armenia[1,2,3]	2010	2 877 314	–	0	–	–	0	–
	2011	2 876 536	–	0	–	–	0	–
	2012	2 884 239	–	0	–	–	0	–
	2013	2 897 593	–	0	–	–	0	–
	2014	2 912 403	–	0	–	–	0	–
	2015	2 925 559	–	0	–	–	0	–
	2016	2 936 147	–	0	–	–	0	–
	2017	2 944 789	–	0	–	–	0	–
	2018	2 951 741	–	0	–	–	0	–
Azerbaijan[1,2]	2010	207 746	–	50	–	–	0	–
	2011	210 364	–	4	–	–	0	–
	2012	213 087	–	3	–	–	0	–
	2013	215 865	–	0	–	–	0	–
	2014	218 629	–	0	–	–	0	–
	2015	221 323	–	0	–	–	0	–
	2016	223 928	–	0	–	–	0	–
	2017	226 442	–	0	–	–	0	–
	2018	228 839	–	0	–	–	0	–

Annex 3 - F. Population at risk and estimated malaria cases and deaths, 2010–2018

WHO region Country/area	Year	Population at risk	Cases			Deaths		
			Lower	Point	Upper	Lower	Point	Upper
EUROPEAN								
Georgia[1,2]	2010	40 990	–	0	–	–	0	–
	2011	40 810	–	0	–	–	0	–
	2012	40 640	–	0	–	–	0	–
	2013	40 487	–	0	–	–	0	–
	2014	40 353	–	0	–	–	0	–
	2015	40 241	–	0	–	–	0	–
	2016	40 154	–	0	–	–	0	–
	2017	40 087	–	0	–	–	0	–
	2018	40 029	–	0	–	–	0	–
Kazakhstan[1,2]	2010	16 252 273	–	0	–	–	0	–
	2011	16 490 669	–	0	–	–	0	–
	2012	16 751 523	–	0	–	–	0	–
	2013	17 026 118	–	0	–	–	0	–
	2014	17 302 619	–	0	–	–	0	–
	2015	17 572 010	–	0	–	–	0	–
	2016	17 830 902	–	0	–	–	0	–
	2017	18 080 023	–	0	–	–	0	–
	2018	18 319 616	–	0	–	–	0	–
Kyrgyzstan[1,2,3]	2010	4 229 392	–	3	–	–	0	–
	2011	4 303 983	–	0	–	–	0	–
	2012	4 384 834	–	0	–	–	0	–
	2013	4 470 423	–	0	–	–	0	–
	2014	4 558 726	–	0	–	–	0	–
	2015	4 648 118	–	0	–	–	0	–
	2016	4 737 975	–	0	–	–	0	–
	2017	4 827 987	–	0	–	–	0	–
	2018	4 917 139	–	0	–	–	0	–
Tajikistan[1,2]	2010	2 514 150	–	111	–	–	0	–
	2011	2 570 967	–	65	–	–	0	–
	2012	2 630 195	–	18	–	–	0	–
	2013	2 691 967	–	3	–	–	0	–
	2014	2 756 444	–	2	–	–	0	–
	2015	2 823 642	–	0	–	–	0	–
	2016	2 893 634	–	0	–	–	0	–
	2017	2 966 010	–	0	–	–	0	–
	2018	3 039 682	–	0	–	–	0	–
Turkey[1,2]	2010	4 701 254	–	0	–	–	0	–
	2011	4 773 811	–	0	–	–	0	–
	2012	4 852 317	–	0	–	–	0	–
	2013	4 935 154	–	0	–	–	0	–
	2014	5 019 902	–	0	–	–	0	–
	2015	5 104 411	–	0	–	–	0	–
	2016	5 188 811	–	0	–	–	0	–
	2017	5 272 569	–	0	–	–	0	–
	2018	5 352 105	–	0	–	–	0	–
Turkmenistan[1,2,3]	2010	5 087 211	–	0	–	–	0	–
	2011	5 174 076	–	0	–	–	0	–
	2012	5 267 906	–	0	–	–	0	–
	2013	5 366 376	–	0	–	–	0	–
	2014	5 466 324	–	0	–	–	0	–
	2015	5 565 283	–	0	–	–	0	–
	2016	5 662 371	–	0	–	–	0	–
	2017	5 757 667	–	0	–	–	0	–
	2018	5 850 902	–	0	–	–	0	–
Uzbekistan[1,2,3]	2010	2 028 390	–	0	–	–	0	–
	2011	2 061 459	–	0	–	–	0	–
	2012	2 095 284	–	0	–	–	0	–
	2013	2 129 847	–	0	–	–	0	–
	2014	2 165 068	–	0	–	–	0	–
	2015	2 200 922	–	0	–	–	0	–
	2016	2 237 184	–	0	–	–	0	–
	2017	2 273 336	–	0	–	–	0	–
	2018	2273336	–	0	–	–	0	–
SOUTH-EAST ASIA								
Bangladesh	2010	15 868 196	59 000	68 774	80 000	6	165	290
	2011	16 050 743	54 000	63 356	73 000	5	155	270
	2012	16 237 042	31 000	35 747	41 000	3	87	150
	2013	16 425 823	23 000	25 366	29 000	2	60	100
	2014	16 614 636	49 000	54 801	61 000	4	133	220
	2015	16 801 613	41 000	45 658	51 000	4	109	180
	2016	16 986 651	29 000	31 662	35 000	2	74	120
	2017	17 170 973	30 000	33 444	37 000	2	77	130
	2018	17 352 837	11 000	12 021	13 000	0	26	44

WHO region Country/area	Year	Population at risk	Cases			Deaths		
			Lower	Point	Upper	Lower	Point	Upper
SOUTH-EAST ASIA								
Bhutan[1,2]	2010	507 271	–	526	–	–	2	–
	2011	513 039	–	228	–	–	1	–
	2012	519 170	–	82	–	–	1	–
	2013	525 573	–	15	–	–	0	–
	2014	532 099	–	19	–	–	0	–
	2015	538 634	–	34	–	–	0	–
	2016	545 162	–	15	–	–	0	–
	2017	551 716	–	11	–	–	0	–
	2018	558 253	–	6	–	–	0	–
Democratic People's Republic of Korea[1,2]	2010	9 585 831	–	13 520	–	–	0	–
	2011	9 634 466	–	16 760	–	–	0	–
	2012	9 684 153	–	21 850	–	–	0	–
	2013	9 734 471	–	14 407	–	–	0	–
	2014	9 784 567	–	10 535	–	–	0	–
	2015	9 833 782	–	7 409	–	–	0	–
	2016	9 882 137	–	2 719	–	–	0	–
	2017	9 929 834	–	4 575	–	–	0	–
	2018	9 976 610	–	3 598	–	–	0	–
India	2010	1 153 311 084	14 840 000	20 200 000	28 480 000	2 730	30 495	57 800
	2011	1 168 267 799	12 770 000	17 240 000	24 290 000	2 370	25 574	48 300
	2012	1 182 743 793	10 290 000	14 020 000	19 840 000	1 920	20 433	38 800
	2013	1 196 817 595	8 172 000	10 960 000	15 210 000	1 490	16 706	31 200
	2014	1 210 608 062	8 383 000	11 140 000	15 520 000	1 350	20 128	37 700
	2015	1 224 205 084	8 941 000	11 840 000	16 220 000	1 470	21 667	40 900
	2016	1 237 627 593	8 826 000	12 370 000	17 930 000	1 550	22 316	44 500
	2017	1 250 859 582	6 832 000	9 348 000	13 250 000	1 210	16 310	31 700
	2018	1 263 908 949	4 659 000	6 737 000	9 541 000	930	9 620	18 300
Indonesia	2010	241 834 226	2 120 000	2 665 491	3 501 000	370	4 260	8 000
	2011	245 115 988	1 930 000	2 424 712	3 190 000	330	3 820	7 160
	2012	248 451 714	1 913 000	2 405 245	3 147 000	320	3 785	7 120
	2013	251 805 314	1 632 000	2 047 233	2 686 000	270	3 256	6 100
	2014	255 128 076	1 241 000	1 556 734	2 041 000	210	2 510	4 700
	2015	258 383 257	1 108 000	1 391 240	1 830 000	190	2 190	4 080
	2016	261 556 386	1 154 000	1 448 007	1 896 000	190	2 516	4 740
	2017	264 650 969	1 428 000	1 792 690	2 338 000	230	3 138	5 890
	2018	267 670 549	933 000	1 034 866	1 154 000	140	1 785	2 930
Myanmar	2010	30 116 448	1 384 000	2 017 346	3 108 000	230	3 882	8 320
	2011	30 348 439	1 014 000	1 319 917	1 761 000	160	2 466	4 620
	2012	30 600 253	1 355 000	1 892 905	2 749 000	220	3 680	7 500
	2013	30 861 393	455 000	611 838	840 000	74	1 169	2 290
	2014	31 116 339	281 000	383 705	535 000	46	729	1 440
	2015	31 354 355	220 000	272 329	328 000	34	482	850
	2016	31 571 282	131 000	161 570	195 000	20	273	480
	2017	31 772 208	98 000	120 755	145 000	15	209	370
	2018	31 966 116	88 000	108 815	131 000	14	172	300
Nepal	2010	7 841 339	15 000	30 320	63 000	3	27	70
	2011	7 849 471	14 000	23 802	45 000	3	9	23
	2012	7 834 359	12 000	18 349	33 000	2	9	20
	2013	7 813 353	7 000	10 222	18 000	1	6	14
	2014	7 810 214	3 000	4 885	9 800	0	3	8
	2015	7 841 869	2 500	4 483	9 600	0	2	7
	2016	7 913 973	2 300	3 372	5 900	0	2	4
	2017	8 021 214	2 500	3 104	4 100	0	1	2
	2018	8 155 623	2 600	3 588	5 300	0	1	2
Sri Lanka[1,2,3]	2010	4 660 199	–	684	–	–	0	–
	2011	4 691 654	–	124	–	–	0	–
	2012	4 722 497	–	23	–	–	0	–
	2013	4 752 502	–	0	–	–	0	–
	2014	4 781 357	–	0	–	–	0	–
	2015	4 808 845	–	0	–	–	0	–
	2016	4 834 870	–	0	–	–	0	–
	2017	4 859 446	–	0	–	–	0	–
	2018	4 882 614	–	0	–	–	0	–
Thailand[1,2]	2010	12 751 063	–	32 480	–	–	80	–
	2011	12 812 422	–	24 897	–	–	43	–
	2012	12 872 689	–	32 569	–	–	37	–
	2013	12 931 240	–	33 302	–	–	47	–
	2014	12 987 073	–	37 921	–	–	38	–
	2015	13 039 404	–	17 427	–	–	33	–
	2016	13 088 134	–	13 451	–	–	27	–
	2017	13 133 254	–	12 515	–	–	15	–
	2018	13 174 743	–	4 782	–	–	8	–

Annex 3 - F. Population at risk and estimated malaria cases and deaths, 2010–2018

WHO region Country/area	Year	Population at risk	Cases			Deaths		
			Lower	Point	Upper	Lower	Point	Upper
SOUTH-EAST ASIA								
Timor-Leste	2010	1 028 463	72 000	102 579	136 000	11	198	380
	2011	1 046 931	26 000	32 736	41 000	3	69	130
	2012	1 065 599	6 500	7 740	9 100	0	10	17
	2013	1 084 678	1 400	1 692	2 000	0	2	3
	2014	1 104 471	480	568	660	0	0	1
	2015	1 125 125	120	139	160	–	0	–
	2016	1 146 752	110	130	150	–	0	–
	2017	1 169 297	31	37	43	–	0	–
	2018	1 192 542	–	0	–	–	0	–
WESTERN PACIFIC								
Cambodia	2010	10 121 505	292 000	353 293	428 000	45	644	1 120
	2011	10 283 605	321 000	368 041	426 000	47	641	1 080
	2012	10 452 648	226 000	260 016	301 000	35	383	640
	2013	10 626 530	147 000	168 806	196 000	23	231	380
	2014	10 802 038	208 000	240 449	282 000	31	399	670
	2015	10 976 665	189 000	218 837	255 000	28	374	630
	2016	11 149 825	107 000	124 137	145 000	16	204	340
	2017	11 321 696	175 000	202 696	237 000	27	336	560
	2018	11 491 692	235 000	272 272	320 000	42	265	430
China[1,2]	2010	575 598 390	–	4 990	–	–	19	–
	2011	578 835 356	–	3 367	–	–	33	–
	2012	582 081 652	–	244	–	–	0	–
	2013	585 315 386	–	86	–	–	0	–
	2014	588 506 114	–	56	–	–	0	–
	2015	591 624 804	–	39	–	–	0	–
	2016	594 665 143	–	3	–	–	0	–
	2017	597 615 756	–	0	–	–	0	–
	2018	600 418 023	–	0	–	–	0	–
Lao People's Democratic Republic	2010	3 251 667	36 000	51 184	69 000	3	127	250
	2011	3 302 866	26 000	35 886	48 000	2	85	160
	2012	3 353 319	70 000	96 451	127 000	9	211	400
	2013	3 403 674	58 000	79 309	105 000	9	145	280
	2014	3 454 907	75 000	103 303	137 000	13	157	300
	2015	3 507 668	57 000	78 225	103 000	10	100	190
	2016	3 562 141	20 000	27 668	37 000	3	33	62
	2017	3 617 940	15 000	20 357	27 000	2	29	56
	2018	3 674 379	11 000	15 437	20 000	1	23	44
Malaysia[1,2]	2010	1 128 321	–	5 194	–	–	13	–
	2011	1 146 038	–	3 954	–	–	12	–
	2012	1 162 727	–	3 662	–	–	12	–
	2013	1 178 756	–	2 921	–	–	10	–
	2014	1 194 664	–	3 147	–	–	4	–
	2015	1 210 838	–	242	–	–	4	–
	2016	1 227 386	–	266	–	–	2	–
	2017	1 244 186	–	85	–	–	10	–
	2018	1 261 121	–	0	–	–	12	–
Papua New Guinea	2010	7 310 512	463 000	1 240 109	2 159 000	110	2 633	6 270
	2011	7 472 196	389 000	1 045 967	1 826 000	87	2 344	5 580
	2012	7 631 003	420 000	1 296 356	2 600 000	100	2 793	7 230
	2013	7 788 388	952 000	1 677 722	2 572 000	140	4 043	8 660
	2014	7 946 733	1 177 000	1 931 287	2 943 000	220	3 728	7 750
	2015	8 107 772	739 000	1 066 533	1 461 000	120	2 227	4 310
	2016	8 271 766	1 056 000	1 469 150	1 965 000	160	3 108	5 970
	2017	8 438 038	1 036 000	1 500 657	2 077 000	170	3 053	5 970
	2018	8 606 324	1 096 000	1 587 573	2 180 000	180	3 124	6 060
Philippines	2010	54 570 270	37 000	53 401	71 000	5	112	220
	2011	55 501 350	17 000	23 891	31 000	2	47	90
	2012	56 455 267	14 000	19 138	25 000	1	35	67
	2013	57 418 668	13 000	17 518	23 000	1	35	68
	2014	58 371 999	11 000	14 543	19 000	0	31	59
	2015	59 301 223	20 000	28 020	37 000	2	62	120
	2016	60 201 722	12 000	17 491	23 000	1	38	74
	2017	61 078 122	13 000	18 685	25 000	1	41	81
	2018	61 936 730	7 700	10 947	15 000	0	24	48
Republic of Korea[1,2]	2010	3 468 194	–	1 267	–	–	1	–
	2011	3 485 030	–	505	–	–	2	–
	2012	3 504 244	–	394	–	–	0	–
	2013	3 524 200	–	383	–	–	0	–
	2014	3 542 553	–	557	–	–	0	–
	2015	3 557 616	–	627	–	–	0	–
	2016	3 568 841	–	602	–	–	0	–
	2017	3 576 748	–	436	–	–	0	–
	2018	3 582 019	–	501	–	–	0	–

WHO region Country/area	Year	Population at risk	Cases			Deaths		
			Lower	Point	Upper	Lower	Point	Upper
WESTERN PACIFIC								
Solomon Islands	2010	522 582	65 000	91 425	130 000	10	163	320
	2011	536 106	44 000	62 676	92 000	7	108	220
	2012	550 505	39 000	52 221	73 000	6	89	170
	2013	565 615	40 000	53 689	74 000	6	83	160
	2014	581 208	25 000	30 591	38 000	3	48	87
	2015	597 101	33 000	39 916	49 000	5	57	99
	2016	613 243	72 000	84 451	101 000	12	103	170
	2017	629 669	80 000	103 482	139 000	15	134	250
	2018	646 327	75 000	86 343	101 000	12	109	180
Vanuatu	2010	236 216	13 000	15 669	19 000	1	20	35
	2011	242 658	8 900	11 631	16 000	1	14	27
	2012	249 505	6 500	8 394	11 000	–	0	–
	2013	256 637	4 100	5 326	7 200	–	0	–
	2014	263 888	1 900	2 427	3 300	–	0	–
	2015	271 128	680	787	920	–	0	–
	2016	278 326	3 200	4 177	5 600	–	0	–
	2017	285 499	1 700	2 266	3 000	–	0	–
	2018	292 675	900	1 167	1 600	–	0	–
Viet Nam	2010	64 831 194	21 000	22 959	26 000	2	45	76
	2011	65 497 232	19 000	20 206	23 000	2	35	58
	2012	66 183 031	22 000	23 838	27 000	2	40	66
	2013	66 883 662	19 000	20 760	23 000	2	33	55
	2014	67 592 098	18 000	19 060	21 000	2	29	47
	2015	68 301 989	10 000	11 283	13 000	1	16	25
	2016	69 011 970	4 600	5 024	5 600	0	7	13
	2017	69 719 633	5 100	5 481	6 100	0	9	15
	2018	70 416 320	5 300	5 794	6 500	0	9	16

"–" refers to not applicable.

[1] The number of indigenous malaria cases registered by the NMPs is reported here without further adjustments.

[2] The number of indigenous malaria deaths registered by the NMPs is reported here without further adjustments.

[3] Certified malaria free countries are included in this listing for historical purposes.

[4] South Sudan became an independent state on 9 July 2011 and a Member State of WHO on 27 September 2011. South Sudan and Sudan have distinct epidemiological profiles comprising high-transmission and low-transmission areas respectively. For this reason, data up to June 2011 from the Sudanese high-transmission areas (10 southern states, which correspond to South Sudan) and low-transmission areas (15 northern states which correspond to contemporary Sudan) are reported separately.

Annex 3 - F. Population at risk and estimated malaria cases and deaths, 2010–2018

WHO region	Year	Population at risk	Cases			Deaths		
			Lower	Point	Upper	Lower	Point	Upper
REGIONAL SUMMARY								
African	2010	742 051 480	199 000 000	219 000 000	245 000 000	507 000	533 000	588 000
	2011	763 387 315	194 000 000	213 000 000	237 000 000	469 000	493 000	537 000
	2012	785 260 919	190 000 000	209 000 000	233 000 000	444 000	469 000	514 000
	2013	807 674 747	185 000 000	204 000 000	229 000 000	419 000	444 000	493 000
	2014	830 636 558	181 000 000	198 000 000	218 000 000	408 000	428 000	462 000
	2015	854 147 991	184 000 000	199 000 000	219 000 000	391 000	411 000	448 000
	2016	878 208 734	189 000 000	206 000 000	229 000 000	371 000	389 000	425 000
	2017	902 801 325	192 000 000	212 000 000	240 000 000	364 000	383 000	423 000
	2018	927 888 238	191 000 000	213 000 000	244 000 000	361 000	380 000	425 000
Americas	2010	126 118 119	744 000	814 000	894 000	220	459	730
	2011	127 739 647	566 000	611 000	666 000	180	444	710
	2012	129 364 372	541 000	580 000	627 000	180	392	600
	2013	130 969 261	520 000	562 000	613 000	180	391	590
	2014	132 522 297	445 000	477 000	512 000	140	289	420
	2015	134 003 416	525 000	566 000	611 000	150	324	460
	2016	135 398 716	640 000	691 000	749 000	210	474	680
	2017	136 722 119	880 000	944 000	1 026 000	250	620	910
	2018	138 017 898	867 000	929 000	1 007 000	220	577	850
Eastern Mediterranean	2010	419 019 843	3 300 000	4 300 000	6 300 000	3 000	8 300	14 400
	2011	427 979 875	3 400 000	4 500 000	6 500 000	3 000	7 500	12 300
	2012	436 754 102	3 200 000	4 200 000	6 000 000	2 900	7 600	12 400
	2013	445 450 169	3 000 000	3 900 000	5 300 000	2 500	6 900	11 100
	2014	454 228 324	3 100 000	4 000 000	5 500 000	2 400	6 900	11 300
	2015	463 210 243	3 000 000	3 800 000	5 200 000	2 300	7 100	12 200
	2016	468 761 159	3 800 000	4 800 000	6 400 000	2 900	8 600	15 300
	2017	478 058 225	3 800 000	4 900 000	6 800 000	3 000	9 200	17 300
	2018	487 588 453	3 700 000	4 900 000	6 800 000	2 600	9 300	17 700
European	2010	37 906 443	–	170	–	–	0	–
	2011	38 469 606	–	69	–	–	0	–
	2012	39 086 200	–	21	–	–	0	–
	2013	39 739 267	–	3	–	–	0	–
	2014	40 405 247	–	2	–	–	0	–
	2015	41 065 655	–	0	–	–	0	–
	2016	41 714 844	–	0	–	–	0	–
	2017	42 352 758	–	0	–	–	0	–
	2018	42 973 389	–	0	–	–	0	–
South-East Asia	2010	1 477 504 120	19 800 000	25 100 000	33 900 000	9 000	39 000	67 000
	2011	1 496 330 952	16 700 000	21 100 000	28 300 000	7 000	32 000	57 000
	2012	1 514 731 269	14 700 000	18 400 000	24 400 000	7 000	28 000	47 000
	2013	1 532 751 942	10 900 000	13 700 000	18 000 000	4 000	21 000	36 000
	2014	1 550 466 894	10 400 000	13 200 000	17 400 000	4 000	24 000	42 000
	2015	1 567 931 968	10 700 000	13 600 000	18 200 000	3 000	25 000	44 000
	2016	1 585 152 940	10 500 000	14 000 000	19 700 000	3 000	25 000	47 000
	2017	1 602 118 493	8 800 000	11 300 000	15 400 000	3 000	20 000	35 000
	2018	1 618 838 836	5 800 000	7 900 000	10 700 000	2 000	12 000	21 000
Western Pacific	2010	721 038 851	1 045 000	1 839 000	2 779 000	800	3 800	7 500
	2011	726 302 437	922 000	1 576 000	2 340 000	600	3 300	6 600
	2012	731 623 901	914 000	1 761 000	3 009 000	700	3 600	8 000
	2013	736 961 516	1 305 000	2 027 000	2 925 000	600	4 600	9 300
	2014	742 256 202	1 588 000	2 345 000	3 339 000	700	4 400	8 500
	2015	747 456 804	1 115 000	1 445 000	1 852 000	500	2 800	5 000
	2016	752 550 363	1 318 000	1 733 000	2 228 000	500	3 500	6 400
	2017	757 527 287	1 392 000	1 854 000	2 420 000	500	3 600	6 500
	2018	762 325 610	1 495 000	1 980 000	2 588 000	500	3 600	6 500
Total	2010	3 523 638 856	231 000 000	251 000 000	278 000 000	541 000	585 000	649 000
	2011	3 580 209 832	222 000 000	241 000 000	266 000 000	499 000	536 000	588 000
	2012	3 636 820 763	214 000 000	234 000 000	260 000 000	474 000	508 000	560 000
	2013	3 693 546 902	205 000 000	224 000 000	250 000 000	446 000	477 000	531 000
	2014	3 750 515 522	202 000 000	218 000 000	239 000 000	434 000	463 000	504 000
	2015	3 807 816 077	203 000 000	219 000 000	240 000 000	416 000	446 000	491 000
	2016	3 861 786 756	210 000 000	227 000 000	251 000 000	398 000	427 000	473 000
	2017	3 919 580 207	211 000 000	231 000 000	259 000 000	390 000	416 000	462 000
	2018	3 977 632 424	206 000 000	228 000 000	258 000 000	384 000	405 000	452 000

Annex 3 - G. Population at risk and reported malaria cases by place of care, 2018

WHO region Country/area	Population			
	UN population	At risk (low + high)	At risk (high)	Number of people living in active foci
AFRICAN				
Algeria	42 228 415	-	-	0
Angola	30 809 787	30 809 787	30 809 787	-
Benin	11 485 035	11 485 035	11 485 035	-
Botswana	2 254 067	1 494 401	94 941	-
Burkina Faso	19 751 466	19 751 466	19 751 466	-
Burundi	11 175 379	11 175 379	11 175 379	-
Cabo Verde	543 764	-	-	162 814
Cameroon	25 216 261	25 216 261	17 903 545	-
Central African Republic	4 666 375	4 666 375	4 666 375	-
Chad	15 477 727	15 308 246	10 425 023	-
Comoros	832 322	832 322	396 019	-
Congo	5 244 363	5 244 363	5 244 363	-
Côte d'Ivoire	25 069 226	25 069 226	25 069 226	-
Democratic Republic of the Congo	84 068 092	84 068 092	81 546 049	-
Equatorial Guinea	1 308 966	1 308 966	1 308 966	-
Eritrea	3 452 797	3 452 797	2 451 486	-
Eswatini	1 136 274	318 157	0	-
Ethiopia	109 224 410	74 272 599	29 709 040	-
Gabon	2 119 275	2 119 275	2 119 275	-
Gambia	2 280 092	2 280 092	2 280 092	-
Ghana	29 767 108	29 767 108	29 767 108	-
Guinea	12 414 292	12 414 292	12 414 292	-
Guinea-Bissau	1 874 304	1 874 304	1 874 304	-
Kenya	51 392 570	51 392 570	36 075 015	-
Liberia	4 818 976	4 818 976	4 818 976	-
Madagascar	26 262 313	26 262 313	23 049 907	-
Malawi	18 143 215	18 143 215	18 143 215	-
Mali	19 077 755	19 077 755	17 389 755	-
Mauritania	4 403 312	4 403 312	2 838 727	-
Mozambique	29 496 009	29 496 009	29 496 009	-
Namibia	2 448 300	1 943 338	1 130 160	-
Niger	22 442 831	22 442 831	22 442 831	-
Nigeria	195 874 685	195 874 685	149 605 167	-
Rwanda	12 301 969	12 301 969	12 301 969	-
Sao Tome and Principe	211 032	211 032	211 032	-
Senegal	15 854 324	15 854 324	15 762 845	-
Sierra Leone	7 650 149	7 650 149	7 650 149	-
South Africa	57 792 520	5 779 252	2 311 701	-
South Sudan[1]	10 975 924	10 975 924	10 975 924	-
Togo	7 889 095	7 889 095	7 889 095	-
Uganda	42 729 032	42 729 032	42 729 032	-
United Republic of Tanzania[2]	56 313 444	56 313 444	55 692 038	-
Mainland	54 720 096	54 720 096	54 720 096	-
Zanzibar	1 593 348	1 593 348	971 942	-
Zambia	17 351 714	17 351 714	17 351 714	-
Zimbabwe	14 438 812	11 369 510	4 131 810	-
AMERICAS				
Belize	383 071	-	-	17 225
Bolivia (Plurinational State of)	11 353 140	5 150 579	283 601	-
Brazil	209 469 320	42 522 272	4 817 794	-
Colombia	49 661 056	10 994 461	4 989 943	-
Costa Rica	4 999 443	-	-	137 832
Dominican Republic	10 627 147	5 853 645	150 374	-
Ecuador	17 084 359	-	-	246 833
El Salvador	6 420 740	-	-	12 700
French Guiana	282 938	156 544	26 115	-
Guatemala	17 247 855	13 020 751	2 353 125	-
Guyana	779 007	779 007	85 021	-

Public sector		Private sector		Community level	
Presumed	Confirmed	Presumed	Confirmed	Presumed	Confirmed
0	1 242 [5]	–	–	–	–
777 685	5 150 575 [3]	–	–	0	241 294
280 134	1 768 450 [4]	323 782	245 807	0	207 362
0	585 [5]	0	2	–	–
1 691 351	10 278 970 [4]	365 492	310 030	20 825	79 954
182 925	4 966 511 [5]	1 399	298 023	0	679 278
0	21 [5]	0	0	–	–
1 221 809	1 249 705	913 574	930 111	70 741	77 817
23 038	972 119 [5]	27 653	147 456	9 858	959
–	1 364 706 [3]	–	–	159 503	222 205
4 069	15 613 [5]	0	427	881	3 642
207 712	116 903 [4]	–	–	–	–
531 449	4 766 477 [5]	0	126 327	0	194 076
1 236 233	16 972 207 [3]	–	–	0	1 372 477
1 964	8 962	–	–	–	–
853	22 955 [4]	–	–	1 033	23 485
0	656 [5]	0	296	–	–
244 804	962 087 [5]	–	–	–	–
685 559	111 719	–	–	–	–
1 206	87 448 [4]	0	1 206	0	4 294
6 222 946	4 931 448 [5]	1 919 308	1 556 857	–	–
384 629	1 214 996 [5]	109 156	53 260	0	299 767
0	171 075 [5]	0	5 854	0	4 318
8 429 215	1 521 566	1 738 477	465 581	128 429	330 943
–	–	–	–	–	–
–	972 790 [4]	262 805	51 693	105 350	108 338
0	5 865 476 [3]	–	–	0	1 045 467
268 629	2 345 475 [5]	0	51 177	0	268 623
145 232	30 609	–	–	–	–
27 629	9 292 928	–	–	7 229	1 011 544
4 300	36 740	–	–	–	–
311 608	3 046 450 [5]	40 112	47 791	0	93 889
5 916 631	12 953 583	498 219	1 487 171	17 725	107 270
0	1 975 926	0	33 854	0	2 222 103
0	2 940 [5]	–	–	–	547
5 801	530 944 [5]	–	–	1 080	143 876
48 024	1 733 831 [3]	18 871	18 230	245 840	561 180
6 174	10 789 [3]	–	–	0	1 675
4 598 663	98 843	–	–	–	–
291 076	1 090 334 [4]	0	291 076	0	621 467
3 136 262	5 759 174 [5]	340 522	372 612	–	–
166 771	6 053 714 [2]	119 178	494 052	0	442
164 733	6 050 382 [4]	119 178	492 692	–	–
2 038	3 332 [4]	0	1 360	0	442
156 044	5 039 679 [3]	–	–	710 465	393 548
0	184 427 [4]	0	8 630	0	79 591
0	7 [5]	0	2	–	–
0	5 354 [3]	–	–	0	93
0	194 512 [4]	–	–	–	–
0	46 217 [5]	–	–	–	–
–	152 [4]	0	4	–	–
0	608	0	84	22	137
0	1 806 [5]	0	10	–	–
0	2	0	1	0	0
–	–	–	–	–	–
–	4 769	0	3	–	–
0	17 038	–	37	0	2 102

Annex 3 - G. Population at risk and reported malaria cases by place of care, 2018

WHO region Country/area	Population			
	UN population	At risk (low + high)	At risk (high)	Number of people living in active foci
AMERICAS				
Haiti	11 123 183	9 937 674	2 696 148	-
Honduras	9 587 523	8 684 378	2 443 668	-
Mexico	126 190 782	-	-	3 120 973
Nicaragua	6 465 502	2 822 192	554 934	-
Panama	4 176 868	4 040 827	176 013	-
Peru	31 989 265	12 564 104	1 601 383	-
Suriname	575 987	85 073	24 456	-
Venezuela (Bolivarian Republic of)	28 887 117	14 443 559	5 990 755	-
EASTERN MEDITERRANEAN				
Afghanistan	37 171 922	28 652 489	10 121 171	-
Djibouti	958 923	719 115	336 659	-
Iran (Islamic Republic of)	81 800 204	835 180	0	-
Pakistan	212 228 288	208 643 752	61 370 054	-
Saudi Arabia	33 702 757	-	-	176 408
Somalia	15 008 225	15 008 225	7 638 736	-
Sudan	41 801 532	41 801 532	36 325 531	-
Yemen	28 498 683	18 373 671	10 964 013	-
SOUTH-EAST ASIA				
Bangladesh	161 376 713	17 352 838	2 038 188	-
Bhutan	754 396	-	-	14 876
Democratic People's Republic of Korea	25 549 606	-	-	12 379 473
India	1 352 642 283	1 263 908 949	164 089 035	-
Indonesia	267 670 549	267 670 549	17 114 855	-
Myanmar	53 708 318	31 966 117	8 491 822	-
Nepal	28 095 712	8 155 623	1 468 563	-
Thailand	69 428 454	13 174 743	1 537 146	-
Timor-Leste	1 267 975	1 192 542	429 432	-
WESTERN PACIFIC				
Cambodia	16 249 795	11 491 693	7 820 376	-
China	1 435 651 150	600 418 024	200 991	-
Lao People's Democratic Republic	7 061 498	3 674 380	3 674 380	-
Malaysia	31 528 033	-	-	3 884
Papua New Guinea	8 606 324	8 606 324	8 089 945	-
Philippines	106 651 394	61 936 731	7 268 293	-
Republic of Korea	51 171 700	3 582 019	0	-
Solomon Islands	652 856	646 327	646 327	-
Vanuatu	292 675	292 675	254 407	-
Viet Nam	95 545 959	70 416 321	6 494 737	-
REGIONAL SUMMARY				
African	1 060 267 778	925 208 992	782 488 842	162 814
Americas	547 304 303	131 055 066	26 193 330	3 535 563
Eastern Mediterranean	451 170 534	314 033 964	126 756 164	176 408
South-East Asia	1 960 494 006	1 603 421 361	195 169 041	12 394 349
Western Pacific	1 753 411 384	761 064 494	34 449 456	3 884
Total	**5 772 648 005**	**3 734 783 877**	**1 165 056 833**	**16 273 018**

UN: United Nations; WHO: World Health Organization.

"–" refers to not applicable or data not available.

[1] In May 2013, South Sudan was reassigned to the WHO African Region (WHA resolution 66.21, http://apps.who.int/gb/ebwha/pdf_files/WHA66/A66_R21-en.pdf).

[2] Where national data for the United Republic of Tanzania are unavailable, refer to Mainland and Zanzibar.

[3] Figures reported for the public sector include cases detected at the community level.

[4] Figures reported for the public sector include cases detected in the private sector.

[5] Figures reported for the public sector include cases detected at the community level and in the private sector.

[6] Figures include all imported or non-human malaria cases; none of them being indigenous malaria cases.

Public sector		Private sector		Community level	
Presumed	Confirmed	Presumed	Confirmed	Presumed	Confirmed
–	9 112 [5]	0	2 049	0	793
0	882	0	73	32	152
0	826 [5]	0	6	–	–
0	15 934	–	–	–	–
0	715	0	3	–	–
0	46 619	–	–	–	–
0	235 [5]	–	16	0	17
0	404 924 [3]	–	–	–	–
51 174	248 689	0	5 365	21 278	69 831
0	25 319	–	474	–	–
0	1 061 [5]	–	–	–	–
591 045	374 510 [4]	0	103 693	–	–
0	2 711	–	–	–	–
9	31 021	–	–	–	–
1 974 469	1 606 833 [4]	–	–	4 434	31 184
75 243	117 652	10 253	36 521	0	3 727
0	1 919	0	56	0	8 548
0	54 [5]	0	5	–	–
0	3 698	–	–	–	–
0	429 928 [3]	–	–	–	199 496
0	223 208 [5]	0	28 759	0	2 804
0	74 392 [5]	0	2 126	0	59 832
2 630	1 158 [5]	544	34	–	–
428	5 389	0	656	0	705
0	8 [5]	–	–	0	0
0	42 285	0	0	0	20 297
5	2 513 [6]	–	–	–	–
0	8 913 [3]	0	1 228	0	1 804
0	4 630 [5,6]	0	52 [6]	–	–
424 444	516 202	–	–	0	0
2 970	1 574	0	295	295	2 772
0	576	0	429	–	–
13 239	59 191	–	–	–	–
0	644 [3]	–	–	0	150
209	6 661 [5]	0	39	–	–
37 210 425	113 681 648	6 678 548	6 997 523	1 478 959	10 401 431
0	749 712	0	2 288	54	3 294
2 691 940	2 407 796	10 253	146 053	25 712	104 742
3 058	739 754	544	31 636	0	271 385
440 867	643 189	0	2 043	295	25 023
40 346 290	**118 222 099**	**6 689 345**	**7 179 543**	**1 505 020**	**10 805 875**

Annex 3 – H. Reported malaria cases by method of confirmation, 2010–2018

WHO region Country/area		2010	2011	2012	2013	2014	2015	2016	2017	2018
AFRICAN										
Algeria[1]	Presumed and confirmed	408	191	887	603	266	747	432	453	1 242
	Microscopy examined	12 224	11 974	15 790	12 762	8 690	8 000	6 628	6 469	10 081
	Confirmed with microscopy	408	191	887	603	266	747	432	453	1 242
	RDT examined	–	–	–	–	–	0	0	0	0
	Confirmed with RDT	–	–	–	–	–	0	0	0	0
	Imported cases	396	187	825	587	260	727	420	446	1 241
Angola	Presumed and confirmed	3 687 574	3 501 953	3 031 546	3 144 100	3 180 021	3 254 270	4 301 146	4 500 221	5 928 260
	Microscopy examined	1 947 349	1 765 933	2 245 223	3 025 258	3 398 029	3 345 693	4 183 727	7 493 969	5 066 780
	Confirmed with microscopy	1 324 264	1 147 473	1 056 563	1 462 941	1 431 313	1 396 773	2 058 128	2 199 810	2 442 500
	RDT examined	639 476	833 753	1 069 483	1 103 815	1 855 400	3 009 305	2 959 282	2 931 055	5 025 981
	Confirmed with RDT	358 606	484 809	440 271	536 927	867 666	1 372 532	1 736 125	1 675 082	2 708 075
	Imported cases	–	–	–	–	–	–	–	–	–
Benin	Presumed and confirmed	1 432 095	1 424 335	1 513 212	1 670 273	1 509 221	1 495 375	1 374 729	1 719 171	2 048 584
	Microscopy examined	–	88 134	243 008	291 479	155 205	296 264	267 405	267 492	349 191
	Confirmed with microscopy	–	68 745	–	99 368	108 714	108 061	104 601	208 823	258 519
	RDT examined	–	475 986	825 005	1 158 526	1 335 582	1 486 667	1 500 047	2 016 767	2 016 745
	Confirmed with RDT	–	354 223	705 839	979 466	935 521	1 160 286	1 219 975	1 487 954	1 509 931
	Imported cases	–	–	–	–	–	–	–	–	–
Botswana	Presumed and confirmed	12 196	1 141	308	506	1 485	340	718	1 902	585
	Microscopy examined	–	–	–	–	–	–	5 178	5 223	872
	Confirmed with microscopy	1 046	432	–	–	–	–	–	–	–
	RDT examined	–	–	–	–	–	1 284	7 806	7 380	13 107
	Confirmed with RDT	–	–	193	456	1 346	326	716	1 900	585
	Imported cases	–	–	–	30	30	48	64	62	51
Burkina Faso	Presumed and confirmed	5 723 481	5 024 697	6 970 700	7 146 026	8 278 408	8 286 453	9 785 822	11 915 816	11 970 321
	Microscopy examined	177 879	400 005	223 372	183 971	198 947	222 190	191 208	133 101	157 824
	Confirmed with microscopy	88 540	83 857	90 089	82 875	83 259	92 589	80 077	46 411	56 989
	RDT examined	940 985	450 281	4 516 273	4 296 350	6 224 055	8 290 188	11 794 810	12 561 490	13 061 136
	Confirmed with RDT	715 999	344 256	3 767 957	3 686 176	5 345 396	6 922 857	9 699 077	10 179 048	10 221 981
	Imported cases	–	–	–	–	–	–	–	–	–
Burundi	Presumed and confirmed	4 255 301	3 298 979	2 570 754	4 469 007	4 831 758	5 243 410	8 383 389	8 133 919	5 149 436
	Microscopy examined	2 825 558	2 859 720	2 659 372	4 123 012	4 471 998	3 254 670	3 941 251	3 814 355	1 542 232
	Confirmed with microscopy	1 599 908	1 485 332	1 484 676	2 366 134	2 718 391	1 964 862	2 520 622	2 269 831	1 148 316
	RDT examined	273 324	181 489	1 148 965	2 933 869	2 903 679	5 076 107	8 307 007	8 058 231	7 009 165
	Confirmed with RDT	163 539	86 542	666 400	1 775 253	1 866 882	3 194 844	5 753 440	5 400 346	3 818 195
	Imported cases	–	–	–	–	–	–	–	–	–
Cabo Verde	Presumed and confirmed	47	36	–	–	46	28	–	446	21
	Microscopy examined	–	–	8 715	10 621	6 894	3 117	8 393	3 857	16 623
	Confirmed with microscopy	47	–	36	46	46	28	75	446	21
	RDT examined	–	26 508	–	–	–	–	–	–	–
	Confirmed with RDT	–	36	–	–	–	–	–	–	–
	Imported cases	–	29	35	24	20	21	27	23	18
Cameroon	Presumed and confirmed	1 845 691	1 829 266	1 589 317	1 824 633	1 369 518	2 321 933	1 790 891	2 488 993	2 471 514
	Microscopy examined	–	1 110 308	1 182 610	1 236 306	1 086 095	1 024 306	1 373 802	627 709	658 017
	Confirmed with microscopy	–	–	–	–	–	592 351	810 367	390 130	428 888
	RDT examined	–	120 466	93 392	591 670	1 254 293	1 128 818	1 740 375	1 420 522	1 337 354
	Confirmed with RDT	–	–	–	–	–	570 433	864 897	801 127	820 817
	Imported cases	–	–	–	–	–	–	–	–	–
Central African Republic	Presumed and confirmed	66 484	221 980	459 999	407 131	495 238	953 535	1 400 526	1 267 673	995 157
	Microscopy examined	–	–	–	63 695	55 943	139 241	189 481	112 007	163 370
	Confirmed with microscopy	–	–	–	36 943	41 436	106 524	144 924	28 855	117 267
	RDT examined	–	–	55 746	136 548	369 208	724 303	1 249 963	483 714	1 181 578
	Confirmed with RDT	–	–	46 759	79 357	253 652	492 309	887 840	354 454	854 852
	Imported cases	–	–	–	–	–	–	–	–	–

WHO region Country/area		2010	2011	2012	2013	2014	2015	2016	2017	2018
AFRICAN										
Chad	Presumed and confirmed	544 243	528 454	660 575	1 272 841	1 513 772	1 490 556	1 402 215	1 659 606	1 175 041
	Microscopy examined	89 749	–	69 789	–	–	–	1 063 293	1 584 525	190 006
	Confirmed with microscopy	75 342	86 348	–	206 082	160 260	149 574	720 765	1 064 354	137 501
	RDT examined	309 927	114 122	–	621 469	1 137 455	937 775	861 561	1 359 070	1 751 483
	Confirmed with RDT	125 106	94 778	–	548 483	753 772	637 472	574 003	898 018	1 227 205
	Imported cases	–	–	–	–	–	–	–	–	–
Comoros	Presumed and confirmed	103 670	76 661	65 139	62 565	2 465	1 517	1 333	2 274	19 682
	Microscopy examined	87 595	63 217	125 030	154 824	93 444	89 634	71 902	130 134	90 956
	Confirmed with microscopy	35 199	22 278	45 507	46 130	1 987	963	559	1 325	9 197
	RDT examined	5 249	20 226	27 714	21 546	9 839	11 479	22 219	60 691	24 567
	Confirmed with RDT	1 339	2 578	4 333	7 026	216	337	507	949	6 416
	Imported cases	–	–	–	–	–	–	–	–	–
Congo	Presumed and confirmed	446 656	277 263	117 640	183 026	248 159	264 574	374 252	297 652	324 615
	Microscopy examined	–	–	–	69 375	88 764	87 547	202 922	153 203	178 017
	Confirmed with microscopy	–	37 744	120 319	43 232	54 523	51 529	134 612	127 939	116 903
	RDT examined	–	–	–	0	19 746	0	60 927	0	0
	Confirmed with RDT	–	–	–	0	11 800	0	37 235	0	0
	Imported cases	–	–	–	–	–	–	–	–	–
Côte d'Ivoire	Presumed and confirmed	1 721 461	2 588 004	2 795 919	4 708 425	4 658 774	3 606 725	3 471 024	3 391 967	5 297 926
	Microscopy examined	–	49 828	195 546	395 914	568 562	811 426	975 507	1 221 845	1 132 659
	Confirmed with microscopy	62 726	29 976	107 563	215 104	306 926	478 870	579 566	588 969	696 124
	RDT examined	–	–	1 572 785	3 384 765	4 904 066	4 174 097	4 202 868	5 007 162	5 042 040
	Confirmed with RDT	–	–	1 033 064	2 291 849	3 405 905	2 897 034	2 891 458	2 685 714	4 070 353
	Imported cases	–	–	–	–	–	–	–	–	–
Democratic Republic of the Congo	Presumed and confirmed	9 252 959	9 442 144	9 128 398	11 363 817	9 749 369	10 878 974	15 397 717	15 272 767	18 208 440
	Microscopy examined	3 678 849	4 226 533	4 329 318	4 126 129	3 533 165	2 877 585	2 810 067	1 981 621	1 926 455
	Confirmed with microscopy	2 374 930	2 700 818	2 656 864	2 611 478	2 126 554	1 902 640	1 847 143	1 291 717	995 577
	RDT examined	54 728	2 912 088	3 327 071	6 096 993	11 114 215	13 574 891	18 630 636	18 994 861	20 671 006
	Confirmed with RDT	42 850	1 861 163	2 134 734	4 103 745	7 842 429	9 724 833	13 483 698	13 885 210	15 976 630
	Imported cases	–	–	–	–	–	–	–	–	–
Equatorial Guinea	Presumed and confirmed	78 095	37 267	20 890	25 162	19 642	8 581	7 542	7 787	6 099
	Microscopy examined	42 585	23 004	33 245	27 039	47 322	21 831	239 938	13 127	8 395
	Confirmed with microscopy	39 636	20 601	13 196	11 235	17 685	8 564	125 623	6 800	4 135
	RDT examined	16 772	2 899	6 826	5 489	9 807	46 227	78 841	78 090	33 174
	Confirmed with RDT	14 177	1 865	1 973	1 894	2 732	6 578	22 091	8 925	4 827
	Imported cases	–	–	–	–	–	–	–	–	–
Eritrea	Presumed and confirmed	53 750	39 567	42 178	34 678	35 725	24 310	47 055	32 444	23 808
	Microscopy examined	79 024	67 190	84 861	81 541	63 766	59 268	83 599	74 962	70 465
	Confirmed with microscopy	13 894	15 308	11 557	10 890	10 993	8 332	24 251	14 519	10 325
	RDT examined	–	25 570	33 758	39 281	53 032	47 744	–	45 144	74 917
	Confirmed with RDT	22 088	19 540	10 258	10 427	19 775	11 040	–	16 967	12 630
	Imported cases	–	–	–	–	–	–	–	–	–
Eswatini	Presumed and confirmed	1 722	797	626	669	–	651	487	1 127	656
	Microscopy examined	–	–	–	–	–	–	1 249	371	1 526
	Confirmed with microscopy	87	130	345	488	711	43	141	68	656
	RDT examined	–	–	–	–	–	–	–	2 841	8 311
	Confirmed with RDT	181	419	217	474	–	152	209	1 059	–
	Imported cases	–	170	153	234	322	282	221	403	348
Ethiopia	Presumed and confirmed	4 068 764	3 549 559	3 876 745	3 316 013	2 513 863	2 174 707	1 962 996	1 755 748	1 206 891
	Microscopy examined	2 509 543	3 418 719	3 778 479	8 573 335	7 062 717	5 679 932	6 367 309	6 246 949	5 668 995
	Confirmed with microscopy	1 158 197	1 480 306	1 692 578	2 645 454	2 118 815	1 867 059	1 718 504	1 530 739	962 087
	RDT examined	–	–	–	–	–	–	–	–	–
	Confirmed with RDT	–	–	–	–	–	–	–	–	–
	Imported cases	–	–	–	–	–	–	–	–	–

Annex 3 - H. Reported malaria cases by method of confirmation, 2010–2018

WHO region Country/area		2010	2011	2012	2013	2014	2015	2016	2017	2018
AFRICAN										
Gabon	Presumed and confirmed	185 105	178 822	188 089	185 196	185 996	217 287	161 508	157 639	797 278
	Microscopy examined	54 714	–	66 018	90 185	90 275	79 308	62 658	70 820	264 676
	Confirmed with microscopy	12 816	–	18 694	26 432	27 687	20 390	22 419	28 297	88 112
	RDT examined	7 887	–	4 129	10 132	11 812	12 761	2 738	18 877	71 787
	Confirmed with RDT	1 120	–	1 059	2 550	4 213	3 477	1 496	6 947	23 607
	Imported cases	–	–	–	–	–	–	–	–	–
Gambia	Presumed and confirmed	194 009	261 967	271 038	279 829	166 229	249 437	155 456	75 559	88 654
	Microscopy examined	290 842	172 241	156 580	236 329	286 111	272 604	165 793	77 491	171 668
	Confirmed with microscopy	52 245	71 588	29 325	65 666	66 253	49 649	26 397	11 343	14 510
	RDT examined	123 564	–	705 862	614 128	317 313	609 852	677 346	508 107	533 994
	Confirmed with RDT	64 108	190 379	271 038	175 126	99 976	190 733	127 377	58 588	72 938
	Imported cases	–	–	–	–	–	–	–	–	–
Ghana	Presumed and confirmed	3 849 536	4 154 261	10 676 731	7 200 797	8 453 557	10 186 510	10 448 267	10 228 988	11 154 394
	Microscopy examined	2 031 674	1 172 838	4 219 097	1 394 249	1 987 959	2 023 581	2 594 918	2 495 536	2 659 067
	Confirmed with microscopy	1 029 384	624 756	2 971 699	721 898	970 448	934 304	1 189 012	1 089 799	1 105 342
	RDT examined	247 278	781 892	1 438 284	1 488 822	3 610 453	5 478 585	5 532 416	5 677 564	6 660 205
	Confirmed with RDT	42 253	416 504	783 467	917 553	2 445 464	3 385 615	3 346 155	3 286 140	3 826 106
	Imported cases	–	–	–	–	–	–	–	–	–
Guinea	Presumed and confirmed	1 092 554	1 189 016	1 220 574	775 341	1 595 828	895 016	992 146	1 335 323	1 599 625
	Microscopy examined	–	43 549	–	–	116 767	78 377	79 233	99 083	131 715
	Confirmed with microscopy	20 936	5 450	191 421	63 353	82 818	52 211	53 805	64 211	77 119
	RDT examined	–	139 066	–	–	–	1 092 523	1 423 802	2 035 460	2 445 164
	Confirmed with RDT	–	90 124	125 779	147 904	577 389	758 768	938 341	1 271 112	1 137 877
	Imported cases	–	–	–	–	–	–	–	–	–
Guinea-Bissau	Presumed and confirmed	140 143	174 986	129 684	132 176	98 952	142 309	150 903	143 554	171 075
	Microscopy examined	48 799	57 698	61 048	58 909	106 882	123 810	146 708	157 970	149 423
	Confirmed with microscopy	30 239	21 320	23 547	17 733	35 546	45 789	53 014	53 770	45 564
	RDT examined	56 455	139 531	97 047	102 079	197 536	261 868	234 488	303 651	320 217
	Confirmed with RDT	20 152	50 662	26 834	36 851	57 885	96 520	97 889	89 784	125 511
	Imported cases	–	–	–	–	–	–	–	–	–
Kenya	Presumed and confirmed	6 071 583	11 120 812	9 335 951	9 750 953	9 655 905	7 676 980	8 322 500	7 961 444	9 950 781
	Microscopy examined	2 384 402	3 009 051	4 836 617	6 606 885	7 444 865	7 772 329	6 167 609	5 952 353	4 282 912
	Confirmed with microscopy	898 531	1 002 805	1 426 719	2 060 608	2 415 950	1 025 508	1 569 045	2 215 665	827 947
	RDT examined	–	–	164 424	655 285	850 884	1 965 661	3 588 676	3 314 695	2 329 005
	Confirmed with RDT	–	–	26 752	274 678	392 981	473 519	1 214 801	999 451	693 619
	Imported cases	–	–	–	–	–	–	–	–	–
Liberia	Presumed and confirmed	2 675 816	2 480 748	1 800 372	1 483 676	1 066 107	1 781 092	2 343 410	1 342 953	–
	Microscopy examined	335 973	728 443	772 362	818 352	1 318 801	509 062	649 096	715 643	–
	Confirmed with microscopy	212 927	577 641	507 967	496 269	302 708	305 981	381 781	425 639	–
	RDT examined	998 043	1 593 676	1 276 521	1 144 405	912 382	947 048	1 304 021	1 045 323	–
	Confirmed with RDT	709 246	1 338 121	899 488	747 951	561 496	625 105	809 356	644 474	–
	Imported cases	–	–	–	–	–	–	–	–	–
Madagascar	Presumed and confirmed	293 910	255 814	395 149	382 495	433 101	752 176	475 333	800 661	965 390
	Microscopy examined	24 393	34 813	38 453	42 573	37 362	39 604	33 085	34 265	43 759
	Confirmed with microscopy	2 173	3 447	3 667	4 947	3 853	4 748	3 734	5 134	7 400
	RDT examined	604 114	739 572	906 080	1 026 110	926 998	1 488 667	1 496 990	1 974 518	2 290 797
	Confirmed with RDT	200 277	221 051	355 753	380 651	374 110	739 355	471 599	795 527	965 390
	Imported cases	–	–	–	–	712	1 167	1 212	–	–
Malawi	Presumed and confirmed	6 851 108	5 338 701	4 922 596	3 906 838	5 065 703	4 933 416	5 165 386	5 936 348	5 865 476
	Microscopy examined	–	119 996	406 907	132 475	198 534	216 643	240 212	127 752	129 575
	Confirmed with microscopy	–	50 526	283 138	44 501	77 635	75 923	96 538	46 099	34 735
	RDT examined	–	580 708	2 763 986	3 029 020	5 344 724	7 030 084	8 661 237	9 413 944	11 384 109
	Confirmed with RDT	–	253 973	1 281 846	1 236 391	2 827 675	3 585 315	4 730 835	4 901 344	5 830 741
	Imported cases	–	–	–	–	–	–	–	–	–

WHO region Country/area		2010	2011	2012	2013	2014	2015	2016	2017	2018
AFRICAN										
Mali	Presumed and confirmed	2 171 542	1 961 070	2 171 739	2 327 385	2 590 643	3 317 001	2 311 098	2 097 797	2 614 104
	Microscopy examined	–	–	–	–	–	–	–	397 723	437 903
	Confirmed with microscopy	–	–	97 995	190 337	219 637	243 151	235 212	276 673	301 880
	RDT examined	1 380 178	974 558	–	1 889 286	–	3 389 449	3 408 254	2 755 935	3 019 364
	Confirmed with RDT	227 482	307 035	788 487	1 176 881	1 820 216	2 052 460	1 921 070	1 821 124	2 043 595
	Imported cases	–	–	–	–	–	–	–	–	–
Mauritania	Presumed and confirmed	244 319	154 003	169 104	128 486	172 326	181 562	159 225	162 572	175 841
	Microscopy examined	5 449	3 752	1 865	5 510	–	–	–	–	–
	Confirmed with microscopy	909	1 130	255	957	–	–	–	–	–
	RDT examined	2 299	7 991	3 293	3 576	47 500	60 253	50 788	51 515	75 889
	Confirmed with RDT	1 085	1 796	1 633	630	15 835	22 631	29 156	20 105	30 609
	Imported cases	–	–	–	–	–	–	–	–	–
Mayotte	Presumed and confirmed	396	92	72	–	–	–	18	19	47
	Microscopy examined	2 023	1 214	1 463	–	–	–	–	–	–
	Confirmed with microscopy	396	92	72	82	15	11	28	19	47
	RDT examined	–	–	–	–	–	–	–	–	–
	Confirmed with RDT	–	–	–	–	–	–	–	–	–
	Imported cases	224	51	47	71	14	10	10	–	44
Mozambique	Presumed and confirmed	3 381 371	3 344 413	3 203 338	3 924 832	5 485 327	5 830 322	7 546 091	8 993 352	9 320 557
	Microscopy examined	1 950 933	2 504 720	2 546 213	2 058 998	2 295 823	2 313 129	1 886 154	1 699 589	1 909 051
	Confirmed with microscopy	644 568	1 093 742	886 143	774 891	1 009 496	735 750	674 697	700 282	743 435
	RDT examined	2 287 536	2 966 853	2 234 994	5 215 893	9 944 222	11 928 263	13 567 501	14 134 096	15 190 949
	Confirmed with RDT	878 009	663 132	927 841	2 223 983	6 108 152	6 983 032	7 845 679	8 220 799	8 549 493
	Imported cases	–	–	–	–	–	–	–	–	–
Namibia	Presumed and confirmed	25 889	14 406	3 163	4 745	15 914	12 050	23 568	66 141	36 451
	Microscopy examined	14 522	13 262	7 875	1 507	1 894	1 471	1 778	1 778	1 215
	Confirmed with microscopy	556	335	194	136	222	118	329	364	289
	RDT examined	–	48 599	–	32 495	185 078	207 612	308 414	616 513	394 822
	Confirmed with RDT	–	1 525	–	4 775	15 692	12 050	24 869	66 141	36 451
	Imported cases	–	–	–	–	–	2 888	3 980	–	–
Niger	Presumed and confirmed	3 643 803	3 157 482	4 592 519	4 288 425	3 222 613	3 817 634	5 056 393	2 638 580	3 358 058
	Microscopy examined	165 514	130 658	1 781 505	1 799 299	2 872 710	295 229	3 198 194	203 583	213 795
	Confirmed with microscopy	49 285	68 529	1 119 929	1 176 711	0	206 660	2 120 515	125 856	121 657
	RDT examined	7 426 774	1 130 514	1 781 505	1 799 299	2 872 710	2 657 057	3 066 101	3 615 853	4 285 516
	Confirmed with RDT	570 773	712 347	1 119 929	1 176 711	1 953 309	2 065 340	2 027 652	2 512 724	2 924 793
	Imported cases	–	–	–	–	–	–	–	–	–
Nigeria	Presumed and confirmed	3 873 463	4 306 945	6 938 519	12 830 911	16 512 127	15 157 491	16 740 560	18 690 954	18 870 214
	Microscopy examined	–	672 185	1 953 399	1 633 960	1 681 469	839 849	901 141	1 055 444	1 428 731
	Confirmed with microscopy	523 513	–	–	–	1 233 654	556 871	618 363	749 118	1 023 273
	RDT examined	45 924	242 526	2 898 052	7 194 960	9 188 933	8 690 087	11 765 893	14 808 335	15 848 248
	Confirmed with RDT	27 674	–	–	–	6 593 300	6 261 971	8 616 024	10 822 840	11 930 310
	Imported cases	–	–	–	–	–	–	–	–	–
Rwanda	Presumed and confirmed	638 669	208 498	483 470	939 076	1 610 812	2 505 794	3 324 678	4 413 473	4 198 029
	Microscopy examined	2 708 973	1 602 271	2 904 793	2 862 877	4 010 202	5 811 267	6 603 261	6 637 571	5 501 455
	Confirmed with microscopy	638 669	208 858	422 224	879 316	1 528 825	2 354 400	2 916 902	2 927 780	1 657 793
	RDT examined	–	–	190 593	201 708	168 004	281 847	898 913	920 295	720 026
	Confirmed with RDT	–	–	61 246	83 302	81 987	151 394	463 666	475 403	318 133
	Imported cases	–	–	–	–	–	–	–	–	–
Sao Tome and Principe	Presumed and confirmed	3 346	8 442	12 550	7 418	1 337	2 058	2 238	2 241	2 940
	Microscopy examined	48 366	83 355	103 773	73 866	33 355	11 941	3 682	2 146	13 186
	Confirmed with microscopy	2 233	6 373	10 706	6 352	569	140	33	109	148
	RDT examined	9 989	33 924	23 124	34 768	58 090	72 407	117 727	94 466	156 697
	Confirmed with RDT	507	2 069	1 844	2 891	1 185	1 918	2 205	2 132	2 792
	Imported cases	–	–	–	–	–	2	4	2	3

Annex 3 – H. Reported malaria cases by method of confirmation, 2010–2018

WHO region Country/area		2010	2011	2012	2013	2014	2015	2016	2017	2018
AFRICAN										
Senegal	Presumed and confirmed	707 772	604 290	634 106	772 222	628 642	502 084	356 272	398 377	536 745
	Microscopy examined	27 793	18 325	19 946	24 205	19 343	26 556	38 748	21 639	12 881
	Confirmed with microscopy	17 750	14 142	15 612	20 801	12 636	17 846	9 918	10 463	3 997
	RDT examined	651 737	555 614	524 971	668 562	697 175	1 384 834	1 513 574	2 011 383	2 077 442
	Confirmed with RDT	325 920	263 184	265 468	325 088	252 988	474 407	339 622	385 243	526 947
	Imported cases	–	–	–	–	–	352	1 905	0	292
Sierra Leone	Presumed and confirmed	934 028	856 332	1 945 859	1 715 851	1 898 852	1 569 606	1 845 727	1 741 512	1 781 855
	Microscopy examined	718 473	46 280	194 787	185 403	66 277	75 025	120 917	10 910	20 155
	Confirmed with microscopy	218 473	25 511	104 533	76 077	39 414	37 820	60 458	5 717	8 719
	RDT examined	1 609 455	886 994	1 975 972	2 377 254	2 056 722	2 176 042	2 805 621	2 834 261	2 827 417
	Confirmed with RDT	715 555	613 348	1 432 789	1 625 881	1 335 062	1 445 556	1 714 848	1 645 519	1 725 112
	Imported cases	–	–	–	–	–	–	–	–	0
South Africa	Presumed and confirmed	8 060	9 866	6 846	8 851	13 988	8 976	4 323	28 295	18 638
	Microscopy examined	–	178 387	121 291	364 021	300 291	13 917	20 653	–	–
	Confirmed with microscopy	3 787	5 986	1 632	2 572	4 101	785	1 219	9 592	2 666
	RDT examined	276 669	204 047	30 053	239 705	240 622	17 446	42 624	56 257	–
	Confirmed with RDT	4 273	3 880	3 997	6 073	7 604	3 572	3 104	18 703	8 123
	Imported cases	–	–	–	–	–	3 568	3 075	6 234	5 742
South Sudan[2]	Presumed and confirmed	900 283	795 784	1 125 039	1 855 501	2 433 991	3 789 475	–	3 602 208	4 697 506
	Microscopy examined	–	–	–	–	27 321	22 721	6 954	800 067	1 204
	Confirmed with microscopy	900 283	112 024	225 371	262 520	18 344	11 272	2 357	335 642	634
	RDT examined	–	–	–	–	102 538	26 507	10 751	2 024 503	1 805 912
	Confirmed with RDT	–	–	–	–	53 033	13 099	5 262	1 152 363	98 209
	Imported cases	–	–	–	–	–	–	–	–	–
Togo	Presumed and confirmed	983 430	519 450	768 287	881 611	1 113 928	1 113 928	1 183 265	1 209 034	1 381 410
	Microscopy examined	478 354	502 977	579 507	560 096	621 119	621 119	435 164	445 035	267 028
	Confirmed with microscopy	224 087	237 305	260 535	272 855	310 207	305 727	231 819	209 626	108 146
	RDT examined	575 245	390 611	660 627	882 475	1 135 581	1 135 581	1 410 290	1 597 463	1 488 587
	Confirmed with RDT	393 014	282 145	436 839	609 575	820 044	808 200	951 446	999 408	982 188
	Imported cases	–	–	–	–	–	–	–	–	–
Uganda	Presumed and confirmed	13 208 169	12 173 358	13 591 932	16 541 563	13 724 345	13 421 804	13 657 887	12 273 076	8 895 436
	Microscopy examined	3 705 284	385 928	3 466 571	3 718 588	2 048 185	3 684 722	4 492 090	5 515 931	1 606 330
	Confirmed with microscopy	1 581 160	134 726	1 413 149	1 502 362	578 289	1 248 576	1 542 091	1 694 441	458 909
	RDT examined	–	194 819	2 449 526	7 387 826	7 060 545	12 126 996	17 473 299	16 803 712	12 741 670
	Confirmed with RDT	–	97 147	1 249 109	–	3 053 650	5 889 086	7 843 041	9 973 390	5 300 265
	Imported cases	–	–	–	–	–	–	–	–	–
United Republic of Tanzania	Presumed and confirmed	12 893 535	10 164 967	8 477 435	8 585 482	7 403 562	7 746 258	6 053 868	5 597 715	6 220 485
	Microscopy examined	3 637 659	5 656 907	6 931 025	6 804 085	727 130	673 223	1 386 389	2 888 538	3 015 052
	Confirmed with microscopy	1 277 024	1 813 179	1 772 062	1 481 275	572 289	412 702	1 262 679	916 742	831 903
	RDT examined	136 123	1 628 092	1 091 615	813 103	17 740 207	16 620 299	15 538 709	15 257 462	19 603 825
	Confirmed with RDT	1 974	337 582	214 893	71 169	107 728	3 830 030	3 930 841	4 437 744	5 221 811
	Imported cases				719	1 583	2 550			1 754
Mainland	Presumed and confirmed	12 819 192	10 160 478	8 474 278	8 582 934	7 399 316	7 741 816	6 050 097	5 593 544	6 215 115
	Microscopy examined	3 573 710	5 513 619	6 784 639	6 720 141	592 320	532 118	1 285 720	2 826 948	2 937 666
	Confirmed with microscopy	1 276 660	1 812 704	1 771 388	1 480 791	571 598	411 741	1 261 650	915 887	830 668
	RDT examined	–	1 315 662	701 477	369 444	17 566 750	16 416 675	15 379 517	15 052 571	19 338 466
	Confirmed with RDT	–	333 568	212 636	69 459	106 609	3 827 749	3 926 855	4 435 250	5 219 714
	Imported cases	–	–	–	–	–	–	–	–	–
Zanzibar	Presumed and confirmed	74 343	4 489	3 157	2 548	4 246	4 442	3 771	4 171	5 370
	Microscopy examined	63 949	143 288	146 386	83 944	134 810	141 105	100 669	61 590	77 386
	Confirmed with microscopy	364	475	674	484	691	961	1 029	855	1 235
	RDT examined	136 123	312 430	390 138	443 659	173 457	203 624	159 192	204 891	265 359
	Confirmed with RDT	1 974	4 014	2 257	1 710	1 119	2 281	3 986	2 494	2 097
	Imported cases	–	–	–	719	1 583	2 550	–	–	1 754

WHO region Country/area		2010	2011	2012	2013	2014	2015	2016	2017	2018
AFRICAN										
Zambia	Presumed and confirmed	4 229 839	4 607 908	4 695 400	5 465 122	5 972 933	5 094 123	5 976 192	6 054 679	5 195 723
	Microscopy examined	–	–	–	–	–	–	–	–	180 697
	Confirmed with microscopy	–	–	–	–	–	–	–	–	49 855
	RDT examined	–	–	–	–	5 964 354	7 207 500	8 502 989	10 403 283	9 718 666
	Confirmed with RDT	–	–	–	–	4 077 547	4 184 661	4 851 319	5 505 639	4 989 824
	Imported cases	–	–	–	–	–	–	–	–	–
Zimbabwe	Presumed and confirmed	648 965	319 935	276 963	422 633	535 983	391 651	280 853	316 392	184 427
	Microscopy examined	–	10 004	–	–	–	–	–	0	2 771
	Confirmed with microscopy	–	–	–	–	–	–	–	0	0
	RDT examined	513 032	470 007	727 174	1 115 005	1 420 894	1 384 893	1 223 509	1 110 705	995 715
	Confirmed with RDT	249 379	319 935	276 963	422 633	535 931	391 651	279 988	316 392	184 427
	Imported cases	–	–	–	–	–	180	358	768	672
AMERICAS										
Argentina[1]	Presumed and confirmed	72	18	4	4	4	11	6	18	23
	Microscopy examined	2 547	7 872	7 027	4 913	5 691	3 862	3 479	2 114	345
	Confirmed with microscopy	72	18	4	4	4	11	7	18	23
	RDT examined	–	–	–	0	0	0	0	0	0
	Confirmed with RDT	–	–	–	0	0	0	0	0	0
	Imported cases	46	18	4	4	4	8	5	15	23
Belize	Presumed and confirmed	150	79	37	26	19	13	5	9	7
	Microscopy examined	27 366	22 996	20 789	25 351	24 122	26 367	20 936	26 995	17 642
	Confirmed with microscopy	150	79	37	26	19	13	5	9	7
	RDT examined	–	–	–	–	–	0	0	0	–
	Confirmed with RDT	–	–	–	–	–	0	0	0	–
	Imported cases	–	7	4	4	0	4	1	2	4
Bolivia (Plurinational State of)	Presumed and confirmed	13 769	7 143	7 415	7 342	7 401	6 907	5 553	4 587	5 354
	Microscopy examined	133 463	143 272	121 944	133 260	124 900	159 167	155 407	151 697	139 938
	Confirmed with microscopy	12 252	6 108	6 293	6 272	7 401	6 907	5 553	4 334	5 261
	RDT examined	7 394	7 390	10 960	10 789	–	–	–	–	–
	Confirmed with RDT	1 517	1 035	1 122	1 070	–	–	–	253	93
	Imported cases	–	–	–	–	–	33	11	15	12
Brazil	Presumed and confirmed	334 668	267 146	242 758	178 546	144 128	143 161	129 246	194 426	194 512
	Microscopy examined	2 711 432	2 476 335	2 325 775	1 873 518	1 744 640	1 573 538	1 341 639	1 656 688	1 753 972
	Confirmed with microscopy	334 667	266 713	237 978	174 048	142 744	139 844	124 210	184 877	181 923
	RDT examined	–	1 486	23 566	19 500	11 820	16 865	23 273	39 378	46 201
	Confirmed with RDT	–	433	4 780	3 719	1 384	3 318	5 034	9 549	12 589
	Imported cases	–	–	–	8 905	4 847	4 915	5 087	4 867	6 819
Colombia	Presumed and confirmed	117 650	64 436	60 179	51 722	40 768	55 866	83 227	54 102	63 143
	Microscopy examined	521 342	396 861	346 599	284 332	325 713	316 451	242 973	244 732	195 286
	Confirmed with microscopy	117 637	60 121	50 938	44 293	36 166	48 059	–	38 349	42 810
	RDT examined	–	21 171	70 168	42 723	77 819	11 983	53 118	9 648	13 252
	Confirmed with RDT	13	4 188	9 241	7 403	4 602	3 535	5 655	5 056	3 407
	Imported cases	–	–	–	–	–	7 785	618	1 297	1 948
Costa Rica	Presumed and confirmed	114	17	8	6	6	8	13	25	108
	Microscopy examined	15 599	10 690	7 485	16 774	4 420	7 373	5 160	9 680	9 000
	Confirmed with microscopy	114	17	8	6	6	8	13	25	108
	RDT examined	–	–	–	0	0	0	0	0	700
	Confirmed with RDT	–	–	–	0	0	0	0	0	44
	Imported cases	4	6	1	4	5	8	9	13	38
Dominican Republic	Presumed and confirmed	2 482	1 616	952	579	496	661	755	324	484
	Microscopy examined	469 052	421 405	415 808	431 683	362 304	317 257	51 329	226 988	33 420
	Confirmed with microscopy	–	1 616	952	579	496	661	484	398	322
	RDT examined	26 585	56 150	90 775	71 000	54 425	7 530	22 450	38 547	42 425
	Confirmed with RDT	932	–	–	–	–	–	–	–	286
	Imported cases	–	–	–	105	37	30	65	57	50

Annex 3 – H. Reported malaria cases by method of confirmation, 2010–2018

WHO region Country/area		2010	2011	2012	2013	2014	2015	2016	2017	2018
AMERICAS										
Ecuador	Presumed and confirmed	1 888	1 232	558	378	242	686	1 191	1 380	1 806
	Microscopy examined	481 030	460 785	459 157	397 628	370 825	261 824	311 920	306 894	237 995
	Confirmed with microscopy	1 888	1 232	558	378	242	686	1 191	1 380	1 589
	RDT examined	7 800	–	–	–	–	–	–	–	6 782
	Confirmed with RDT	–	–	–	–	–	–	–	–	217
	Imported cases	–	14	14	10	–	59	233	105	153
El Salvador[3]	Presumed and confirmed	24	15	21	7	8	9	14	4	2
	Microscopy examined	115 256	100 883	124 885	103 748	106 915	89 267	81 904	70 022	52 216
	Confirmed with microscopy	24	–	21	7	8	9	14	4	2
	RDT examined	–	1	–	–	0	0	0	0	0
	Confirmed with RDT	–	1	–	–	0	0	0	0	0
	Imported cases	7	6	6	1	2	7	1	3	2
French Guiana	Presumed and confirmed	1 608	1 209	900	877	448	434	258	597	–
	Microscopy examined	14 373	14 429	13 638	22 327	14 651	11 558	9 430	–	–
	Confirmed with microscopy	–	505	401	–	242	297	173	468	–
	RDT examined	–	–	–	–	–	–	–	–	–
	Confirmed with RDT	944	704	499	551	206	137	58	129	–
	Imported cases	–	–	–	–	–	60	41	43	–
Guatemala	Presumed and confirmed	7 198	6 817	5 346	6 214	4 931	5 538	4 854	3 744	3 021
	Microscopy examined	235 075	195 080	186 645	153 731	250 964	295 246	333 535	372 158	438 833
	Confirmed with microscopy	7 198	6 817	5 346	6 214	–	–	4 854	3 744	3 021
	RDT examined	2 000	–	0	0	50 025	6 500	74 859	0	75 300
	Confirmed with RDT	0	–	0	0	–	1 298	–	0	1 748
	Imported cases	–	–	–	–	1	2	1	2	3
Guyana	Presumed and confirmed	22 935	29 471	31 610	31 479	12 354	9 984	11 108	13 936	17 038
	Microscopy examined	212 863	201 693	196 622	205 903	142 843	132 941	110 891	100 096	99 806
	Confirmed with microscopy	22 935	–	–	31 479	12 354	9 984	–	13 734	15 599
	RDT examined	–	35	–	0	0	0	5 409	–	0
	Confirmed with RDT	–	35	55	0	0	0	1 461	202	1 439
	Imported cases	–	–	–	–	–	–	411	–	–
Haiti	Presumed and confirmed	84 153	32 969	25 423	26 543	17 696	17 583	21 430	19 135	8 828
	Microscopy examined	270 427	184 934	167 726	165 823	134 766	69 659	61 428	62 539	59 803
	Confirmed with microscopy	84 153	–	–	20 957	10 893	5 224	4 342	2 119	1 586
	RDT examined	–	–	46	5 586	126 637	233 081	245 133	232 741	228 491
	Confirmed with RDT	–	–	–	–	6 803	12 359	18 115	17 739	7 526
	Imported cases	–	–	–	–	–	–	–	–	–
Honduras	Presumed and confirmed	9 685	7 618	6 439	5 428	3 380	3 575	4 097	1 287	653
	Microscopy examined	152 961	152 451	155 165	144 436	151 420	150 854	167 836	148 160	142 780
	Confirmed with microscopy	–	7 465	–	5 364	–	3 555	3 695	1 251	653
	RDT examined	4 000	4 000	4 000	237	1 427	3 052	14 930	17 376	18 620
	Confirmed with RDT	–	45	10	64	102	20	401	35	229
	Imported cases	–	–	–	–	2	0	3	10	21
Mexico	Presumed and confirmed	1 226	1 124	833	499	666	551	596	765	826
	Microscopy examined	1 192 081	1 035 424	1 025 659	1 017 508	900 578	867 853	798 568	644 174	548 247
	Confirmed with microscopy	1 233	1 130	842	499	–	551	596	765	826
	RDT examined	–	–	–	0	0	0	0	0	0
	Confirmed with RDT	–	–	–	0	0	0	0	0	0
	Imported cases	7	6	9	4	10	34	45	29	23
Nicaragua	Presumed and confirmed	692	925	1 235	1 194	1 163	2 307	6 284	10 949	15 934
	Microscopy examined	535 914	521 904	536 278	519 993	605 357	604 418	553 615	660 452	831 077
	Confirmed with microscopy	692	925	1 235	1 194	1 163	2 307	6 284	10 949	15 934
	RDT examined	18 500	14 201	16 444	19 029	0	–	800	2 680	44 905
	Confirmed with RDT	0	–	0	–	0	–	–	–	0
	Imported cases	–	–	–	34	21	29	12	3	17

WHO region Country/area		2010	2011	2012	2013	2014	2015	2016	2017	2018
AMERICAS										
Panama	Presumed and confirmed	418	354	844	705	874	562	811	689	715
	Microscopy examined	141 038	116 588	107 711	93 624	80 701	64 511	50 772	38 270	23 383
	Confirmed with microscopy	418	354	844	705	874	562	811	689	715
	RDT examined	–	0	0	0	0	0	0	0	–
	Confirmed with RDT	–	0	0	0	0	0	0	0	–
	Imported cases	–	–	–	9	10	16	42	40	31
Paraguay[1]	Presumed and confirmed	27	10	15	11	8	8	10	5	–
	Microscopy examined	62 178	48 611	31 499	24 806	24 832	6 687	3 192	8 014	–
	Confirmed with microscopy	27	10	15	11	8	8	–	5	–
	RDT examined	–	–	–	–	–	0	1	1 267	–
	Confirmed with RDT	–	–	–	–	–	0	1	0	–
	Imported cases	9	9	15	11	8	8	10	5	–
Peru	Presumed and confirmed	31 545	25 005	31 436	48 719	65 252	63 865	56 623	55 367	45 619
	Microscopy examined	744 627	702 894	758 723	863 790	864 413	865 980	566 230	388 699	304 785
	Confirmed with microscopy	–	–	31 436	48 719	65 252	66 609	56 623	55 367	45 619
	RDT examined	23	58	562	858	1 634	0	–	13 924	160 000
	Confirmed with RDT	1	34	–	–	–	–	–	2 325	1 000
	Imported cases	–	–	–	–	0	0	0	–	176
Suriname	Presumed and confirmed	1 771	795	569	729	729	376	327	551	235
	Microscopy examined	16 533	15 135	17 464	13 693	17 608	15 083	14 946	12 536	11 799
	Confirmed with microscopy	1 574	751	306	530	–	345	315	412	218
	RDT examined	541	1 025	4 008	6 043	15 489	153	8 498	9 498	8 037
	Confirmed with RDT	138	20	50	199	303	31	12	139	17
	Imported cases	–	–	–	204	–	274	251	414	198
Venezuela (Bolivarian Republic of)	Presumed and confirmed	45 155	45 824	52 803	78 643	91 918	137 996	242 561	411 586	404 924
	Microscopy examined	400 495	382 303	410 663	476 764	522 617	625 174	852 556	1 144 635	699 130
	Confirmed with microscopy	45 155	45 824	52 803	78 643	91 918	137 996	240 613	411 586	404 924
	RDT examined	–	–	–	–	–	–	–	–	48 117
	Confirmed with RDT	–	–	–	–	–	–	–	–	48 117
	Imported cases	–	–	–	1 677	1 210	1 594	1 948	2 941	2 125
EASTERN MEDITERRANEAN										
Afghanistan	Presumed and confirmed	392 463	482 748	391 365	319 742	295 050	366 526	384 943	326 625	299 863
	Microscopy examined	524 523	531 053	511 408	507 145	514 466	538 789	598 556	611 904	665 200
	Confirmed with microscopy	69 397	77 549	54 840	46 114	83 920	103 377	151 528	194 866	180 156
	RDT examined	–	0	0	0	–	–	94 975	161 925	216 240
	Confirmed with RDT	–	0	0	0	–	–	38 631	53 823	68 533
	Imported cases	–	–	–	–	–	–	–	–	–
Djibouti	Presumed and confirmed	1 010	230	27	1 684	9 439	9 557	13 804	14 671	25 319
	Microscopy examined	–	124	1 410	7 189	39 284	10 502	19 492	24 504	–
	Confirmed with microscopy	1 010	–	22	1 684	9 439	1 764	2 280	1 283	–
	RDT examined	–	–	–	–	–	–	–	50 104	104 800
	Confirmed with RDT	–	–	3	–	–	7 709	11 524	13 388	25 319
	Imported cases	–	–	–	–	–	–	–	–	–
Iran (Islamic Republic of)[3]	Presumed and confirmed	3 031	3 239	1 629	1 373	1 238	799	705	939	625
	Microscopy examined	614 817	530 470	479 655	385 172	468 513	610 337	418 125	383 397	477 914
	Confirmed with microscopy	3 031	3 239	1 629	1 373	1 243	799	705	939	625
	RDT examined	–	–	0	–	–	–	–	–	64 061
	Confirmed with RDT	–	–	0	–	–	–	–	–	436
	Imported cases	1 184	1 529	842	853	867	632	612	868	602
Pakistan	Presumed and confirmed	4 281 356	4 065 802	4 285 449	3 472 727	3 666 257	3 776 244	2 121 958	2 209 768	1 069 248
	Microscopy examined	4 281 346	4 168 648	4 497 330	3 933 321	4 343 418	4 619 980	5 046 870	4 539 869	4 324 570
	Confirmed with microscopy	220 870	287 592	250 526	196 078	193 952	137 401	154 541	132 580	119 099
	RDT examined	279 724	518 709	410 949	628 504	779 815	691 245	1 296 762	1 821 139	2 207 613
	Confirmed with RDT	19 721	46 997	40 255	85 677	81 197	64 612	169 925	237 237	255 411
	Imported cases	–	–	–	–	–	–	–	–	–

Annex 3 - H. Reported malaria cases by method of confirmation, 2010–2018

WHO region Country/area		2010	2011	2012	2013	2014	2015	2016	2017	2018
EASTERN MEDITERRANEAN										
Saudi Arabia	Presumed and confirmed	1 941	2 788	3 406	–	2 305	2 620	5 382	3 151	2 711
	Microscopy examined	944 723	1 062 827	1 186 179	1 309 783	1 249 752	1 306 700	1 267 933	1 073 998	1 015 953
	Confirmed with microscopy	1 941	2 788	3 406	2 513	2 305	2 620	5 382	3 151	2 711
	RDT examined	–	–	0	–	–	–	–	–	–
	Confirmed with RDT	–	–	0	–	–	–	–	–	–
	Imported cases	1 912	2 719	3 324	2 479	2 254	2 537	5 110	2 974	2 517
Somalia	Presumed and confirmed	24 553	41 167	23 202	9 135	26 174	39 169	58 021	37 156	31 030
	Microscopy examined	20 593	26 351	–	–	–	–	–	–	–
	Confirmed with microscopy	5 629	1 627	–	–	–	–	–	–	–
	RDT examined	200 105	35 236	37 273	67 464	64 480	100 792	183 360	226 894	253 211
	Confirmed with RDT	18 924	1 724	6 817	7 407	11 001	20 953	35 628	35 138	31 021
	Imported cases	–	–	–	–	–	–	–	–	–
Sudan	Presumed and confirmed	1 465 496	1 214 004	964 698	989 946	1 207 771	1 102 186	897 194	1 562 821	3 581 302
	Microscopy examined	–	–	–	–	–	3 586 482	3 236 118	2 426 329	6 668 355
	Confirmed with microscopy	625 365	506 806	526 931	592 383	579 038	586 827	378 308	588 100	1 251 544
	RDT examined	1 653 300	2 222 380	2 000 700	1 800 000	788 281	–	632 443	422 841	1 080 601
	Confirmed with RDT	95 192	–	–	–	489 468	–	187 707	132 779	355 289
	Imported cases	–	–	–	–	–	–	–	–	–
Yemen	Presumed and confirmed	198 963	142 152	165 687	149 451	122 812	104 831	144 628	114 004	192 895
	Microscopy examined	645 463	645 093	685 406	723 691	643 994	561 644	960 860	1 070 020	419 415
	Confirmed with microscopy	78 269	60 751	71 300	63 484	51 768	42 052	45 886	28 936	64 233
	RDT examined	97 289	108 110	150 218	157 457	141 519	121 464	174 699	560 449	219 250
	Confirmed with RDT	28 428	30 203	41 059	39 294	34 939	34 207	52 815	85 068	53 419
	Imported cases	–	–	–	–	–	–	–	–	–
EUROPEAN										
Armenia[1]	Presumed and confirmed	1	0	4	0	1	1	1	2	–
	Microscopy examined	31 026	–	–	–	–	1 213	465	350	–
	Confirmed with microscopy	1	–	–	–	–	2	2	2	–
	RDT examined	–	–	–	–	–	0	0	0	–
	Confirmed with RDT	–	–	–	–	–	0	0	0	–
	Imported cases	1	0	4	0	1	1	1	2	–
Azerbaijan[3]	Presumed and confirmed	52	8	4	4	2	1	1	1	–
	Microscopy examined	456 652	449 168	497 040	432 810	399 925	405 416	465 860	373 562	–
	Confirmed with microscopy	52	8	4	4	2	1	1	1	–
	RDT examined	–	–	–	–	–	0	0	0	–
	Confirmed with RDT	–	–	–	–	–	0	0	0	–
	Imported cases	2	4	1	4	2	1	1	1	–
Georgia[3]	Presumed and confirmed	0	6	5	7	6	5	7	8	–
	Microscopy examined	2 368	2 032	1 046	192	440	294	318	416	–
	Confirmed with microscopy	0	6	5	7	6	5	7	8	–
	RDT examined	–	–	–	–	–	0	0	0	–
	Confirmed with RDT	–	–	–	–	–	0	0	0	–
	Imported cases	0	5	4	7	5	5	7	8	–
Kyrgyzstan[1]	Presumed and confirmed	6	5	3	4	0	1	6	2	–
	Microscopy examined	30 190	27 850	18 268	54 249	35 600	75 688	62 537	8 459	–
	Confirmed with microscopy	6	5	3	4	0	1	6	2	–
	RDT examined	–	–	–	–	–	0	0	0	–
	Confirmed with RDT	–	–	–	–	–	0	0	0	–
	Imported cases	3	5	3	4	0	1	6	2	–
Tajikistan[3]	Presumed and confirmed	112	78	33	14	7	5	1	3	–
	Microscopy examined	173 523	173 367	209 239	213 916	200 241	188 341	198 766	191 284	–
	Confirmed with microscopy	112	78	33	14	7	5	1	3	–
	RDT examined	–	–	–	–	–	–	34 570	41 218	–
	Confirmed with RDT	–	–	–	–	–	–	1	3	–
	Imported cases	1	25	15	11	5	5	1	3	–

WHO region Country/area		2010	2011	2012	2013	2014	2015	2016	2017	2018
EUROPEAN										
Turkey[3]	Presumed and confirmed	90	132	376	285	249	221	209	214	–
	Microscopy examined	507 841	421 295	337 830	255 125	189 854	211 740	144 499	115 557	–
	Confirmed with microscopy	78	128	376	285	249	221	209	214	–
	RDT examined	–	–	–	–	–	–	–	–	–
	Confirmed with RDT	–	–	–	–	–	–	–	–	–
	Imported cases	81	128	376	251	249	221	208	214	–
Turkmenistan[1]	Presumed and confirmed	0	0	0	0	0	0	0	0	–
	Microscopy examined	81 784	–	–	–	–	83 675	85 536	84 264	–
	Confirmed with microscopy	0	–	–	–	–	0	0	0	–
	RDT examined	–	–	–	–	–	0	0	0	–
	Confirmed with RDT	–	–	–	–	–	0	0	0	–
	Imported cases	0	0	0	0	0	0	0	0	–
Uzbekistan[1]	Presumed and confirmed	5	1	1	3	1	0	0	0	–
	Microscopy examined	921 364	886 243	805 761	908 301	812 347	800 912	797 472	655 112	–
	Confirmed with microscopy	5	1	1	3	1	0	0	0	–
	RDT examined	–	–	–	–	–	0	0	0	–
	Confirmed with RDT	–	–	–	–	–	0	0	0	–
	Imported cases	2	1	1	3	1	0	0	0	–
SOUTH-EAST ASIA										
Bangladesh	Presumed and confirmed	91 227	51 773	9 901	3 864	10 216	6 608	5 063	5 133	1 919
	Microscopy examined	308 326	270 253	253 887	74 755	78 719	69 093	65 845	70 267	57 557
	Confirmed with microscopy	20 519	20 232	4 016	1 866	3 249	1 612	1 022	1 077	377
	RDT examined	152 936	119 849	35 675	19 171	46 482	53 713	73 128	80 251	75 990
	Confirmed with RDT	35 354	31 541	5 885	1 998	6 967	4 996	3 765	3 835	1 542
	Imported cases	–	–	–	–	–	129	109	19	41
Bhutan	Presumed and confirmed	487	207	82	–	–	104	74	62	54
	Microscopy examined	54 709	44 481	42 512	31 632	33 586	26 149	23 442	22 885	19 778
	Confirmed with microscopy	436	194	82	45	48	84	59	51	49
	RDT examined	–	–	–	–	–	47 938	95 399	19 250	113 720
	Confirmed with RDT	–	–	–	–	–	20	15	0	5
	Imported cases	–	–	0	23	0	70	56	38	34
Democratic People's Republic of Korea	Presumed and confirmed	15 392	18 104	23 537	15 673	11 212	7 409	5 113	4 626	3 698
	Microscopy examined	25 147	26 513	39 238	71 453	38 201	29 272	22 747	16 835	28 654
	Confirmed with microscopy	13 520	16 760	21 850	14 407	10 535	7 010	4 890	4 463	3 446
	RDT examined	–	–	0	0	0	61 348	182 980	172 499	657 050
	Confirmed with RDT	–	–	0	0	0	12	143	140	252
	Imported cases	–	–	0	0	0	205	0	0	0
India	Presumed and confirmed	1 599 986	1 310 656	1 067 824	881 730	1 102 205	1 169 261	1 087 285	844 558	429 928
	Microscopy examined	108 679 429	108 969 660	109 033 790	113 109 094	124 066 331	121 141 970	124 933 348	110 769 742	111 123 775
	Confirmed with microscopy	1 599 986	1 310 656	1 067 824	881 730	1 102 205	1 169 261	1 087 285	306 768	230 432
	RDT examined	10 600 000	10 500 384	13 125 480	14 782 104	14 562 000	19 699 260	19 606 260	15 208 057	13 489 707
	Confirmed with RDT	–	–	–	–	–	–	–	537 790	199 496
	Imported cases	–	–	–	–	–	–	–	–	–
Indonesia	Presumed and confirmed	465 764	422 447	417 819	343 527	252 027	217 025	218 450	261 617	223 208
	Microscopy examined	1 335 445	962 090	1 429 139	1 447 980	1 300 835	1 224 504	1 092 093	1 045 994	1 111 931
	Confirmed with microscopy	465 764	422 447	417 819	343 527	252 027	217 025	218 450	261 617	190 522
	RDT examined	255 734	250 709	471 586	260 181	249 461	342 946	365 765	395 685	362 705
	Confirmed with RDT	–	–	–	–	–	–	–	–	32 686
	Imported cases	–	–	–	–	–	–	–	–	11
Myanmar	Presumed and confirmed	693 124	567 452	481 204	333 871	205 658	182 616	110 146	85 019	76 518
	Microscopy examined	275 374	312 689	265 135	138 473	151 258	99 025	122 078	107 242	58 126
	Confirmed with microscopy	103 285	91 752	75 192	26 509	12 010	6 782	6 717	4 648	2 577
	RDT examined	729 878	795 618	1 158 420	1 162 083	1 415 837	2 564 707	3 063 167	3 261 455	3 041 650
	Confirmed with RDT	317 523	373 542	405 394	307 362	193 648	175 986	103 429	80 371	71 815
	Imported cases	–	–	–	–	–	345	–	–	–

Annex 3 - H. Reported malaria cases by method of confirmation, 2010–2018

WHO region Country/area		2010	2011	2012	2013	2014	2015	2016	2017	2018
SOUTH-EAST ASIA										
Nepal	Presumed and confirmed	96 383	71 752	71 410	38 113	25 889	19 375	10 185	3 269	2 930
	Microscopy examined	102 977	95 011	152 780	100 336	127 130	63 946	84 595	163 323	160 904
	Confirmed with microscopy	3 115	1 910	1 659	1 197	1 469	1 112	1 009	1 293	1 158
	RDT examined	17 887	25 353	22 472	32 989	48 444	49 649	52 432	48 625	93 378
	Confirmed with RDT	779	1 504	433	777	–	725	–	329	0
	Imported cases	–	1 069	592	–	667	521	502	670	539
Thailand	Presumed and confirmed	32 480	24 897	32 569	41 362	37 921	14 755	11 522	7 342	5 817
	Microscopy examined	1 695 980	1 354 215	1 130 757	1 830 090	1 756 528	1 358 953	1 302 834	1 117 648	908 540
	Confirmed with microscopy	22 969	14 478	32 569	33 302	37 921	14 135	11 301	7 154	5 171
	RDT examined	81 997	96 670	–	97 495	–	10 888	158 173	31 898	12 580
	Confirmed with RDT	9 511	10 419	–	8 300	–	0	221	188	218
	Imported cases	–	–	–	–	–	9 890	5 724	4 020	1 618
Timor-Leste[3]	Presumed and confirmed	119 072	36 064	6 458	1 240	406	101	107	26	0
	Microscopy examined	109 806	82 175	64 318	56 192	30 515	30 237	35 947	37 705	45 976
	Confirmed with microscopy	40 250	19 739	5 208	1 025	347	80	94	17	8
	RDT examined	85 643	127 272	117 599	121 991	86 592	90 817	114 385	91 470	108 840
	Confirmed with RDT	7 887	–	–	–	0	0	0	–	–
	Imported cases	–	–	–	–	–	–	0	13	7
WESTERN PACIFIC										
Cambodia	Presumed and confirmed	47 910	51 611	45 553	24 130	26 278	29 957	23 492	36 932	39 584
	Microscopy examined	90 175	86 526	80 212	54 716	48 591	49 357	42 802	38 188	42 834
	Confirmed with microscopy	14 277	13 792	10 124	4 598	5 288	7 423	3 695	5 908	8 318
	RDT examined	103 035	130 186	108 974	94 600	92 525	114 323	123 893	130 057	123 804
	Confirmed with RDT	35 079	43 631	30 352	16 711	19 864	26 507	19 797	31 024	33 967
	Imported cases	–	–	–	–	–	–	–	–	–
China[3]	Presumed and confirmed	7 855	4 498	2 716	4 127	–	3 116	3 143	2 675	2 518
	Microscopy examined	7 115 784	9 189 270	6 918 657	5 554 960	4 403 633	4 052 588	3 194 915	2 409 280	1 904 290
	Confirmed with microscopy	4 990	3 367	2 603	4 086	2 921	3 088	3 129	2 666	2 513
	RDT examined	–	–	–	–	–	–	–	–	–
	Confirmed with RDT	–	–	–	–	–	–	–	–	–
	Imported cases	–	–	2 399	4 007	2 864	3 055	3 125	2 663	2 506
Lao People's Democratic Republic	Presumed and confirmed	23 047	17 904	46 819	41 385	38 754	36 056	11 753	9 336	8 913
	Microscopy examined	150 512	213 578	223 934	202 422	133 916	110 084	89 998	110 450	89 622
	Confirmed with microscopy	4 524	6 226	13 232	10 036	8 018	4 167	1 597	1 549	1 091
	RDT examined	127 790	77 825	145 425	133 337	160 626	173 919	133 464	163 856	197 259
	Confirmed with RDT	16 276	11 306	32 970	28 095	40 053	31 889	9 626	7 779	7 822
	Imported cases	–	–	–	–	–	0	–	–	0
Malaysia[3]	Presumed and confirmed	–	–	–	–	3 923	2 311	2 302	4 114	4 630
	Microscopy examined	1 619 074	1 600 439	1 566 872	1 576 012	1 443 958	1 066 470	1 153 108	1 046 163	1 070 356
	Confirmed with microscopy	6 650	5 306	4 725	3 850	3 923	2 311	2 302	4 114	4 630
	RDT examined	–	–	–	–	–	–	0	0	0
	Confirmed with RDT	–	–	–	–	–	–	0	0	0
	Imported cases	831	1 142	924	865	766	435	428	423	485
Papua New Guinea	Presumed and confirmed	1 379 787	1 151 343	878 371	1 125 808	644 688	553 103	728 798	881 697	940 646
	Microscopy examined	198 742	184 466	156 495	139 972	83 257	112 864	146 242	139 910	121 766
	Confirmed with microscopy	75 985	70 603	67 202	70 658	68 114	64 719	80 472	70 449	59 605
	RDT examined	20 820	27 391	228 857	468 380	475 654	541 760	772 254	857 326	967 566
	Confirmed with RDT	17 971	13 457	82 993	209 336	213 068	233 068	398 025	407 891	456 597
	Imported cases	–	–	–	–	–	–	–	–	–
Philippines	Presumed and confirmed	19 106	9 617	8 154	7 720	4 972	8 301	6 690	1 335	1 477
	Microscopy examined	301 031	327 060	332 063	317 360	287 725	224 843	255 302	171 424	122 502
	Confirmed with microscopy	18 560	9 552	7 133	5 826	3 618	5 694	2 860	874	569
	RDT examined	–	–	–	1 523	28 598	35 799	66 536	113 140	156 913
	Confirmed with RDT	–	–	–	688	1 285	2 572	3 820	2 953	1 005
	Imported cases	–	–	–	–	–	18	55	69	79

WHO region Country/area		2010	2011	2012	2013	2014	2015	2016	2017	2018
WESTERN PACIFIC										
Republic of Korea	Presumed and confirmed	–	–	–	–	638	699	673	515	576
	Microscopy examined	–	–	–	–	–	247	673	515	576
	Confirmed with microscopy	1 772	838	555	443	638	699	673	515	576
	RDT examined	–	–	–	–	–	–	–	–	–
	Confirmed with RDT	–	–	–	–	–	–	–	–	–
	Imported cases	56	64	47	50	78	65	67	79	75
Solomon Islands	Presumed and confirmed	95 006	80 859	57 296	53 270	51 649	50 916	84 513	68 676	72 430
	Microscopy examined	212 329	182 847	202 620	191 137	173 900	124 376	152 690	89 061	89 169
	Confirmed with microscopy	35 373	23 202	21 904	21 540	13 865	14 793	26 187	15 978	17 825
	RDT examined	17 300	17 457	13 987	26 216	26 658	40 750	92 109	133 560	142 115
	Confirmed with RDT	4 331	3 455	2 479	4 069	4 539	9 205	28 244	36 505	41 366
	Imported cases	–	–	–	–	–	–	–	–	–
Vanuatu	Presumed and confirmed	16 831	5 764	3 309	2 381	982	697	2 147	1 072	644
	Microscopy examined	29 180	19 183	16 981	15 219	18 135	4 870	6 704	9 187	5 935
	Confirmed with microscopy	4 013	2 077	733	767	190	15	225	120	53
	RDT examined	10 246	12 529	16 292	13 724	17 435	9 794	14 501	21 126	20 996
	Confirmed with RDT	4 156	2 743	2 702	1 614	792	408	1 643	952	591
	Imported cases	–	–	–	–	–	0	0	1	12
Viet Nam	Presumed and confirmed	54 297	45 588	43 717	35 406	27 868	19 252	10 446	8 411	4 451
	Microscopy examined	2 760 119	2 791 917	2 897 730	2 684 996	2 357 536	2 204 409	2 082 986	2 009 233	1 674 897
	Confirmed with microscopy	17 515	16 612	19 638	17 128	15 752	9 331	4 161	4 548	4 813
	RDT examined	7 017	491 373	514 725	412 530	416 483	459 332	408 055	603 161	492 270
	Confirmed with RDT	–	–	–	–	–	–	–	1 594	1 848
	Imported cases	–	–	–	–	–	–	–	–	–

	2010	2011	2012	2013	2014	2015	2016	2017	2018
REGIONAL SUMMARY (presumed and confirmed malaria cases)									
African	103 145 240	100 204 662	110 881 358	124 426 890	128 466 431	131 302 726	142 439 439	148 718 852	152 909 417
Americas	677 230	493 823	469 385	439 651	392 491	450 101	568 969	773 486	763 232
Eastern Mediterranean	6 368 813	5 952 130	5 835 463	4 944 058	5 331 046	5 401 932	3 626 635	4 269 135	5 202 993
European	266	230	426	317	266	234	225	230	-
South-East Asia	3 113 915	2 503 352	2 110 804	1 659 380	1 645 534	1 617 254	1 447 945	1 211 652	744 072
Western Pacific	1 643 839	1 367 184	1 085 935	1 294 227	799 752	704 408	873 957	1 014 763	1 075 869
Total	**114 949 303**	**110 521 381**	**120 383 371**	**132 764 523**	**136 635 520**	**139 476 655**	**148 957 170**	**155 988 118**	**160 695 583**

RDT: rapid diagnostic test; WHO: World Health Organization.

"–" refers to not applicable or data not available.

* The table indicates cases reported at health facilities and excludes cases at community level.

[1] Certified malaria free countries are included in this listing for historical purposes.

[2] In May 2013, South Sudan was reassigned to the WHO African Region (WHA resolution 66.21, http://apps.who.int/gb/ebwha/pdf_files/WHA66/A66_R21-en.pdf).

[3] There is no local transmission.

Note: The table indicates cases reported at health facilities and excludes cases at community level.

Annex 3 – I. Reported malaria cases by species, 2010–2018

WHO region Country/area		2010	2011	2012	2013	2014	2015	2016	2017	2018
AFRICAN										
Algeria[1]	Suspected	12 224	11 974	15 790	12 762	8 690	8 000	6 628	6 469	10 081
	Indigenous: *P. falciparum*	–	–	–	–	–	0	0	0	0
	Indigenous: *P. vivax*	–	–	–	–	–	0	0	0	0
	Indigenous: mixed	–	–	–	–	–	0	0	0	0
	Indigenous: other species	0	0	0	0	0	0	0	0	0
Angola	Suspected	4 591 529	4 469 357	4 849 418	5 273 305	6 134 471	6 839 963	7 649 902	11 050 353	10 870 446
Benin	Suspected	1 432 095	1 565 487	1 875 386	2 041 444	1 955 773	2 009 959	1 817 605	2 306 653	2 646 070
	Total: *P. falciparum*	–	68 745	0	–	1 044 235	1 268 347	1 324 576	1 696 777	1 768 450
	Total: *P. vivax*	–	0	0	–	0	0	0	0	0
	Total: mixed cases	–	0	0	–	0	0	0	0	0
	Total: other species	–	0	0	–	0	0	0	0	0
Botswana	Suspected	12 196	1 141	308	506	1 485	1 298	12 986	12 605	13 979
	Total: *P. falciparum*	1 046	432	193	456	1 346	326	703	1 891	585
	Total: *P. vivax*	0	0	0	0	0	0	0	0	0
	Total: mixed cases	0	0	0	0	0	0	13	9	0
	Total: other species	0	0	0	0	0	0	0	0	0
Burkina Faso	Suspected	6 037 806	5 446 870	7 852 299	7 857 296	9 272 755	9 783 385	11 992 686	14 384 948	14 910 311
Burundi	Suspected	5 590 736	4 768 314	4 228 015	7 384 501	7 622 162	8 414 481	12 357 585	12 336 328	8 734 322
Cabo Verde	Suspected	47	26 508	8 715	10 621	6 894	3 117	8 393	3 857	16 623
	Indigenous: *P. falciparum*	–	–	–	–	26	7	48	423	2
	Indigenous: *P. vivax*	–	–	–	–	0	0	0	0	0
	Indigenous: mixed	–	–	–	–	0	0	0	0	0
	Indigenous: other species	0	0	0	0	0	0	0	0	0
Cameroon	Suspected	1 845 691	3 060 040	2 865 319	3 652 609	3 709 906	3 312 273	3 229 804	3 345 967	3 217 180
	Total: *P. falciparum*	–	–	–	–	–	592 351	1 675 264	1 191 257	1 249 705
	Total: *P. vivax*	–	–	–	–	–	0	0	0	0
	Total: mixed cases	–	–	–	–	–	0	0	0	0
	Total: other species	–	–	–	–	–	0	0	0	0
Central African Republic	Suspected	66 484	221 980	468 986	491 074	625 301	1 218 246	1 807 206	1 480 085	1 367 986
	Total: *P. falciparum*	–	–	–	–	295 088	598 833	1 032 764	383 309	972 119
	Total: *P. vivax*	–	–	–	–	0	0	0	0	0
	Total: mixed cases	–	–	–	–	0	0	0	0	0
	Total: other species	–	–	–	–	0	0	0	0	0
Chad	Suspected	743 471	528 454	730 364	1 272 841	1 737 195	1 641 285	2 032 301	2 943 595	1 941 489
Comoros	Suspected	159 976	135 248	168 043	185 779	103 545	101 330	94 388	190 825	119 592
	Total: *P. falciparum*	33 791	21 387	43 681	45 669	2 203	1 300	1 066	2 274	15 613
	Total: *P. vivax*	528	334	637	72	0	0	0	0	0
	Total: mixed cases	0	0	0	363	0	0	0	0	0
	Total: other species	880	557	0	363	0	0	0	0	0
Congo	Suspected	446 656	277 263	117 640	209 169	290 346	300 592	466 254	322 916	385 729
	Total: *P. falciparum*	–	37 744	120 319	43 232	66 323	51 529	171 847	127 939	116 903
	Total: *P. vivax*	–	0	0	0	0	0	0	0	0
	Total: mixed cases	–	0	0	0	0	0	0	0	0
	Total: other species	–	0	0	0	0	0	0	0	0
Côte d'Ivoire	Suspected	1 721 461	2 607 856	3 423 623	5 982 151	6 418 571	5 216 344	5 178 375	6 346 291	6 706 148
	Total: *P. falciparum*	–	–	–	2 506 953	3 712 831	3 375 904	3 471 024	3 274 683	4 766 477
	Total: *P. vivax*	–	–	–	0	0	0	0	0	0
	Total: mixed cases	–	–	–	0	0	0	0	0	0
	Total: other species	–	–	–	0	0	0	0	0	0
Democratic Republic of the Congo	Suspected	10 568 756	12 018 784	11 993 189	14 871 716	14 647 380	16 452 476	21 507 579	21 072 322	23 833 694
	Total: *P. falciparum*	0	0	0	0	–	–	–	–	–
	Total: *P. vivax*	0	0	0	0	–	–	–	–	–
	Total: mixed cases	0	0	0	0	–	–	–	–	–
	Total: other species	0	0	0	0	–	–	–	–	–

WHO region Country/area		2010	2011	2012	2013	2014	2015	2016	2017	2018
AFRICAN										
Equatorial Guinea	Suspected	83 639	40 704	45 792	44 561	57 129	68 058	318 779	91 217	43 533
	Total: *P. falciparum*	53 813	22 466	15 169	13 129	17 452	-	-	-	-
	Total: *P. vivax*	0	0	0	0	0	-	-	-	-
	Total: mixed cases	0	0	0	0	0	-	-	-	-
	Total: other species	0	0	0	0	0	-	-	-	-
Eritrea	Suspected	96 792	97 479	138 982	134 183	121 755	111 950	106 403	121 064	146 235
	Total: *P. falciparum*	9 785	10 263	12 121	12 482	23 787	14 510	20 704	21 849	16 553
	Total: *P. vivax*	3 989	4 932	9 204	7 361	6 780	4 780	2 999	9 185	6 108
	Total: mixed cases	63	94	346	1 391	166	70	543	429	268
	Total: other species	57	19	0	83	35	12	5	23	26
Eswatini	Suspected	1 722	797	626	669	711	651	1 386	3 212	9 837
	Total: *P. falciparum*	87	130	345	487	710	195	350	1 127	656
	Total: *P. vivax*	0	0	0	0	1	0	0	0	0
	Total: mixed cases	0	0	0	0	0	0	0	0	0
	Total: other species	0	0	0	1	0	0	0	0	0
Ethiopia	Suspected	5 420 110	5 487 972	5 962 646	9 243 894	7 457 765	5 987 580	6 611 801	6 471 958	5 913 799
	Total: *P. falciparum*	732 776	814 547	946 595	1 687 163	1 250 110	1 188 627	1 142 235	1 059 847	859 675
	Total: *P. vivax*	390 252	665 813	745 983	958 291	868 705	678 432	576 269	470 892	102 412
	Total: mixed cases	73 801	0	0	0	0	0	0	0	0
	Total: other species	0	0	0	0	0	0	0	0	0
Gabon	Suspected	233 770	178 822	238 483	256 531	256 183	285 489	202 989	212 092	1 022 022
	Total: *P. falciparum*	2 157	-	-	26 432	26 117	-	23 915	35 244	111 719
	Total: *P. vivax*	720	-	-	0	0	-	0	0	0
	Total: mixed cases	55	-	-	0	0	-	0	0	0
	Total: other species	0	-	-	0	1 570	-	0	0	0
Gambia	Suspected	492 062	261 967	862 442	889 494	603 424	891 511	844 821	591 226	706 868
	Total: *P. falciparum*	64 108	190 379	271 038	240 792	99 976	240 382	153 685	69 931	87 448
	Total: *P. vivax*	0	0	0	0	0	0	0	0	0
	Total: mixed cases	0	0	0	0	0	0	0	0	0
	Total: other species	0	0	0	0	0	0	0	0	0
Ghana	Suspected	5 056 851	5 067 731	12 578 946	8 444 417	10 636 057	13 368 757	14 040 434	14 026 149	15 542 218
	Total: *P. falciparum*	926 447	593 518	3 755 166	1 629 198	3 415 912	4 319 919	4 421 788	4 266 541	4 808 163
	Total: *P. vivax*	0	0	0	0	0	0	0	0	0
	Total: mixed cases	0	0	0	0	0	0	83 654	82 153	0
	Total: other species	102 937	31 238	0	0	0	0	29 725	27 245	27 635
Guinea	Suspected	1 092 554	1 276 057	1 220 574	775 341	1 595 828	1 254 937	1 503 035	2 134 543	2 961 508
	Total: *P. falciparum*	20 936	5 450	191 421	63 353	660 207	810 979	992 146	1 335 323	1 214 996
	Total: *P. vivax*	0	0	0	0	0	0	0	0	0
	Total: mixed cases	0	0	0	0	0	0	0	0	0
	Total: other species	0	0	0	0	0	0	0	0	0
Guinea-Bissau	Suspected	195 006	300 233	237 398	238 580	309 939	385 678	381 196	461 621	469 640
	Total: *P. falciparum*	-	-	-	-	-	96 520	97 889	89 784	125 511
	Total: *P. vivax*	-	-	-	-	-	0	0	0	0
	Total: mixed cases	-	-	-	-	-	0	0	0	0
	Total: other species	-	-	-	-	-	0	0	0	0
Kenya	Suspected	7 557 454	13 127 058	12 883 521	14 677 837	15 142 723	15 915 943	15 294 939	14 013 376	15 041 132
	Total: *P. falciparum*	898 531	1 002 805	1 453 471	2 335 286	2 808 931	1 499 027	2 783 846	3 215 116	1 521 566
	Total: *P. vivax*	0	0	0	0	0	0	0	0	0
	Total: mixed cases	0	0	0	0	0	0	0	0	0
	Total: other species	0	0	0	0	0	0	0	0	0
Liberia	Suspected	3 087 659	2 887 105	2 441 800	2 202 213	2 433 086	2 306 116	3 105 390	2 033 806	
	Total: *P. falciparum*	212 927	577 641	1 407 455	1 244 220	864 204	2 086 600	1 191 137	1 760 966	-
	Total: *P. vivax*	0	0	0	0	0	0	0	0	-
	Total: mixed cases	0	0	0	0	0	0	0	0	-
	Total: other species	0	0	0	0	0	0	0	0	-
Madagascar	Suspected	719 967	805 701	980 262	1 068 683	1 019 498	1 536 344	1 530 075	2 008 783	2 334 556

Annex 3 – I. Reported malaria cases by species, 2010–2018

WHO region Country/area		2010	2011	2012	2013	2014	2015	2016	2017	2018
AFRICAN										
Malawi	Suspected	6 851 108	5 734 906	6 528 505	5 787 441	7 703 651	8 518 905	9 239 462	10 530 601	11 513 684
	Total: *P. falciparum*	–	–	1 564 984	1 280 892	2 905 310	3 585 315	4 730 835	4 901 344	5 830 741
	Total: *P. vivax*	–	–	0	0	0	0	0	0	0
	Total: mixed cases	–	–	0	0	0	0	0	0	0
	Total: other species	–	–	0	0	0	0	0	0	0
Mali	Suspected	3 324 238	2 628 593	2 171 739	2 849 453	2 590 643	4 410 839	3 563 070	3 333 079	3 725 896
Mauritania	Suspected	239 795	191 726	209 955	190 446	203 991	233 362	192 980	214 087	221 121
Mayotte	Suspected	2 023	1 214	1 463	82	15	–	12	–	–
	Indigenous: *P. falciparum*	–	–	–	–	–	–	–	–	–
	Indigenous: *P. vivax*	–	–	–	–	–	–	–	–	–
	Indigenous: mixed	–	–	–	–	–	–	–	–	–
	Indigenous: other species	0	0	0	0	0		0	–	–
Mozambique	Suspected	6 097 263	7 059 112	6 170 561	8 200 849	12 240 045	14 241 392	15 453 655	15 905 956	17 127 629
	Total: *P. falciparum*	878 009	663 132	927 841	2 998 874	7 117 648	7 718 782	8 520 376	8 921 081	9 292 928
	Total: *P. vivax*	0	0	0	0	0	0	0	0	0
	Total: mixed cases	0	0	0	0	0	0	0	0	0
	Total: other species	0	0	0	0	0	0	0	0	0
Namibia	Suspected	39 855	74 407	10 844	34 002	186 972	209 083	310 192	618 291	400 337
	Total: *P. falciparum*	556	335	194	136	15 914	12 050	329	364	280
	Total: *P. vivax*	0	0	0	0	0	0	0	0	0
	Total: mixed cases	0	0	0	0	0	0	0	0	0
	Total: other species	0	0	0	0	0	0	0	0	0
Niger	Suspected	10 616 033	3 637 778	5 915 671	5 533 601	7 014 724	4 497 920	7 172 521	3 819 436	4 810 919
	Total: *P. falciparum*	601 455	757 449	2 185 060	2 306 354	3 828 486	2 267 867	3 961 178	2 638 580	3 046 450
	Total: *P. vivax*	0	0	0	0	0	0	0	0	0
	Total: mixed cases	17 123	21 370	22 399	46 068	78 102	0	0	0	0
	Total: other species	0	0	0	0	0	4 133	186 989	0	0
Nigeria	Suspected	3 873 463	5 221 656	11 789 970	21 659 831	19 555 575	17 388 046	20 173 207	22 982 775	23 193 610
	Total: *P. falciparum*	523 513	–	–	–	–	–	–	–	–
	Total: *P. vivax*	0	–	–	–	–	–	–	–	–
	Total: mixed cases	0	–	–	–	–	–	–	–	–
	Total: other species	0	–	–	–	–	–	–	–	–
Rwanda	Suspected	2 708 973	1 602 271	3 095 386	3 064 585	4 178 206	6 093 114	7 502 174	7 557 866	6 221 481
	Total: *P. falciparum*	638 669	208 858	483 470	962 618	1 623 176	–	–	2 927 780	1 657 793
	Total: *P. vivax*	0	0	0	0	0	–	–	0	0
	Total: mixed cases	0	0	0	0	0	–	–	0	0
	Total: other species	0	0	0	0	0	–	–	0	0
Sao Tome and Principe	Suspected	58 961	117 279	126 897	108 634	91 445	84 348	121 334	96 612	169 883
	Total: *P. falciparum*	2 219	6 363	10 700	9 242	1 754	2 057	2 238	2 241	2 940
	Total: *P. vivax*	14	4	1	1	0	0	0	0	0
	Total: mixed cases	0	0	0	0	0	0	0	0	0
	Total: other species	0	6	0	0	0	1	0	0	0
Senegal	Suspected	739 714	628 096	655 294	802 227	741 835	1 421 221	1 559 054	2 035 693	2 096 124
	Total: *P. falciparum*	343 670	277 326	281 080	345 889	265 624	492 253	349 540	395 706	530 944
	Total: *P. vivax*	0	0	0	0	0	0	0	0	0
	Total: mixed cases	0	0	0	0	0	0	0	0	0
	Total: other species	0	0	0	0	0	0	0	0	0
Sierra Leone	Suspected	2 327 928	1 150 747	2 579 296	2 576 550	2 647 375	2 337 297	2 996 959	2 935 447	2 895 596
	Total: *P. falciparum*	218 473	25 511	1 537 322	1 701 958	1 374 476	1 483 376	1 775 306	1 651 236	1 733 831
	Total: *P. vivax*	0	0	0	0	0	0	0	0	0
	Total: mixed cases	0	0	0	0	0	0	0	0	0
	Total: other species	0	0	0	0	0	0	0	0	0

WHO region Country/area		2010	2011	2012	2013	2014	2015	2016	2017	2018
AFRICAN										
South Africa	Suspected	276 669	382 434	152 561	603 932	543 196	35 982	63 277	56 257	-
	Indigenous: *P. falciparum*	-	-	-	-	-	554	1 113	21 442	9 540
	Indigenous: *P. vivax*	-	-	-	-	-	0	0	0	0
	Indigenous: mixed	-	-	-	-	-	1	0	0	0
	Indigenous: other species	0	0	0	0	0	0	0	0	0
South Sudan[2]	Suspected	900 283	795 784	1 125 039	1 855 501	2 492 473	3 814 332	17 705	4 938 773	6 405 779
	Total: *P. falciparum*	-	112 024	-	-	0	24 371	7 619	1 488 005	3 242
	Total: *P. vivax*	-	0	-	-	0	0	0	0	0
	Total: mixed cases	-	0	-	-	0	0	0	0	0
	Total: other species	-	0	-	-	0	0	0	0	0
Togo	Suspected	1 419 928	893 588	1 311 047	1 442 571	1 756 700	1 756 701	1 845 454	2 042 498	2 046 691
	Total: *P. falciparum*	224 080	237 282	260 526	272 847	1 130 234	1 113 910	1 174 116	1 208 957	1 090 110
	Total: *P. vivax*	0	0	0	0	0	0	0	0	0
	Total: mixed cases	0	0	0	8	0	0	0	0	0
	Total: other species	7	23	0	8	17	17	9 149	77	224
Uganda	Suspected	15 294 306	12 340 717	16 845 771	26 145 615	19 201 136	22 095 860	26 238 144	22 319 643	17 484 262
	Total: *P. falciparum*	1 565 348	231 873	2 662 258	1 502 362	3 631 939	7 137 662	9 385 132	11 667 831	5 759 174
	Total: *P. vivax*	15 812	0	0	0	0	0	0	0	0
	Total: mixed cases	47 435	0	0	0	0	0	0	0	0
	Total: other species	0	0	0	0	0	0	0	0	0
United Republic of Tanzania	Suspected	15 388 319	15 299 205	14 513 120	14 650 226	25 190 882	20 797 048	17 786 690	18 389 229	22 785 648
	Total: *P. falciparum*	2 338	4 489	2 730	2 194	1 810	414 983	5 015	1 733	2 240
	Total: *P. vivax*	0	0	0	0	0	0	0	0	0
	Total: mixed cases	0	0	212 837	69 511	106 764	175	89	1 606	1 020
	Total: other species	0	0	0	0	0	0	0	10	26
Mainland	Suspected	15 116 242	14 843 487	13 976 370	14 122 269	24 880 179	20 451 119	17 526 829	18 121 926	22 440 865
	Total: *P. falciparum*	-	-	0	0	0	411 741			
	Total: *P. vivax*	-	-	0	0	0	0			
	Total: mixed cases	-	-	212 636	69 459	106 609	0			
	Total: other species	-	-	0	0	0	0			
Zanzibar	Suspected	272 077	455 718	536 750	527 957	310 703	345 929	259 861	267 303	344 783
	Total: *P. falciparum*	2 338	4 489	2 730	2 194	1 810	3 242	5 015	1 733	2 240
	Total: *P. vivax*	0	0	0	0	0	0	0	0	0
	Total: mixed cases	0	0	201	52	155	175	89	1 606	1 020
	Total: other species	0	0	0	0	0	0	0	10	26
Zambia	Suspected	4 229 839	4 607 908	4 695 400	5 465 122	7 859 740	8 116 962	9 627 862	10 952 323	10 055 407
	Total: *P. falciparum*	-	-	-	-	4 077 547	4 184 661	4 851 319	5 505 639	5 039 679
	Total: *P. vivax*	-	-	-	-	0	0	0	0	0
	Total: mixed cases	-	-	-	-	0	0	0	0	0
	Total: other species	-	-	-	-	0	0	0	0	0
Zimbabwe	Suspected	912 618	480 011	727 174	1 115 005	1 420 946	1 384 893	1 224 374	1 110 705	998 486
	Total: *P. falciparum*	249 379	319 935	276 963	422 633	535 931	391 651	279 988	316 392	184 427
	Total: *P. vivax*	0	0	0	0	0	0	0	0	0
	Total: mixed cases	0	0	0	0	0	0	0	0	0
	Total: other species	0	0	0	0	0	0	0	0	0

Annex 3 – I. Reported malaria cases by species, 2010–2018

WHO region Country/area		2010	2011	2012	2013	2014	2015	2016	2017	2018
AMERICAS										
Argentina[1]	Suspected	2 547	7 872	7 027	4 913	5 691	3 862	3 479	2 114	345
	Indigenous: *P. falciparum*	0	–	–	–	0	0	0	0	0
	Indigenous: *P. vivax*	14	–	–	–	0	0	0	0	0
	Indigenous: mixed	–	–	–	–	0	0	0	0	0
	Indigenous: other species	0	0	0	0	0	0	0	0	0
Belize	Suspected	27 366	22 996	20 789	25 351	24 122	26 367	20 936	26 995	17 642
	Indigenous: *P. falciparum*	–	0	0	0	0	0	0	0	1
	Indigenous: *P. vivax*	–	72	33	20	19	9	4	5	2
	Indigenous: mixed	–	–	–	0	0	0	0	2	0
	Indigenous: other species	0	0	0	0	0	0	0	0	0
Bolivia (Plurinational State of)	Suspected	140 857	150 662	132 904	144 049	124 900	159 167	155 407	151 697	139 938
	Total: *P. falciparum*	1 557	526	385	959	325	84	6	4	0
	Total: *P. vivax*	13 694	7 635	8 141	6 346	7 060	6 811	5 544	4 583	5 354
	Total: mixed cases	35	17	11	37	16	12	3	0	0
	Total: other species	0	0	0	0	0	0	0	0	0
Brazil	Suspected	2 711 433	2 477 821	2 349 341	1 893 018	1 756 460	1 590 403	1 364 917	1 695 805	1 800 173
	Indigenous: *P. falciparum*	–	–	–	26 178	21 295	14 762	13 160	18 614	17 852
	Indigenous: *P. vivax*	–	–	–	141 391	117 009	122 746	110 340	169 887	168 499
	Indigenous: mixed	–	–	–	2 090	939	683	669	1 032	1 331
	Indigenous: other species	0	0	0	31	28	38	8	26	11
Colombia	Suspected	521 342	418 032	416 767	327 055	403 532	332 706	296 091	265 077	225 464
	Indigenous: *P. falciparum*	–	–	–	–	–	27 875	47 232	29 558	29 953
	Indigenous: *P. vivax*	–	–	–	–	–	19 002	32 635	22 132	30 063
	Indigenous: mixed	–	–	–	–	–	739	2 742	1 115	1 179
	Indigenous: other species	0	0	0	0	0	0	0	0	0
Costa Rica	Suspected	15 599	10 690	7 485	16 774	4 420	7 373	5 160	9 680	9 700
	Indigenous: *P. falciparum*	–	–	–	0	0	0	0	0	9
	Indigenous: *P. vivax*	110	10		0	0	0	4	12	61
	Indigenous: mixed	–	–	–	0	0	0	0	0	0
	Indigenous: other species	0	0	0	0	0	0	0	0	0
Dominican Republic	Suspected	495 637	477 555	506 583	502 683	416 729	324 787	302 600	265 535	76 007
	Total: *P. falciparum*	2 480	1 614	950	576	491	651	479	366	575
	Total: *P. vivax*	0	0	0	3	5	10	5	28	29
	Total: mixed cases	0	0	0	0	0	0	0	4	2
	Total: other species	0	0	0	0	0	0	0	0	1
Ecuador	Suspected	488 830	460 785	459 157	397 628	370 825	261 824	311 920	306 894	244 777
	Indigenous: *P. falciparum*	–	–	–	–	–	184	403	309	149
	Indigenous: *P. vivax*	–	–	–	–	–	434	788	963	1 504
	Indigenous: mixed	–	–	–	–	–	0	0	3	0
	Indigenous: other species	0	0	0	0	0	0	0	0	0
El Salvador[3]	Suspected	115 256	100 884	124 885	103 748	106 915	89 267	81 904	70 022	52 216
	Indigenous: *P. falciparum*	–	–	–	0	0	0	0	0	0
	Indigenous: *P. vivax*	–	–	–	6	6	2	13	0	0
	Indigenous: mixed	–	–	–	0	0	0	0	0	0
	Indigenous: other species	0	0	0	0	0	0	0	0	0
French Guiana	Suspected	14 373	14 429	13 638	22 327	14 651	11 558	9 457	597	–
	Total: *P. falciparum*	987	584	382	304	136	84	72	70	–
	Total: *P. vivax*	476	339	257	220	129	230	119	400	–
	Total: mixed cases	561	496	381	348	182	120	67	127	–
	Total: other species	5	5	2	0	1	0	0	0	–

WHO region Country/area		2010	2011	2012	2013	2014	2015	2016	2017	2018
AMERICAS										
Guatemala	Suspected	237 075	195 080	186 645	153 731	300 989	301 746	408 394	372 158	514 133
	Total: *P. falciparum*	30	64	54	101	25	43	4	4	3
	Total: *P. vivax*	7 163	6 707	5 278	6 062	4 839	5 487	4 849	3 739	4 766
	Total: mixed cases	5	3	14	51	67	8	0	1	0
	Total: other species	0	0	0	0	0	0	1	0	0
Guyana	Suspected	212 863	201 728	196 622	205 903	142 843	132 941	116 300	100 096	99 806
	Total: *P. falciparum*	11 244	15 945	16 722	13 655	3 943	3 219	4 200	5 141	6 032
	Total: *P. vivax*	8 402	9 066	11 244	13 953	7 173	6 002	7 144	7 645	9 853
	Total: mixed cases	3 157	4 364	3 607	3 770	1 197	731	966	1 078	1 089
	Total: other species	132	96	92	101	41	32	57	72	64
Haiti	Suspected	270 427	184 934	167 772	176 995	261 403	302 740	302 044	295 572	288 294
	Total: *P. falciparum*	84 153	32 969	25 423	20 957	17 696	17 583	22 457	19 858	9 112
	Total: *P. vivax*	0	0	0	0	0	0	0	0	0
	Total: mixed cases	0	0	0	0	0	0	0	0	0
	Total: other species	0	0	0	0	0	0	0	0	0
Honduras	Suspected	156 961	156 559	159 165	144 673	152 847	153 906	182 767	165 536	161 400
	Total: *P. falciparum*	866	585	560	1 113	564	904	1 310	131	98
	Total: *P. vivax*	8 759	7 044	5 865	4 269	2 881	2 642	2 747	1 155	778
	Total: mixed cases	120	34	24	46	37	29	40	0	2
	Total: other species	0	0	0	0	0	0	0	0	1
Mexico	Suspected	1 192 081	1 035 424	1 025 659	1 017 508	900 580	867 853	798 568	644 174	548 247
	Indigenous: *P. falciparum*	–	–	–	0	0	0	0	0	0
	Indigenous: *P. vivax*	–	–	–	495	656	517	551	736	803
	Indigenous: mixed	–	–	–	0	0	0	0	0	0
	Indigenous: other species	0	0	0	0	0	0	0	0	0
Nicaragua	Suspected	554 414	536 105	552 722	539 022	605 357	604 418	554 415	663 132	875 982
	Indigenous: *P. falciparum*	–	–	–	208	155	338	1 285	1 836	1 319
	Indigenous: *P. vivax*	–	–	–	954	985	1 937	4 965	9 080	14 553
	Indigenous: mixed	–	–	–	0	2	4	22	33	45
	Indigenous: other species	0	0	0	0	0	0	0	0	0
Panama	Suspected	141 038	116 588	107 711	93 624	80 701	64 511	50 772	38 270	23 383
	Indigenous: *P. falciparum*	–	–	–	–	0	0	21	1	0
	Indigenous: *P. vivax*	–	–	–	–	864	546	748	648	684
	Indigenous: mixed	–	–	–	–		0	0	0	0
	Indigenous: other species	0	0	0	0	0	0	0	0	0
Paraguay[1]	Suspected	62 178	48 611	31 499	24 806	24 832	6 687	3 193	9 281	–
	Indigenous: *P. falciparum*	–	–	–	–	–	0	0	0	–
	Indigenous: *P. vivax*	18	1	–	–	–	0	0	0	–
	Indigenous: mixed	–	–	–	–	–	0	0	0	–
	Indigenous: other species	0	0	0	0	0	0	0	0	–
Peru	Suspected	744 650	702 952	759 285	864 648	866 047	867 980	566 230	402 623	464 785
	Total: *P. falciparum*	2 291	2 929	3 399	7 890	10 416	12 569	15 319	13 173	9 456
	Total: *P. vivax*	29 169	21 984	28 030	40 829	54 819	49 287	41 287	42 044	36 157
	Total: mixed cases	83	89	102	213	0	0	0	148	0
	Total: other species	3	3	7	11	17	9	17	2	6
Suriname	Suspected	17 133	16 184	21 685	19 736	33 425	15 236	23 444	22 034	19 836
	Total: *P. falciparum*	638	310	115	322	165	108	100	146	55
	Total: *P. vivax*	817	382	167	322	78	242	216	378	150
	Total: mixed cases	83	21	11	85	158	26	11	27	30
	Total: other species	36	17	2	0	0	0	0	0	0
Venezuela (Bolivarian Republic of)	Suspected	400 495	382 303	410 663	476 764	522 617	625 174	932 556	1 144 635	747 247
	Total: *P. falciparum*	10 629	9 724	10 978	22 777	21 375	24 412	46 503	69 076	80 587
	Total: *P. vivax*	32 710	34 651	39 478	50 938	63 695	102 016	179 554	316 401	344 106
	Total: mixed cases	286	909	2 324	4 882	6 833	11 555	14 655	26 080	28 339
	Total: other species	60	6	23	46	15	13	25	29	9

Annex 3 - I. Reported malaria cases by species, 2010–2018

WHO region Country/area		2010	2011	2012	2013	2014	2015	2016	2017	2018
EASTERN MEDITERRANEAN										
Afghanistan	Suspected	847 589	936 252	847 933	787 624	743 183	801 938	939 389	932 096	932 614
	Total: *P. falciparum*	6 142	5 581	1 231	1 877	3 000	4 004	6 369	6 907	6 437
	Total: *P. vivax*	63 255	71 968	53 609	43 369	58 362	82 891	132 407	154 468	166 583
	Total: mixed cases	0	0	0	0	0	0	311	403	473
	Total: other species	0	0	0	0	0	0	0	0	0
Djibouti	Suspected	1 010	354	1 410	7 189	39 284	10 586	19 492	74 608	104 800
	Total: *P. falciparum*	1 010	-	20	0	-	-	11 781	9 290	16 130
	Total: *P. vivax*	0	-	0	0	-	-	2 041	5 381	9 189
	Total: mixed cases	0	-	0	0	-	-	0	0	0
	Total: other species	0	-	0	0	-	-	0	0	0
Iran (Islamic Republic of)[3]	Suspected	614 817	530 470	479 655	385 172	468 513	630 886	418 125	383 397	541 975
	Indigenous: *P. falciparum*	-	-	-	-	-	8	0	2	0
	Indigenous: *P. vivax*	-	-	-	-	-	157	79	55	0
	Indigenous: mixed	-	-	-	-	-	1	2		0
	Indigenous: other species	0	0	0	0	0	0	0	0	0
Pakistan	Suspected	8 601 835	8 418 570	8 902 947	7 752 797	8 514 341	8 885 456	8 072 464	8 122 212	7 123 228
	Total: *P. falciparum*	73 857	73 925	95 095	46 067	33 391	30 075	42 011	54 467	55 832
	Total: *P. vivax*	143 136	205 879	228 215	283 661	232 332	163 872	257 962	300 623	314 385
	Total: mixed cases	0	0	2 901	10 506	9 426	8 066	24 493	14 787	4 489
	Total: other species	0	0	0	0	0	0	0	0	0
Saudi Arabia	Suspected	944 723	1 062 827	1 186 179	1 309 783	1 249 752	1 306 700	1 267 933	1 073 998	1 015 953
	Indigenous: *P. falciparum*	-	-	82	-	-	83	270	172	57
	Indigenous: *P. vivax*	-	-	-	-	-	0	2	5	4
	Indigenous: mixed	-	-	-	-	-	0	0	0	0
	Indigenous: other species	0	0	0	0	0	0	0	0	0
Somalia	Suspected	220 698	99 403	53 658	69 192	79 653	119 008	205 753	228 912	253 220
	Total: *P. falciparum*	5 629	-	-	-	-	-	-	-	-
	Total: *P. vivax*	0	-	-	-	-	-	-	-	-
	Total: mixed cases	0	-	-	-	-	-	-	-	-
	Total: other species	0	-	-	-	-	-	-	-	-
Sudan	Suspected	2 398 239	2 929 578	2 438 467	2 197 563	1 207 771	4 101 841	4 199 740	3 691 112	9 723 425
	Total: *P. falciparum*	-	-	-	-	-	-	333 009	580 145	1 286 915
	Total: *P. vivax*	-	-	-	-	-	-	82 175	58 335	143 314
	Total: mixed cases	-	-	-	-	-	-	32 557	82 399	187 270
	Total: other species	-	-	-	-	-	-	24 105	0	0
Yemen	Suspected	835 018	804 401	888 952	927 821	821 618	711 680	1 181 486	1 630 469	713 908
	Total: *P. falciparum*	77 271	59 689	109 504	102 369	86 428	75 898	45 469	109 849	112 823
	Total: *P. vivax*	966	478	398	408	267	334	347	1 833	970
	Total: mixed cases	30	7	0	0	12	27	70	2 322	63
	Total: other species	2	33	0	0	0	0	0	0	69
EUROPEAN										
Armenia[1]	Suspected	31 026	0	821 860	825 443	-	-	-	350	-
	Indigenous: *P. falciparum*	0	0	0	0	0	0	0	0	-
	Indigenous: *P. vivax*	0	0	0	0	0	0	0	0	-
	Indigenous: mixed	0	0	0	0	0	0	0	0	-
	Indigenous: other species	0	-	-	-	-	0	0	0	-
Azerbaijan[3]	Suspected	456 652	449 168	497 040	432 810	399 925	405 416	465 860	373 562	-
	Indigenous: *P. falciparum*	0	0	0	0	0	0	0	0	-
	Indigenous: *P. vivax*	50	4	3	0	0	0	0	0	-
	Indigenous: mixed	0	0	0	0	0	0	0	0	-
	Indigenous: other species	0	0	0	0	0	0	0	0	-

WHO region Country/area		2010	2011	2012	2013	2014	2015	2016	2017	2018
EUROPEAN										
Georgia[3]	Suspected	2 368	2 032	1 046	192	440	294	318	416	-
	Indigenous: *P. falciparum*	0	0	0	0	0	0	0	0	-
	Indigenous: *P. vivax*	0	1	1	0	0	0	0	0	-
	Indigenous: mixed	0	0	0	0	0	0	0	0	-
	Indigenous: other species	0	0	0	0	0	0	0	0	-
Kyrgyzstan[1]	Suspected	30 190	27 850	18 268	54 249	35 600				-
	Indigenous: *P. falciparum*	0	0	0	0	0	0	0	0	-
	Indigenous: *P. vivax*	3	0	0	0	0	0	0	0	-
	Indigenous: mixed	0	0	0	0	0	0	0	0	-
	Indigenous: other species	0	0	0	0	0	0	0	0	-
Tajikistan[1]	Suspected	173 523	173 367	209 239	213 916	200 241	188 341	233 336	232 502	-
	Indigenous: *P. falciparum*	0	0	0	0	0	0	0	0	-
	Indigenous: *P. vivax*	111	65	18	7	2	0	0	0	-
	Indigenous: mixed	0	0	0	0	0	0	0	0	-
	Indigenous: other species	0	0	0	0	0	0	0	0	-
Turkey[3]	Suspected	507 841	421 295	337 830	255 125	189 854	221	144 499	115 557	-
	Indigenous: *P. falciparum*	0	0	0	0	0	0	0	0	-
	Indigenous: *P. vivax*	9	4	219	34	5	0	0	0	-
	Indigenous: mixed	0	0	0	0	0	0	0	0	-
	Indigenous: other species	0	0	0	0	0	0	0	0	-
Turkmenistan[1]	Suspected	81 784	-	-	-	-	83 675	85 536	84 264	-
	Indigenous: *P. falciparum*	0	0	0	0	0	0	0	0	-
	Indigenous: *P. vivax*	0	0	0	0	0	0	0	0	-
	Indigenous: mixed	0	0	0	0	0	0	0	0	-
	Indigenous: other species	0	0	0	0	0	0	0	0	-
Uzbekistan[1]	Suspected	921 364	886 243	805 761	908 301	812 347	800 912	797 472	655 112	-
	Indigenous: *P. falciparum*	0	0	0	0	0	0	0	0	-
	Indigenous: *P. vivax*	3	0	0	0	0	0	0	0	-
	Indigenous: mixed	0	0	0	0	0	0	0	0	-
	Indigenous: other species	0	0	0	0	0	0	0	0	-
SOUTH-EAST ASIA										
Bangladesh	Suspected	461 262	390 102	309 179	93 926	125 201	122 806	138 973	150 518	133 547
	Total: *P. falciparum*	52 012	49 084	9 428	3 597	8 981	5 351	3 509	4 224	1 609
	Total: *P. vivax*	3 824	2 579	396	262	489	488	427	522	280
	Total: mixed cases	37	110	36	5	746	769	851	166	30
	Total: other species	0	0	0	0	0	0	0	0	0
Bhutan	Suspected	54 760	44 494	42 512	31 632	33 586	74 087	118 841	42 146	133 498
	Indigenous: *P. falciparum*	-	-	-	-	-	13	1	0	1
	Indigenous: *P. vivax*	-	-	-	-	-	21	13	11	5
	Indigenous: mixed	-	-	-	-	-	0	1	0	0
	Indigenous: other species	0	0	0	0	0	0	0	0	0
Democratic People's Republic of Korea	Suspected	27 019	27 857	40 925	72 719	38 878	91 007	205 807	189 357	685 704
	Total: *P. falciparum*	0	0	0	0	0	0	0	0	0
	Total: *P. vivax*	13 520	16 760	21 850	14 407	10 535	7 022	5 033	4 603	3 598
	Total: mixed cases	0	0	0	0	0	0	0	0	0
	Total: other species	0	0	0	0	0	0	0	0	0

Annex 3 - I. Reported malaria cases by species, 2010–2018

WHO region Country/area		2010	2011	2012	2013	2014	2015	2016	2017	2018
SOUTH-EAST ASIA										
India	Suspected	119 279 429	119 470 044	122 159 270	127 891 198	138 628 331	140 841 230	144 539 608	125 977 799	124 613 482
	Total: *P. falciparum*	830 779	662 748	524 370	462 079	720 795	774 627	706 257	525 637	204 733
	Total: *P. vivax*	765 622	645 652	534 129	417 884	379 659	390 440	375 783	315 028	222 730
	Total: mixed cases	3 585	2 256	0	1 767	1 751	4 194	5 245	3 893	2 465
	Total: other species	0	0	0	0	0	0	0	0	0
Indonesia	Suspected	1 591 179	1 212 799	1 900 725	1 708 161	1 550 296	1 567 450	1 457 858	1 441 679	1 474 636
	Total: *P. falciparum*	220 077	200 662	199 977	170 848	126 397	103 315	118 844	143 926	101 736
	Total: *P. vivax*	187 583	187 989	187 583	150 985	107 260	94 267	81 748	95 694	70 867
	Total: mixed cases	21 964	31 535	29 278	20 352	16 410	13 105	16 751	18 899	16 068
	Total: other species	2 547	2 261	981	1 342	1 960	1 387	1 106	1 818	1 902
Myanmar	Suspected	1 277 568	1 210 465	1 423 555	1 300 556	1 567 095	2 663 732	3 185 245	3 368 697	3 099 776
	Total: *P. falciparum*	70 941	59 604	314 650	223 303	138 311	110 539	62 917	50 730	37 566
	Total: *P. vivax*	29 944	28 966	135 386	99 037	61 830	65 590	43 748	32 070	31 389
	Total: mixed cases	2 054	3 020	30 419	12 255	5 511	6 632	3 476	2 214	1 474
	Total: other species	346	162	103	25	6	14	5	5	3
Nepal	Suspected	213 353	188 702	243 432	168 687	200 631	131 654	146 705	214 265	256 912
	Total: *P. falciparum*	550	219	612	273	195	250	137	103	47
	Total: *P. vivax*	2 349	1 631	1 480	1 659	1 154	1 516	846	1 173	1 106
	Total: mixed cases	216	30	0	22	120	71	26	17	5
	Total: other species	0	0	0	0	0	0	0	0	0
Sri Lanka[1]	Suspected	1 001 107	985 060	948 250	1 236 580	1 069 817	1 156 151	1 090 760	1 104 796	1 149 897
	Indigenous: *P. falciparum*	6	3	4	-	-	0	0	0	0
	Indigenous: *P. vivax*	668	119	19	-	-	0	0	0	0
	Indigenous: mixed	-	-	-	-	-	0	0	0	0
	Indigenous: other species	0	0	0	0	0	0	0	0	0
Thailand	Suspected	1 777 977	1 450 885	1 130 757	1 927 585	1 756 528	1 370 461	1 461 007	1 149 546	921 548
	Indigenous: *P. falciparum*	-	-	-	-	-	3 291	1 609	846	447
	Indigenous: *P. vivax*	-	-	-	-	-	4 655	5 765	4 802	3 575
	Indigenous: mixed	-	-	-	-	-	57	40	36	34
	Indigenous: other species	0	0	0	0	0	19	14	10	21
Timor-Leste[3]	Suspected	266 386	225 858	182 857	178 200	117 107	121 054	150 333	129 175	154 816
	Indigenous: *P. falciparum*	-	-	-	-	-	-	46	5	0
	Indigenous: *P. vivax*	-	-	-	-	-	-	8	3	0
	Indigenous: mixed	-	-	-	-	-	-	28	8	0
	Indigenous: other species	0	0	0	0	0	0	0	0	0
WESTERN PACIFIC										
Cambodia	Suspected	193 210	216 712	194 263	152 137	142 242	163 680	166 695	168 245	166 638
	Total: *P. falciparum*	8 213	7 054	14 896	7 092	8 332	17 830	12 156	20 328	10 525
	Total: *P. vivax*	4 794	5 155	19 575	11 267	10 356	13 146	9 816	15 207	30 680
	Total: mixed cases	1 270	1 583	4 971	2 418	6 464	2 954	1 520	1 397	1 080
	Total: other species	0	0	0	0	0	0	0	0	0
China[3]	Suspected	7 118 649	9 190 401	6 918 770	5 555 001	4 403 633	4 052 616	3 194 929	2 409 280	1 904 295
	Indigenous: *P. falciparum*	-	-	-	-	-	1	0	0	0
	Indigenous: *P. vivax*	-	-	-	-	-	26	3	0	0
	Indigenous: mixed	-	-	-	-	-	0	0	0	0
	Indigenous: other species	0	0	0	0	0	6	0	0	0
Lao People's Democratic Republic	Suspected	280 549	291 775	369 976	339 013	294 542	284 003	223 992	274 314	286 881
	Total: *P. falciparum*	4 393	5 770	37 692	24 538	23 928	14 430	4 255	4 550	4 726
	Total: *P. vivax*	122	442	7 634	12 537	22 625	20 804	6 795	4 590	4 077
	Total: mixed cases	8	0	769	956	1 517	822	173	193	110
	Total: other species	1	14	0	1	1	0	0	0	0

WHO region Country/area		2010	2011	2012	2013	2014	2015	2016	2017	2018
WESTERN PACIFIC										
Malaysia[3]	Suspected	1 619 074	1 600 439	1 566 872	1 576 012	1 443 958	1 066 470	1 153 108	1 046 163	1 070 356
	Indigenous: *P. falciparum*	–	–	–	–	–	110	67	18	0
	Indigenous: *P. vivax*	–	–	–	–	–	84	178	59	0
	Indigenous: mixed	–	–	–	–	–	22	9	1	0
	Indigenous: other species	0	0	0	0	0	26	12	7	0
Papua New Guinea	Suspected	1 505 393	1 279 140	1 113 528	1 454 166	922 417	909 940	1 168 797	1 400 593	1 513 776
	Total: *P. falciparum*	56 735	59 153	58 747	119 469	120 641	118 452	183 686	163 160	174 818
	Total: *P. vivax*	13 171	9 654	7 108	7 579	78 846	62 228	95 328	113 561	138 006
	Total: mixed cases	4 089	1 164	0	1 279	79 574	115 157	197 711	200 186	201 658
	Total: other species	1 990	632	0	1 279	2 125	1 950	1 772	1 433	1 767
Philippines	Suspected	301 577	327 125	333 084	320 089	316 323	280 222	321 838	284 564	282 385
	Total: *P. falciparum*	11 824	6 877	4 774	4 968	3 760	4 781	5 320	3 160	1 370
	Total: *P. vivax*	2 885	2 380	2 189	1 357	834	760	826	538	129
	Total: mixed cases	214	166	0	83	235	196	391	83	26
	Total: other species	175	127	0	67	74	87	142	46	49
Republic of Korea	Suspected	1 772	838	555	443	638	699	0	0	576
	Indigenous: *P. falciparum*	–	–	–	–	–	0	0	0	0
	Indigenous: *P. vivax*	–	–	–	–	–	628	602	436	501
	Indigenous: mixed	–	–	–	–	–	0	0	0	0
	Indigenous: other species	0	0	0	0	0	0	0	0	0
Solomon Islands	Suspected	284 931	254 506	249 520	245 014	233 803	192 044	274 881	238 814	244 523
	Total: *P. falciparum*	22 892	14 454	14 748	13 194	9 835	10 478	16 607	15 400	15 771
	Total: *P. vivax*	12 281	8 665	9 339	11 628	7 845	12 150	33 060	30 169	35 072
	Total: mixed cases	200	83	232	446	724	1 370	4 719	6 917	8 341
	Total: other species	0	0	0	0	0	0	46	33	7
Vanuatu	Suspected	48 088	32 656	33 273	28 943	35 570	14 938	21 484	30 313	26 931
	Total: *P. falciparum*	1 545	770	1 257	1 039	279	150	186	273	49
	Total: *P. vivax*	2 265	1 224	1 680	1 342	703	273	1 682	799	595
	Total: mixed cases	193	81	470	0	0	0	0	0	0
	Total: other species	10	2	0	0	0	0	0	0	0
Viet Nam	Suspected	2 803 918	3 312 266	3 436 534	3 115 804	2 786 135	2 673 662	2 497 326	2 614 663	2 167 376
	Total: *P. falciparum*	12 763	10 101	11 448	9 532	8 245	4 327	2 323	2 858	2 966
	Total: *P. vivax*	4 466	5 602	7 220	6 901	7 220	4 756	1 750	1 608	1 751
	Total: mixed cases	0	0	0	0	287	234	73	70	83
	Total: other species	0	0	0	0	0	14	15	12	13

P.: *Plasmodium*; WHO: World Health Organization.

"–" refers to not applicable or data not available.

[1] Certified malaria free countries are included in this listing for historical purposes.

[2] In May 2013, Sudan was reassigned to the WHO African Region (WHA resolution 66.21, https://apps.who.int/gb/ebwha/pdf_files/WHA66/A66_R21-en.pdf).

[3] There is no local transmission.

Note: Suspected cases include indigenous and imported cases. For countries in the WHO Region of the Americas, the number of Total: *P. falciparum*, Total: *P. vivax*, Total: mixed cases and Total: other species are indigenous cases from 2013 onwards (data from 2010–2012 signifies all reported cases).

Annex 3 - J. Reported malaria deaths, 2010–2018

WHO region Country/area	2010	2011	2012	2013	2014	2015	2016	2017	2018
AFRICAN									
Algeria[1]	*1*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
Angola	8 114	6 909	5 736	7 300	5 714	7 832	15 997	13 967	11 814
Benin	964	1 753	2 261	2 288	1 869	1 416	1 646	2 182	2 138
Botswana	8	8	3	7	22	5	3	17	9
Burkina Faso	9 024	7 001	7 963	6 294	5 632	5 379	3 974	4 144	4 294
Burundi	2 677	2 233	2 263	3 411	2 974	3 799	5 853	4 414	2 481
Cabo Verde	*1*	*1*	*0*	*0*	*1*	*0*	*1*	*1*	*0*
Cameroon	4 536	3 808	3 209	4 349	4 398	3 440	2 639	3 195	3 256
Central African Republic	526	858	1 442	1 026	635	1 763	2 668	3 689	1 292
Chad	886	1 220	1 359	1 881	1 720	1 572	1 686	2 088	1 948
Comoros	53	19	17	15	0	1	0	3	8
Congo	–	892	623	2 870	271	435	733	229	131
Côte d'Ivoire	1 023	1 389	1 534	3 261	4 069	2 604	3 340	3 222	3 133
Democratic Republic of the Congo	23 476	23 748	21 601	30 918	25 502	39 054	33 997	27 458	18 030
Equatorial Guinea	30	52	77	66	–	28	109	–	–
Eritrea	27	12	30	6	15	12	21	8	5
Eswatini	8	1	3	4	4	5	3	20	2
Ethiopia	1 581	936	1 621	358	213	662	510	356	158
Gabon	182	74	134	273	159	309	101	218	591
Gambia	151	440	289	262	170	167	79	54	60
Ghana	3 859	3 259	2 855	2 506	2 200	2 137	1 264	599	428
Guinea	735	743	979	108	1 067	846	867	1 174	1 267
Guinea-Bissau	296	472	370	418	357	477	191	296	244
Kenya	26 017	713	785	360	472	15 061	603	–	–
Liberia	1 422	–	1 725	1 191	2 288	1 379	1 259	758	–
Madagascar	427	398	552	641	551	841	443	370	927
Malawi	8 206	6 674	5 516	3 723	4 490	3 799	4 000	3 613	2 967
Mali	3 006	2 128	1 894	1 680	2 309	1 544	1 344	1 050	1 001
Mauritania	60	66	106	46	19	39	315	67	–
Mayotte	*0*	*0*	*0*	*0*	*0*	*0*	*0*	–	–
Mozambique	3 354	3 086	2 818	2 941	3 245	2 467	1 685	1 114	968
Namibia	63	36	4	21	61	45	65	104	82
Niger	3 929	2 802	2 825	2 209	2 691	2 778	2 226	2 316	3 576
Nigeria	4 238	3 353	7 734	7 878	6 082	–	–	–	–
Rwanda	670	380	459	409	496	516	715	376	341
Sao Tome and Principe	14	19	7	11	0	0	1	1	0
Senegal	553	472	649	815	500	526	325	284	555
Sierra Leone	8 188	3 573	3 611	4 326	2 848	1 107	1 345	1 298	1 949
South Africa	83	54	72	105	174	110	34	301	69
South Sudan[2]	1 053	406	1 321	1 311	–	–	–	3 483	1 191
Togo	1 507	1 314	1 197	1 361	1 205	1 205	847	995	905
Uganda	8 431	5 958	6 585	7 277	5 921	6 100	5 635	5 111	3 302
United Republic of Tanzania	15 867	11 806	7 820	8 528	5 373	6 313	5 046	3 685	2 753
Mainland	15 819	11 799	7 812	8 526	5 368	6 311	5 045	3 684	2 747
Zanzibar	48	7	8	2	5	2	1	1	6
Zambia	4 834	4 540	3 705	3 548	3 257	2 389	1 827	1 425	1 209
Zimbabwe	255	451	351	352	406	200	351	527	192
AMERICAS									
Argentina[1]	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
Belize	0	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
Bolivia (Plurinational State of)	0	0	0	0	1	*0*	*0*	*0*	*0*
Brazil	76	70	60	40	36	35	35	34	*44*
Colombia	42	23	24	10	17	*18*	*36*	*19*	*9*
Costa Rica	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
Dominican Republic	15	10	8	5	*4*	*3*	*1*	*1*	*1*
Ecuador	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
El Salvador[3]	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
French Guiana	1	2	2	3	0	*0*	*0*	*0*	–
Guatemala	0	0	0	1	1	1	0	*0*	*0*
Guyana	24	36	35	14	11	12	13	11	6
Haiti	8	5	6	10	9	15	13	12	12
Honduras	3	2	1	1	2	0	*0*	*1*	*1*
Mexico	0	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*

WHO region Country/area	2010	2011	2012	2013	2014	2015	2016	2017	2018
AMERICAS									
Nicaragua	1	1	2	0	*0*	*1*	*2*	*1*	*3*
Panama	1	0	1	0	0	*0*	*0*	*0*	*0*
Paraguay[1]	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
Peru	0	1	7	4	4	5	7	*10*	*4*
Suriname	1	1	0	1	1	*0*	*0*	*1*	*0*
Venezuela (Bolivarian Republic of)	18	16	10	6	5	8	105	333	257
EASTERN MEDITERRANEAN									
Afghanistan	22	40	36	24	32	49	47	10	1
Djibouti	0	0	0	17	28	23	5	-	-
Iran (Islamic Republic of)[3]	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
Pakistan	-	4	260	244	56	34	33	113	102
Saudi Arabia	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
Somalia	6	5	10	23	14	27	13	20	31
Sudan	1 023	612	618	685	823	868	698	1 534	3 129
Yemen	92	75	72	55	23	14	65	37	57
EUROPEAN									
Armenia[1]	0	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
Azerbaijan[3]	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
Georgia[3]	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
Kyrgyzstan[1]	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
Tajikistan[3]	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
Turkey[3]	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
Turkmenistan[1]	0	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
Uzbekistan[1]	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
SOUTH-EAST ASIA									
Bangladesh	37	36	11	15	45	9	17	13	7
Bhutan	2	1	1	*0*	*0*	*0*	*0*	*0*	*0*
Democratic People's Republic of Korea	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
India	1 018	754	519	440	562	384	331	194	96
Indonesia	432	388	252	385	217	157	161	47	34
Myanmar	788	581	403	236	92	37	21	30	19
Nepal	6	2	0	0	0	0	*3*	*0*	*0*
Sri Lanka[1]	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
Thailand	80	43	37	47	38	33	27	15	8
Timor-Leste[3]	58	16	6	3	1	0	*0*	*0*	*0*
WESTERN PACIFIC									
Cambodia	151	94	45	12	18	10	3	1	0
China[3]	19	33	*0*	*0*	*0*	*0*	*0*	*0*	*0*
Lao People's Democratic Republic	24	17	44	28	4	2	1	2	6
Malaysia[4]	*13*	*12*	*12*	*10*	*4*	*4*	*2*	*10*	*12*
Papua New Guinea	616	523	381	307	203	163	306	273	216
Philippines	30	12	16	12	10	20	*7*	*3*	*1*
Republic of Korea	*1*	*2*	*0*	*0*	*0*	*0*	*0*	*0*	*0*
Solomon Islands	34	19	18	18	23	13	20	27	7
Vanuatu	1	1	0	0	0	*0*	*0*	*0*	*0*
Viet Nam	21	14	8	6	6	3	*2*	*5*	*1*
REGIONAL SUMMARY									
African	150 335	104 057	104 105	116 354	99 380	118 362	103 748	94 212	73 276
Americas	190	167	156	95	91	98	212	423	337
Eastern Mediterranean	1 143	736	996	1 048	976	1 015	861	1 714	3 320
European	0	0	0	0	0	0	0	0	0
South-East Asia	2 421	1 821	1 229	1 126	955	620	560	299	164
Western Pacific	910	727	524	393	268	215	341	321	243
Total	**154 999**	**107 508**	**107 010**	**119 016**	**101 670**	**120 310**	**105 722**	**96 969**	**77 340**

[1] Certified malaria free countries are included in this listing for historical purposes.

[2] In May 2013, South Sudan was reassigned to the WHO African Region (WHA resolution 66.21, https://apps.who.int/gb/ebwha/pdf_files/WHA66/A66_R21-en.pdf).

[3] There is no local transmission.

[4] In Malaysia, there is no local transmission of human malaria in 2018. Malaria deaths are imported non-human malaria.

Note: Deaths reported before 2000 can be probable and confirmed or only confirmed deaths depending on the country. Indigenous malaria deaths are in italics.

Notes

Notes

Notes

Imperial College London

For further information please contact:

Global Malaria Programme
World Health Organization
20, avenue Appia
CH-1211 Geneva 27
Web: www.who.int/malaria
Email: infogmp@who.int

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Speaker: David Scales, M.D.
Date: March 22, 2021
Time: 1:00pm – 2:00pm
Title: Humanitarian Crisis: Global Health

Zoom info: https://weillcornell.zoom.us/j/98591461353 **Meeting ID**: 985 9146 1353 **Passcode**: 264130

Summary: Be able to define humanitarian emergency and syndemic; Understand the intertwined health risks after humanitarian crises and initial approaches to address them.

Suggested Readings:

Kohrt, B. A. & Carruth, L. (2020). Syndemic effects in complex humanitarian emergencies: A framework for understanding political violence and improving multi-morbidity health outcomes. Social Science & Medicine, 113378. https://doi.org/10.1016/j.socscimed.2020.113378

Case Study:

Please take particular note of Case Study #2 in the above reading: "diabetes, anxiety, persistent wounds, and humoral dysfunction in the Somali Region of Ethiopia"

Discussion Questions:

Based on this reading, be prepared to share an example from a country you are familiar with about how the emergency conditions created by the Covid-19 pandemic may lead to a syndemic among certain vulnerable populations. What are the intertwined social, political, economic and health forces that are leading to increased disease vulnerability?

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Syndemic effects in complex humanitarian emergencies: A framework for understanding political violence and improving multi-morbidity health outcomes

Brandon A. Kohrt, MD, PhD [a,*], Lauren Carruth, PhD [b]

[a] Department of Psychiatry and Behavioral Sciences, School of Medicine and Health Sciences, Department of Global Health, Milken School of Public Health, George Washington University, USA
[b] School of International Service, American University, Washington, DC, 20016, USA

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ABSTRACT

A hallmark of complex humanitarian emergencies is the collective exposure, often over extended periods of time, to political violence in the forms of war, terrorism, political intimidation, repression, unlawful detention, and forced displacement. Populations in complex humanitarian emergencies have higher risks of multiple co-morbidities: mental disorders, infectious diseases, malnutrition, and chronic non-communicable diseases. However, there is wide variation in the health impacts both across and within humanitarian emergencies. Syndemic theory is an approach to conceptualizing disease and social determinants to understand differential patterns of multi-morbidity, elucidate underlying mechanisms, and better design interventions. Syndemic theory, if applied to complex humanitarian emergencies, has the potential to uncover origins of localized patterns of multi-morbidity resulting from political violence and historical inequities. In this paper, we present two case studies based on mixed-methods research to illustrate how syndemic models can be applied in complex humanitarian emergencies. First, in a Nepal case study, we explore different patterns of posttraumatic stress disorder (PTSD) and depression co-morbidity among female former child soldiers returning home after war. Despite comparable exposure to war-related traumas, girl soldiers in high-caste Hindu communities had 63% co-morbidity of PTSD and depression, whereas girl soldiers in communities with mixed castes and religions, had 8% PTSD prevalence, but no cases of PTSD and depression co-morbidity. In the second case study, we explore the high rates of type 2 diabetes during a spike in political violence and population displacement. Despite low rates of obesity and other common risk factors, Somalis in Ethiopia experienced rising cases of and poor outcomes from type-2 diabetes. Political violence shapes healthcare resources, diets, and potentially, this epidemiological anomaly. Based on these case studies we propose a humanitarian syndemic research agenda for observational and intervention studies, with the central focus being that public health efforts need to target violence prevention at family, community, national, and global levels.

1. Introduction

Political violence – including internal conflicts, international wars, terrorism, political intimidation and repression, unlawful detentions of dissidents, and population displacement – is commonplace around the world and has devastating consequences on human health (Herbert et al., 2011; Krug et al., 2002; Wenzel et al., 2015). The presence of political violence distinguishes *complex* humanitarian emergencies from other humanitarian emergencies. A "complex humanitarian emergency" is defined as a crisis when there is a breakdown in a country's political system or sovereign authority resulting from internal or external conflict, necessitating an international response (Burkle, 2006). As such, complex humanitarian emergencies are defined by their association with various forms of political violence (Edkins, 1996; Macrae and Zwi, 1994), their embeddedness in long histories of inequity, colonialism, and conflict (Albala-Bertrand, 2000), and a subsequent cascading effects on population health (Hammer et al., 2018; Salama et al., 2004; Toole and Waldman, 1997).

Populations affected by complex humanitarian emergencies experience increased rates of physical injuries, increased rates of acute and

* Corresponding author.
E-mail addresses: bkohrt@gwu.edu (B.A. Kohrt), lcarruth@american.edu (L. Carruth).

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chronic forms of malnutrition, increased risk of infectious diseases, increased rates of mental illness, and disruptions or gaps in care for chronic and non-communicable conditions (Charlson et al., 2019; Chen et al., 1999; Hammer et al., 2018; Jobanputra et al., 2016; Salama et al., 2004; Toole and Waldman, 1997). Multi-morbidity is more the rule than the exception. However, little epidemiological or other research examines how exposures to political violence affect subsequent patterns of multi-morbidity in humanitarian emergency-affected populations. Epidemiological research in complex humanitarian emergencies predominantly presents descriptive data on the patterns of health outcomes in a population with less attention to how different health conditions, exposures to different forms of violence, and contextual factors interact.

Health needs vary significantly during complex humanitarian settings. Within populations affected by the same conflict, there may be tremendous epidemiological heterogeneity in the burdens of disease, capacities to manage disease across different demographic groups and parties to the conflicts at hand. Standard epidemiological models often have been limited in understanding patterns of health outcomes in complex humanitarian emergencies and in determining how best to respond or prevent the confluence and interactions of multiple health problems. Guidelines for responding to health needs in humanitarian crises such as the Sphere Handbook (2018) continue to rely upon single-disorder approaches to disease classification, rather than employing an integrative or interactive perspective on the potential of interacting multi-morbidities, i.e., standard reporting does not routinely present rates and prevalences of multi-morbidities.

Syndemic theory presents an innovative way to conceptualize and advocate for responses in complex humanitarian emergencies to address multi-morbidity and the exponentiation of interacting negative health outcomes (Kohrt et al., 2019). The basic principle of syndemic theory is that particular sociocultural settings can contribute to increased risk of co-morbid conditions. The concept of syndemic emerged early in understanding HIV in the United States. The medical anthropologist Merrill Singer observed that HIV rates were especially high among persons with substance abuse disorders who also had experiences of exposure to violence (Singer, 1996). The pattern was not simply explained by HIV transmission in the context of substance abuse (e.g., sharing needles), it was also important to account for violence histories that shaped risk-taking behaviors and limited people's access to and use of social and health services. Singer's *Substance Abuse Violence AIDS* (SAVA) syndemic model was instrumental in understanding variation in exposure to and rates of HIV in different communities. More recently, the *Violence Immigration Depression and Diabetes* (VIDDA) syndemic model has been used to understand why Mexican immigrants are more likely to have greater co-morbidity of depression and diabetes compared to the non-immigrant, non-Mexican populations in Chicago (Mendenhall, 2012).

Notably, each of these models integrates measures of people's exposure to different forms of violence to better understand the exacerbation of risks for compounding negative health outcomes. In the case of SAVA, Singer highlights the manifold effects of different forms of community violence. In the VIDDA model, Mendenhall examines the manifold effects of intimate partner violence. Violence, in both models, is key to the exacerbation of risk of multi-morbidity. The role of violence is similarly important to understand interacting multi-morbidity in the context of complex humanitarian emergencies. Violence has both internal effects on the body and external effects on lived experience. Witnessing violence, experiencing violence, and the threat of violence impact stress pathways both to trigger inflammatory processes and to suppress viral responses (Lindqvist et al., 2014; Kohrt et al., 2016). Exposure to violence impacts metabolism, cardiovascular function, and pain pathways (Alhalal et al., 2018; Kaur, 2017; Kliewer et al., 2019; Konstam and Konstam, 2019; Liu et al., 2020; Rivara et al., 2019). Outside the body, violence transforms the social world by reducing access to restorative social relationships, decreasing access to health, educational, and social services, and limiting economic and livelihood opportunities (Carruth, 2014; Willman and Team, 2009; Yodanis et al., 2000). In the context of political violence, these impacts are not limited to a few individuals but transforms entire societies (Galtung, 1969, 1990). Given these internal and external impacts of political violence, we cannot assume that health conditions will follow the same epidemiological and clinical profiles as one observes among populations with less exposure to state-level, community, and interpersonal violence.

Just as human bodies and minds bring different resources and vulnerabilities to the impact of violence, people's histories also influence how violence transforms health. For example, in societies with long histories of economic exploitation, colonial occupation, social divisions in the form of gender, racial, ethnic, and religious discrimination, and the undermining of civic institutions, political violence is more likely to have dramatic health impacts (Farmer, 2003). This is evident more than ever with the major disparities in COVID-19 morbidity and mortality among populations subjected to prolonged histories of structural and direct violence, as demonstrated by the health burden among Black American, Latinx, and immigrant communities in the United States (Gravlee, 2020; Poteat et al., 2020). The COVID-19 syndemic of pre-existing health conditions, COVID-19, and exposure to violence highlights the need to advance syndemic research among populations affected by political violence.

To explore this proposed model of syndemic effects in the context of complex humanitarian emergencies, we present two case studies. These studies did not involve an *a priori* test of syndemic models in these two contexts, but instead we apply a conceptual model of syndemic effects to prior research conducted in complex humanitarian emergencies. We retrospectively examine data collected during separate research projects in Nepal and Ethiopia (Carruth et al., 2020; Carruth and Mendenhall, 2019; Kohrt et al., 2008, 2010a) to theorize how the notion of syndemics potentially helps to overcome both the fragmentation of humanitarian responses and the siloed nature of epidemiological research during these emergencies. This sets the stage for a research agenda on syndemic effects and syndemic-informed care in complex humanitarian emergencies. In the first case study, we evaluate the co-morbidity of PTSD and depression among female former child soldiers in Nepal. We explore why some communities had low rates of PTSD and depression co-morbidity, whereas other communities had extremely high rates. These findings can best be understood via the interaction of political violence exposure with differences in historical and current discrimination against women.

In the second case study, we explore high-rates of type-2 diabetes alongside food insecurity among Somalis in Ethiopia. Given the low prevalence of common risk factors for type-2 diabetes, such as obesity and smoking, among people there, diabetes prevalence and symptoms are surprising. However, attention to the potential physiological effects of political violence on the body and recognition of how political violence has changed local diets, may help explain these health outcomes. We conclude with recommendations for designing both epidemiological studies and healthcare responses for complex humanitarian emergencies within a model of syndemic effects.

2. Case study 1: differential co-morbidity of depression and PTSD among child soldiers in Nepal

The first case study explores patterns of mental health co-morbidity in Nepal among adolescent girls exposed to war, including girls who became child soldiers. From 1996 to 2006, there was a civil war in Nepal between the Communist Party of Nepal (Maoists) and the Hindu monarchy government. The Maoists regularly recruited minors into their armed forces. By the end of the war in 2006, there were more than 9000 youth under the age of 18 who were part of the fighting forces. One of the striking features of the Maoist conflict in Nepal was that girls were typically recruited as combatants in the same roles as boys. This contrasts with East and West Africa where girls were more likely kidnapped and forced into sexual relationships and marriage with male

combatants.

Through a study commissioned by UNICEF, the rates of mental health problems of youth who had informally returned home at the end of war were studied (Kohrt et al., 2008). (Ethical approval provided by the Nepal Health Research Council and Emory University.) "Informal return" refers to the process where youth left the armed forces and returned home independently rather than through formal Disarmament, Demobilization, and Reintegration programs (DDR). In DDR programs, standing militaries are first inspected by humanitarian actors. Then persons under 18 years of age are removed and entered in temporary housing programs while family members to receive them are identified. After this, they can be formally returned to the community with service packages. Our study, in contrast to traditional DDR processes, worked with the informally returning youth and found wide variations in the rates of mental health problems among former child soldiers and youth throughout the country. In some regions of the country, more than half of former child soldiers were above cut-offs for depression and PTSD on culturally and clinically validated assessment tools (Kohrt et al., 2011). However, in other regions of the country, rates were only to 1 out of 10. The disparity in prevalence rates was strongest among girl soldiers. Moreover, the rates of co-morbidity varied widely, with some regions showing an association between PTSD and depression, but not in other regions.

2.1. Ethnographic research to identify sociocultural and contextual contributors to a syndemic pattern

Ethnographic research and other qualitative methods were used to explore why these differences existed, to propose statistical analyses, and to determine what needed to be done to address the burden of mental health and psychosocial problems (Kohrt et al., 2010b). A team of Nepali researchers were trained in qualitative and ethnographic methods and the first author spent time conducting participant observation in different regions of the country. The team found that although the types of traumatic events during the war appeared to be similar for child soldiers across the country, the experience of reintegration varied widely (Kohrt et al., 2010a). In some regions of the country, child soldiers were discriminated against when they came home. Female former child soldiers, in particular, were discriminated against by their families and communities. However, in other regions of the country, girl soldiers were welcomed back into their families and communities, even without formal programs from UNICEF or other humanitarian agencies.

The ethnographic and other qualitative work suggested that the discrimination against women in these communities played a role in these reintegration differences (Kohrt et al., 2010b). In some communities, discrimination against women in general and discrimination against girl soldiers was frequently described. In these communities, the girl soldiers were more likely to described high levels of distress. In other communities, there was less qualitatively reported general gender discrimination, and less discrimination against girl soldiers specifically. One distinguishing feature between the two types of communities was that the communities with high levels of gender discrimination and stigmatization of former girl soldiers were more likely to be predominantly high-caste Hindu groups.

In the high-caste Hindu communities, there was more focus on describing girls in terms of their ritual purity, with former girl solders described as being 'polluted' (Nepali: *jutho*) and no longer religiously pure (*choko*). In contrast, in regions with mixed caste/ethnicity including high- and low-caste as well as Buddhist ethnic groups, the former child soldiers were less likely to describe experiencing discrimination in with the framing of these Hindu concepts of purity. The gender discrimination played out in other differences between the communities, such as lower female literacy, lower female school completion, and other performance on Gender Development Indices (Kohrt et al., 2010a). This suggests that although trauma levels were comparable for the girls in the two types of communities, the differences in gender discrimination likely set the stage for differences in mental health sequelae of the trauma.

2.2. Assessing differences in comorbidities by sociocultural context

Based on our prior quantitative and qualitative findings, we conducted exploratory analyses to assess a potential syndemic model. In our model, the specific co-morbidity of interest was PTSD and depression. Globally—whether referring to humanitarian conflicts in low-income countries or working with veterans in high-income countries—PTSD is often co-morbid with depression (Nesterko et al., 2020; Peconga and Høgh Thøgersen, 2019; Stander et al., 2014). However, the rates of co-morbidity vary widely by populations and settings. In some conflict affected populations rates of depression without PTSD are high, and other in other populations there may be high comorbidity of depression and PTSD (Kohrt et al., 2012; Nesterko et al., 2020; Trief et al., 2006). We wanted to determine the rates of co-morbidity in the child soldier and civilian children populations in post-conflict Nepal. The socio-cultural context of interest was the comparison of predominantly high-caste Hindu communities with communities that were more mixed by ethnicity and caste.

Because the socio-cultural context appeared to particularly influence girls' mental health, we limited our syndemic analysis to female former child soldiers and comparison civilian girls. The sample included 148 girls: 75 female former child soldiers, and 73 civilian girls (see Kohrt et al., 2008 for recruitment and sample details). We analyzed the samples comparing girls living in predominantly high-caste Hindu communities (63 child soldiers and 60 civilians) vs. girls in mixed ethnic and caste communities (12 child soldiers and 13 civilians). Because the study was not originally designed to test this syndemic association, the sample sizes are not equal between the two types of communities.

We then evaluated whether female former child soldiers in the high-caste Hindu communities and female civilians in the mixed ethnic-caste communities had comparable levels of war-related and other traumas. We found that female former child soldiers in both communities had similar levels of exposure to war traumas (witnessing violent death, witnessing torture, experiencing bombing, war-related fires, and exposure to combat) and pre-war traumas (domestic violence and physical abuse), see Fig. 1.

We then evaluated co-morbidity rates of PTSD and depression in the two communities. We found that PTSD and depression symptom scores were not correlated in the mixed religious/caste communities ($r = 0.04$, $p = 0.87$). However, the PTSD and depression symptom scores were strongly correlated in the high-caste Hindu communities ($r = 0.58$, $p < 0.001$). Using a culturally and clinically validated cut-off for PTSD and depression (Kohrt et al., 2011), we then identified the number of child soldier and civilian girls scoring above the cut-offs for these conditions. In the mixed religious and ethnicity communities, 8% of female child soldiers and 8% of female civilians scored above the cut-off for PTSD, but none of the girls in either group were above the cut-off for depression. In the high-caste Hindu communities, among civilian girls, 17% had PTSD only, 32% had depression only, and 8% had co-morbid PTSD and depression. For female former child soldiers, 11% had PTSD only, 11% had depression only, and 63% had co-morbid PTSD and depression (see Fig. 2).

It is striking that female former child soldiers with comparable levels of trauma exposure had such different mental health profiles: in the mixed religious and ethnic communities, no girls had co-morbid PTSD and depression, but in high-caste communities, 6 out of 10 girl soldiers had co-morbid PTSD and depression. These findings were supported by assessment of discrimination and stigma, with both civilian and child soldier girls in high-caste communities reporting higher levels of discrimination compared to girls in mixed-religious communities; in prior analyses, we have shown that children in high-caste Hindu districts reported experiencing greater levels of family and community discrimination and lower levels of supports (Kohrt et al., 2010a). One possible

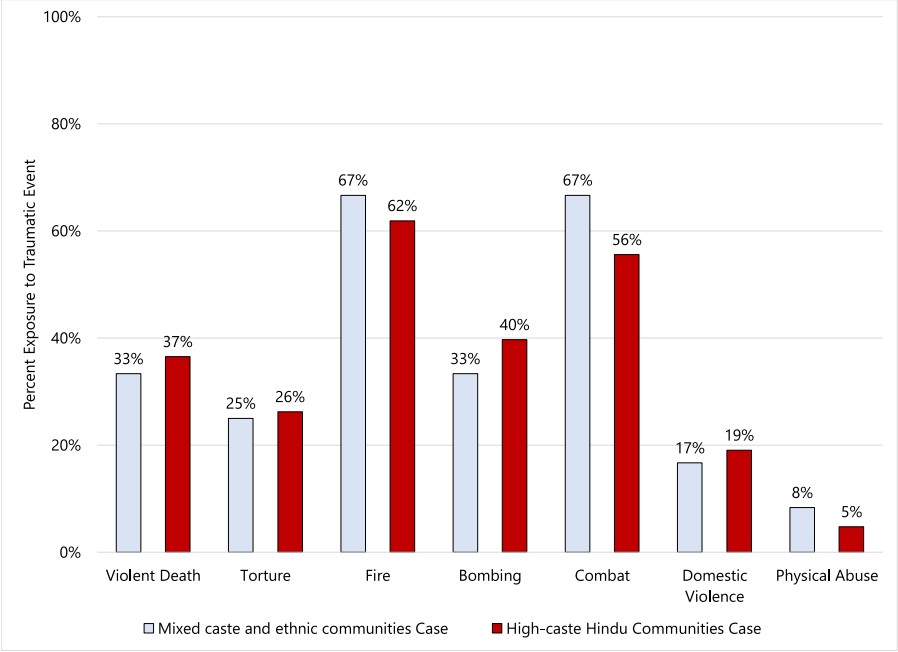

Fig. 1. Exposure to traumatic events among female former child soldiers in mixed caste/ethnic communities vs. high-caste communities.

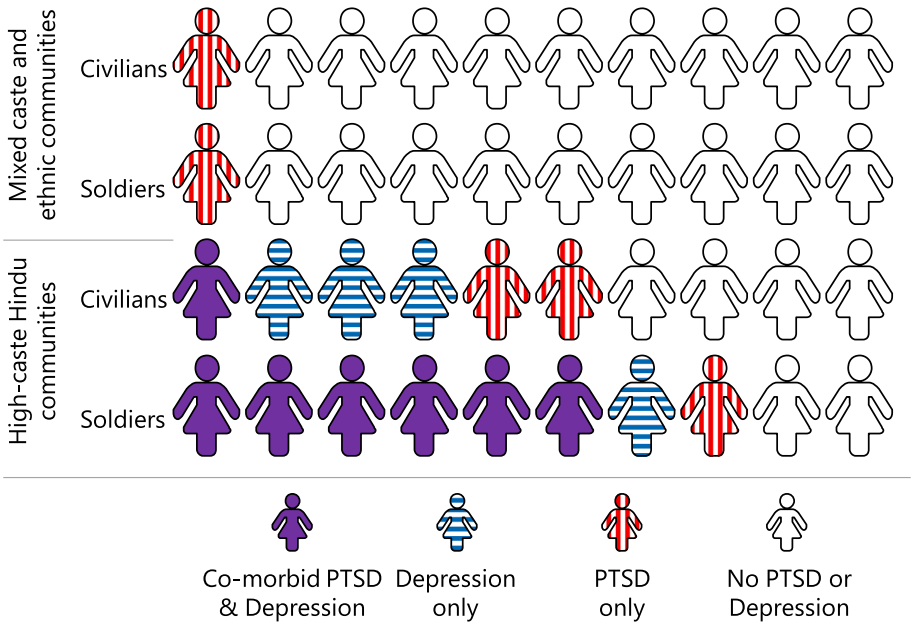

Fig. 2. Percentage of civilian girls and girls soldiers with PTSD and depression by type of community.

explanation for the differences is that the likelihood of developing depression was already greater in the high-caste Hindu communities. There is evidence to support this with large gender differences in depression rates in high-caste Hindu regions of Nepal (Kohrt et al., 2009, 2012). Therefore, the girls in these communities were already likely to develop depression during adolescence and young adulthood. Then, the traumatic experience in the context of gender discrimination, low social support, and a social context predisposing for depression contributed to the increased likelihood of developing PTSD.

This provides a useful illustration for how syndemics may work in humanitarian settings. Although the traumas of interest (combat and other war-related exposures) were comparable for girl soldiers in two different types of communities, the rates of mental health problems and co-morbidities were strikingly different. This suggests that it is vital to understand the community context that trauma survivors grow up in and return to after their exposure to being a child soldier. These findings suggest that differences in the religious/ethnic composition of the communities influenced the experiences of children in the community and particularly the experience of female former child soldiers (Kohrt et al., 2010b). From a mechanistic perspective, caste-based Hindu discrimination may contribute to greater levels of stress in daily living for girls which is a risk factor for depression, and depression may then increase the likelihood of PTSD. It is also possible that the discrimination leads to lower levels of social support, which we documented, and this increases the risk of PTSD, with the greater severity of PTSD increasing likelihood of depression. This points to the need to target aspects of

gender-based discrimination related to high-caste Hindu culture to interrupt the interaction of PTSD and depression in this context.

2.3. Interventions targeting sociocultural components of syndemics

Using a syndemic lens, it is possible to re-evaluate how interventions for former child soldiers may have worked in post-conflict Nepal. Given that the sociocultural context of the returning soldiers appeared to play a major role in determining the regional differences in burden and co-morbidity of mental health problems, we developed an intervention that focused on community-level support of former child soldiers (Kohrt et al., 2015), rather than an exclusively trauma-focused individual treatment. From a syndemic perspective, the sociocultural context of high rates of discrimination and social exclusion was contributing to the comorbid depression and PTSD (see Fig. 3). The intervention involved training cadres of community psychosocial workers (CPSWs) with a 28-day curriculum delivered in 4 different modules over a 4-month period (Kohrt et al., 2015). CPSWs were trained to work with teachers, community leaders, parents and relatives, religious leaders, health workers, and other community stakeholders engaged in children's and adolescents' lives. This program emphasized activities such as reducing discrimination by teachers in schools directed toward former girl soldiers. CPSWs worked with teachers to help reduce the teachers' biases and discrimination against girl soldiers. In addition, through UNICEF support programs, girl soldiers were given opportunities to pursue activities they were most interested in for their future, including returning to formal schools, informal education, skills training (e.g., seamstress), and livelihood programs (e.g., receiving livestock and training).

Rates of depression and PTSD among former child soldiers significantly reduced one year after the program and reached comparable levels to civilian children; in contrast, socioeconomic interventions (e.g., education, livelihood training, small grants) that targeted specific children (rather than the community) did not show relative differences in benefit (Kohrt et al., 2015, Adhikari et al., 2014). This suggests that the community level effects may have been more beneficial than individual supports received by a specific child. These findings highlight that when differences in sociocultural risk factors are found to be associated with differences in multi-morbidity, then intervening on the sociocultural risk factors may contribute to reduction in health problems. Ultimately, mitigating the effects of political violence on multi-morbidity likely requires addressing current social inequities that shape the form and severity of trauma's impact.

3. Case study 2: diabetes, anxiety, persistent wounds, and humoral dysfunction in the Somali Region of Ethiopia

The case study on diabetes in Somali communities in eastern Ethiopia builds on findings from the second author's long-term ethnographic research on medical care and humanitarian assistance in the Somali Region of Ethiopia during five extended research stints from 2007 to 2018 (Carruth, 2014; Carruth, 2016; Carruth, 2018). During this larger project, even during droughts and outbreaks of political violence, local clinicians remarked on several occasions that rates of type-2 diabetes mellitus among Somalis in Ethiopia seemed to be rising and were unexpectedly high given low rates of obesity, but there was (and still is) no systematic, population-based research to investigate this possibility.

In response to this, four researchers who have known each other for 10 years collected additional data related to diabetes and diet among Somali Ethiopians in Ethiopia: a university professor, two local Somali research assistants, and a local community health worker (in Ethiopia, called a "health extension worker"). Another university professor with experience in studying diabetes and public health assisted with research design and data analysis (Carruth, 2020). The field team in Ethiopia recruited and collected basic survey and anthropometric data from 108 individuals including 85 Somali-Ethiopians who self-reported a type-2 diabetes diagnosis and 23 additional persons who are adult siblings of these persons with diabetes living in communities nearby. Anthropometric data included weight, height, and both hip and waist circumferences. We used these metrics to calculate participants' Body Mass Index (BMI) as well as their waist-to-hip ratio as a proxy of abdominal adiposity, as recommended by the World Health Organization and diabetes researchers working in sub-Saharan Africa (Mbanya et al., 2010; Vazquez et al., 2007; World Health Organization, 2008). We collected basic survey data including, as appropriate, age, residential location, typical diet, dietary changes, seasonal dietary shifts, food insecurity, therapeutic regimens, current and past symptoms, and more. Additionally, with all 108 participants we collected finger stick blood samples, which were placed on Dried Blood Spot (DBS) cards, refrigerated, and mailed to the University of Washington Department of Laboratory Medicine for analysis. The DBS samples were analyzed for levels of hemoglobin A1c (abbreviated as HbA1c), cholesterol (CHO), high-density lipoproteins (HDL), triglycerides (TRG), and C-Reactive Protein (CRP); see Table 1 for a summary of anthropometric and biological results.

At the time of the biological and anthropometric data collection, we also conducted 16 in-depth semi-structured qualitative interviews with a sub-set of patients with T2DM diagnoses and two semi-structured interviews with their siblings living in close proximity. We also carried out

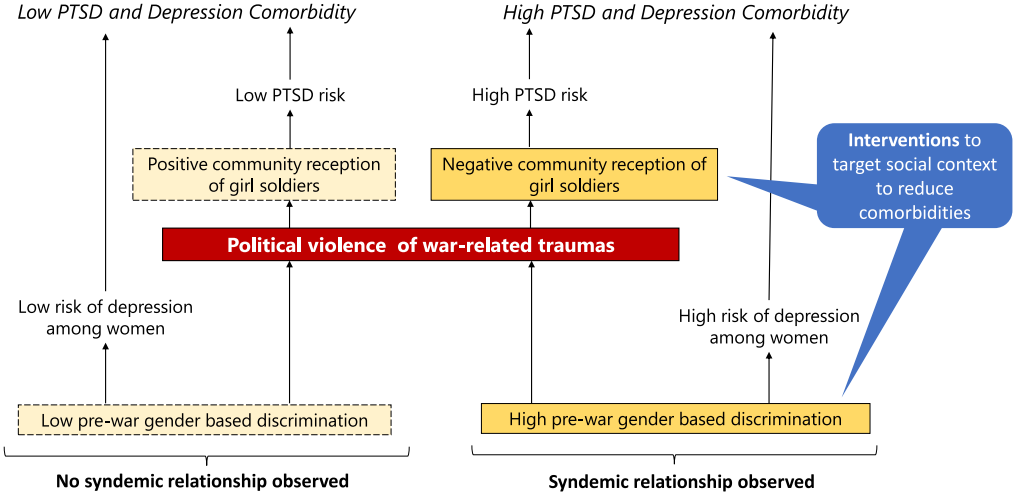

Fig. 3. Pathways in different types of communities leading to low vs. high rates of PTSD and depression comorbidity based on absence or presence of a symdemic relationship.

Table 1
Anthropometrics and Biomarkers associated with chronic anxiety and stress and higher risk additional chronic non-communicable diseases.

	Women (n = 68)	Men (n = 40)	No Diabetes Diagnosis (n = 23)	Diabetes Diagnosed (n = 85)	Total (n = 108)
Age	46.7 years	48.9 years	41.6 years	49.1 years	47.5 years
BMI	27.4	22.1	27.9	24.7	25.4
Waist-to-Hip Ratio	0.89	0.92	0.88	0.91	0.90
HbA1c (direct)	7.66	7.34	6.06	8.8	7.5
Cholesterol (direct)	165	156	113	123	161
HDL (Direct)	55.4	55.6	40.6	36.5	55.5
TRG (Direct)	254.6	257.1	220.7	226.0	255.5
CRP (Direct)	4.83	2.98	3.42	2.97	4.13

*all data are reported as averages per group unless otherwise specified.

in-depth interviews plus additional participant-observation over the course of eight weeks in rural and urban clinics, hospitals, and community spaces where patients with T2DM work and live, and we carried out several informal conversations and semi-structured qualitative interviews with two local community health workers, two physicians serving the Somali patient population, one hospital administrator, two persons who served as health policymakers within the regional government, and three policymakers within international nongovernmental agencies (totaling 28 qualitative interview participants). This study was approved by the IRBs at Anonymized University, Anonymized University, and Anonymized University in Ethiopia.

3.1. Repeated conflicts, displacements, and disasters in the Somali Region of Ethiopia

Ethiopia has achieved remarkably high and consistent economic growth rates over the last fifteen years and is a model "developmental state" (Clapham, 2018). Ethiopia is also frequently portrayed as a global health model (Østebø et al., 2018). Its governmental health extension worker program, for example, has deployed thousands of healthcare providers to rural parts of the country and helped to improve many Ethiopian's access to basic primary healthcare and vaccinations (Maes, 2016). This and other programs have contributed to a nearly halving of nationwide infant and child mortality rates, and rates of both acute and chronic forms of malnutrition among children continue to fall (Demographic and Health Survey Program, 2016; UNICEF, 2019).

However, disparities between the Somali Region and the rest of Ethiopia persist (Demographic and Health Survey Program, 2016; UNICEF, 2018, 2019). Infant and maternal mortality rates in the Somali Region are higher than almost anywhere else in the country; people's access to and use of regulated primary healthcare facilities is lower there than in other regions; and major investments in technology, industry, and agriculture are few and far between in the Somali Region compared to other parts of Ethiopia (Demographic and Health Survey Program, 2016; Human Rights Watch, 2018). Despite notable political reforms since the ascension of Prime Minister Abiy Ahmed to the office of Prime Minister in 2018 (Devermont and Temin, 2019), political insecurity, population displacement, human rights abuses, and outbreaks of violence in eastern Ethiopia continue (Human Rights Watch, 2018; International Organization for Migration, 2019; ReliefWeb, 2019).

Recurrent droughts in different parts of the Somali Region prior to this field work in 2003–2004, 2008–2009, 2010–2012, and again in 2015–2016, together with increases in the numbers of violent conflicts and population displacements from 2016 to 2018, increased local rates of food insecurity and malnutrition throughout the region (Integrated Regional Information Network, 2017). Cases of water-borne diarrheal diseases, including cholera and dysentery, repeatedly spiked in emergency-affected places and in camps of displaced people (UNICEF, 2018; UNICEF, 2019). Markets of fresh milk, sorghum, and livestock declined in these difficult years, and prices for staple goods increased. Many families were forced to sell their livestock or resettle elsewhere. Droughts also exacerbated fights over access to pastureland and water along regional boundaries (Integrated Regional Information Network, 2017; ReliefWeb, 2019; UNOCHA, 2018).

Data collection for the case study of diabetes among Somalis happened during a period of political violence and a complex humanitarian emergency characterized by internal population displacement, political violence, and increases in incidences of diarrheal diseases and malnutrition in July–August 2018. Specifically, in, in early August 2018, conflict erupted in and around Jigjiga when the Ethiopian Prime Minister Abiy Ahmed ordered the arrest of the Somali Regional President Abdi Iley. The President's loyalists protested and retaliated against government officials and suspected traitors in and around the regional capital. At least 100 people were killed and nearly 150,000 people fled the immediate area (Human Rights Watch, 2018; UNICEF, 2018; UNOCHA, 2018). Due to this violence and other conflicts, by December 2018, there were nearly 3 million internally displaced persons (or IDPs) throughout Ethiopia (UNICEF, 2018)–more than any other country in the world (International Organization for Migration, 2019).

When violence broke out in Jigjiga mid-way through this study, members of the field team fled for safety to the outskirts of the city of Dire Dawa and then traveled to stay in rural communities closer to the borders of Djibouti and Somaliland. We continued recruiting and enrolling participants throughout this period, even as people were frequently displaced or away from their homes. Consequently, the humanitarian crisis unfolding around us presented an opportunity to better understand the challenges patients and caregivers face in accessing medical care and treatments during periods of concurrent social upheaval in the context of chronic food insecurity.

3.2. Surprising symptoms and comorbidities

Anthropometric and biological data collected with the diabetes patients and a few of their siblings living nearby revealed a few important patterns. First, as we discuss in greater detail in other publications (Carruth et al., 2020), persons who had received a previous diabetes diagnosis were on average older, shorter, lighter in weight, compared to their siblings who had not been diagnosed with diabetes, and had a body mass index within the international standard "healthy range" of between 20 and 25. The diabetes patients also had smaller waist and hip circumferences compared to those who had not received a diabetes diagnosis, although they had a slightly larger waist-hip ratio. Overall, overweight and obesity were not significantly associated with diabetes outcomes, although a larger sample size would help elucidate additional potential associations.

Persons in our sample who had received a diabetes diagnosis previously had higher HbA1c levels (a measure of average blood glucose levels, across the previous two to three months), in the range that indicates their diabetes was poorly controlled, compared to those without a diabetes diagnosis who on average demonstrate no diabetes or low diabetes risk. Those with a previous diabetes diagnosis also had higher cholesterol and triglycerides, but lower HDL and C-Reactive Protein compared to those who had never been diagnosed with diabetes, indicating a higher average risk of chronic comorbidities like cardiovascular disease, compared to their non-diabetic siblings (see Table 1) (see also Carruth et al., 2020).

At the time of their diagnosis, the patients with a diagnosis with type-2 diabetes reported insatiable thirst and frequent urination. However in addition to these expected symptoms, patients also reported dramatic and progressive weight loss (*weydow),* loss of appetite, progressively worsening bodily weakness (*daal*), slowed wound healing and recurrent infections in their extremities, and loss of teeth and tooth decay, that in all but two cases, did not improve with standard, recommended

biomedical treatments of metformin and/or insulin. Three of the elderly patients >60 years old had previously lost toes, and continued to struggle to manage multiple chronic infections in their extremities. Compliance with therapeutic regimens did not result in control of average blood glucose levels and an amelioration of symptoms, comorbidities, and other related medical complications (Carruth and Mendenhall, 2019).

3.3. Humoral and digestive dysfunctions as comorbidities

In the medical literature, type 2 diabetes is described as partially hereditary and triggered by combinations of obesity, individual behaviors like poor diet and smoking tobacco, and increasingly, exposure to environmental toxins such as air pollution (Zimmet, 2017). Among Somalis in Ethiopia, by contrast, diabetes is typically defined as a humoral pathology, marked by disruptions or excesses of humoral flows (Carruth, 2020; Carruth and Mendenhall, 2019). Consequently, in discussions about their experience of type 2 diabetes, most people with diabetes mentioned comorbid humoral dysfunctions including indigestion, gastritis, heartburn, and most commonly, constipation (*calool istaag*). Additionally, the most common symptoms that motivated people to seek medical care were also described to us as humoral dysfunctions, including frequent urination and sudden weight loss. In other words, what was most concerning for these patients was the uncontrolled and continuous draining of their humoral flows (Carruth, 2020). The pathological losses of their urine and healthy fatness (*subaq*) were perceived as physical symptoms of deeper disease, depletion, and stress – including but not limited to diabetes and the anxiety chronic disease produces.

Humoral pathologies were also discussed not as individual problems related solely to behaviors or choices like sugar consumption, but as consequent of widespread food insecurity and the progressive sedentarization and displacement of pastoralist and semi-pastoralist livestock herders throughout the region. Diets low in fresh, locally-grown foods, but high in "oily" (*saliid leh*), "soft," (*jilicsan*) or "sweet" (*macaan*) foods, seen as the products of these broader social and economic changes, were perceived to disrupt humoral flows and increase vulnerability to diseases including diabetes (Carruth and Mendenhall, 2019). A change from living out of doors, walking long distances to care for livestock and trade, and living on "fresh foods," patients opined, caused community-wide increases in internal, humoral disruptions including type-2 diabetes.

In general, multiple simultaneous and interacting humoral pathologies including diabetes were managed by Somalis through compliance with recommended courses of medications, but in addition to this, through self-induced vomiting or gut evacuation (*bixin*), consuming camel milk, taking herbal remedies such as special teas or oils, feasting, fasting, or otherwise changing the diet (*buulee*), and halting consumption of *khat* leaves (a popular mild narcotic). The management of internal humoral dysfunctions including type-2 diabetes required regulating what was consumed and felt from the external environment.

3.4. Emergency as etiology

Self-reported feelings of anxiety and stress were also perceived by our respondents to trigger and manifest alongside diabetes (Carruth and Mendenhall, 2019). This echoes findings elsewhere: stress, trauma, clinical depression, and violence play a causal role in the diagnosis and experience of diabetes, as well as their own interpretations of diabetes etiologies in places around the world (Carruth and Mendenhall, 2018; Lee et al., 2014; Mendenhall, 2019; Smith-Morris, 2008; Solomon, 2016; Wiedman, 2012). Exposures to stressful life events and intense emotions were the most commonly reported proximate cause of diabetes among these crisis-affected Somalis. Many people described the onset of their symptoms as consequent of sudden and forced migrations, loss of livestock, local outbreaks of violence, anxiety about the actions of the police or military, anger (*cadho*) between persons within their household, and/or what people called "thinking too much" (*fikir badan*)–an idiom of distress documented elsewhere in East Africa and in Latin America (Kaiser et al., 2015).

Other persons we spoke with also suspected diet changes pursuant to recurrent complex humanitarian emergencies and dependence on limited food aid rations caused or contributed to their diabetes. Many explained that years ago, especially prior to crises in the mid-1980s, people would eat what they called in Somali traditional foods (*cunto dhaqmeed*) such as whole-grain sorghum with fresh or soured livestock milk, maize alone or made into a porridge, bone broths, and occasional goat, sheep, cattle, or camel meat. But today, most people's diets have dramatically changed. Most of the people we spoke with – in rural and urban locations – consumed pasta or rice on a daily basis. Our respondents also reported daily consumption of candy, sodas, and heavily sweetened, spiced tea. In rural communities outside the cities of Jigjiga and Dire Dawa, persons additionally reported chronic food insecurity and a lack of fresh vegetables and fruits for months at a time (including during the long winter dry season, or *jiilal*, and during drought years).

The diabetes patients who had experienced recent temporary displacements due to political insecurity or attacks on their livestock or property also reported lacking some or all of the kinds of fresh ingredients their doctors recommended. Additionally, most of the people with diabetes we spoke to belonged to households that were chronically food insecure and as such, qualified for occasional or regular distributions of food aid – most often bags of wheat grains, bags of corn-soy blended flour, lentils, split peas, and/or cans of vegetable oil. In times of crisis, when people sought refuge with family members or traveled frequently, it was difficult or impossible for them to manage a diet different from what their family members and hosts were already eating, or outside the limited rations offered by international aid organizations.

In sum, Somali diabetes patients in eastern Ethiopia, during this recent time of political upheaval and displacement, experienced a form of diabetes frequently concomitant with several other conditions including humoral dysfunctions, digestive problems, slow wound-healing, infections of the extremities, tooth decay, tooth loss, and anxiety and stress over their individual and collective circumstances. These diabetes patients also experienced chronic weight loss, loss of appetite, lethargy, weakness, high cholesterol, high triglycerides, and persistently high HbA1c even while taking prescribed medications and/or insulin. Furthermore, these patients described type-2 diabetes not as a chronic condition, but rather an acute and life-threatening disease.

In the four months preceding data collection, two individuals in their mid-30's and 40's in communities the field team knew well died of complications of diabetes. Then in the fourteen months following data collection, a total of four of the 85 diabetes patients we spoke to also passed away. Several of the patients and healthcare providers we spoke with for this research expressed to us their fear of untimely death and "wasting away" from diabetes. "It is like an epidemic among Somalis," one aid worker in the city of Jigjiga said to us. The lack of preventive care, dietary support, insulin supplies, and refrigeration diabetes patients require are absolutely matters of life and death – especially during humanitarian emergencies. What local Somali healthcare providers and policymakers suggested to us were humanitarian interventions that better met the needs of both adults with chronic diseases like diabetes as well as children and their parents, and programs to address people's both chronic conditions as well as acute infections associated with crisis and displacement.

Humanitarian crisis-affected persons in eastern Ethiopia needed and desired dietary support including vegetables, fruits, and high-fiber grains like whole-grain *teff* and sorghum (and not standard foods supplied in ration distributions, like biscuits, wheat, and oil) beyond the food commodities provided in rations. Higher quality and greater variety of foods offered in humanitarian responses would surely improve the health outcomes for all food aid recipients, but for diabetes patients, access to these foods was absolutely necessary to maintain their digestive health, humoral flows, and ability to resist or recover from

infections. Patients additionally needed better access to healthcare providers who could prescribe and monitor responses to medications and insulin, as well as access to local refrigeration to store insulin supplies. Patients needed dental care and wound-care specialists, and needed their local healthcare providers to also have training in the community-based management of common complications and chronic comorbidities in general. Humanitarian responses that narrowly target children and mothers, or offer only interventions for singular infectious diseases and undernutrition in children would fail to address many of the most pressing health needs in these communities.

4. Discussion

The most pressing health concerns that emerge during relief operations typically highlight not the general patterns of morbidity and mortality across different humanitarian emergencies, but rather, the longstanding healthcare needs of the particular communities facing a complex humanitarian emergency. The constellations of multi-morbidities that emerge are the products of particular local contexts and long histories of recurrent crises. Humanitarian crises can worsen individuals' existing health problems and at the same time exacerbate existing collective health inequities, as well as thwart efforts to provide comprehensive and community-based primary healthcare. The most pressing health concerns that emerge during humanitarian responses may often reflect the longstanding needs of communities facing complex humanitarian emergencies. Our prior research in two different contexts suggests that outbreaks of political violence, for example, can increase risks of both acute and chronic diseases, as well as communicable and non-communicable conditions, making many chronic, non-communicable diseases matters of immediate concern. At the same time, political violence can also prevent the efficient recognition and effective and continuous management of both mental illness and other chronic noncommunicable diseases more difficult.

However, reconceptualizing complex humanitarian crises as sites of discernible syndemics may help reorient and broaden humanitarian interventions to focus on the exacerbation and interplay of these long-standing and multifaceted healthcare challenges in crisis-affected communities, rather than remaining focused on reactionary interventions to address single health domains or narrow demographic groups. Recognition of these contingent and cascading constellations of risks and outcomes demands intervention designs focused on integrated chronic disease, infectious disease, and mental health care – in other words, expansive and sustainable primary health care – even in the face of overwhelmed or disintegrated health systems. Consequently, efforts to improve health outcomes must address both the multi-morbidity that clusters in humanitarian crisis-affected populations and the roots of political violence. This kind of syndemic approach can elucidate the specific effects and patterns of negative health outcomes and violence within populations and help improve humanitarian interventions.

In Nepal, we found that rates of mental health problems varied substantially among female former child soldiers despite comparable burdens of trauma exposure. In some parts of the country, female former child soldiers had high rates of PTSD and depression co-morbidity, but in other communities there were lower rates of PTSD and depression. A syndemic theory that connects co-morbidities and the sociocultural context interacting with political violence is helpful to interpret these differences. One contributor to the differences appeared to be the sociocultural context that former child soldiers returned to after the war, with some communities having greater levels of gender-based discrimination, that likely preceded the war and also influenced how women were treated after the war. Girls in communities dominated by high-caste Hindu groups reported more experiences of discrimination compared to girls in mixed caste/ethnic communities (Kohrt et al., 2010b). A community-based intervention designed to increase social supports and social inclusion appeared to mitigate some of the burden of PTSD and depression.

In the case of providing better health care to Somalis in Ethiopia during a complex humanitarian emergency characterized by population displacement and political upheaval, it may be necessary for responses to attend to cases of acute malnutrition and the spread of infectious diseases, but also, to consider how complex humanitarian emergencies precipitate and exacerbate suffering from type-2 diabetes, chronic disease prevention and care in general, mental health concerns such as anxiety, chronic digestive and humoral dysfunctions, persistent infections and wounds, and even loss of teeth and dental caries consequent of these other outcomes. Diabetes as it manifests in this emergency-affected population involved unexpected symptoms including dramatic and persistent weight loss, loss of appetite, lethargy, and weakness despite patients' compliance with recommended medications and/or insulin, which are more typical of later-stage diabetes rather than the ongoing chronic management seen in most high-income settings or stable, peacetime context in settings with functioning health systems. Patients lacked continuing health care, access to diets of fresh foods, and refrigeration for their insulin, and these challenges were made worse during the acute phase of the emergency. Our research therefore suggests that persons with pre-existing and/or undiagnosed chronic conditions may be at heightened risk of infectious diseases, malnutrition, or poor health outcomes. Persons may also struggle to access the medications, treatments, regular preventive healthcare, and technologies their health depends on.

4.1. Limitations

The main limitation of this study is that the case studies were not designed *a priori* to test syndemic models of causality. Intriguing patterns were identified in the findings in these complex humanitarian emergencies that raised the potential for considering them in light of syndemic relationships. To statistically demonstrate the exponentiation of health effects needed to identify the presence of a syndemic relationship, we would need samples powered for appropriate moderator effects on associations by context. Future studies should follow recommendations for analyses to empirically test for syndemics (Tsai and Venkataramani, 2016; Tsai, 2018). Therefore, the current findings should be taken as case studies to reflect upon how syndemics may present in complex humanitarian emergencies, but the findings are not definitive for specific syndemics given the retrospective analysis of studies designed with other analytic models in mind.

4.2. Agenda for applying syndemic theory in complex humanitarian emergencies

Given the nature of complex humanitarian emergencies and the effects of political violence on other health outcomes, our case studies support Willen et al.'s model for intervening in syndemics when human rights are threatened: "(1) mapping the effect of social, political, and structural determinants on health; (2) identifying opportunities for upstream intervention; and (3) working collaboratively to tackle the structures, institutions, and processes that cause and exacerbate health inequities," (Willen et al., 2017). Below, we apply these three tenets to syndemic health responses in complex humanitarian emergencies (see Fig. 4).

1. *In humanitarian emergencies, it is important to map not only the differential distribution of health problems, but also the regional and local differences in political, structural, and historical determinants of health, and the clustering of multi-morbidities.* Whereas most humanitarian emergency responses are moving to digital based approaches such as Global Positioning System (GPS) tagging of regions with infectious disease outbreaks and, malnutrition cases, etc., it would be helpful to also have tracking that merges this information with mental health and other non-communicable disease epidemiology. In addition, human rights documentation of political violence, exposure to sexual

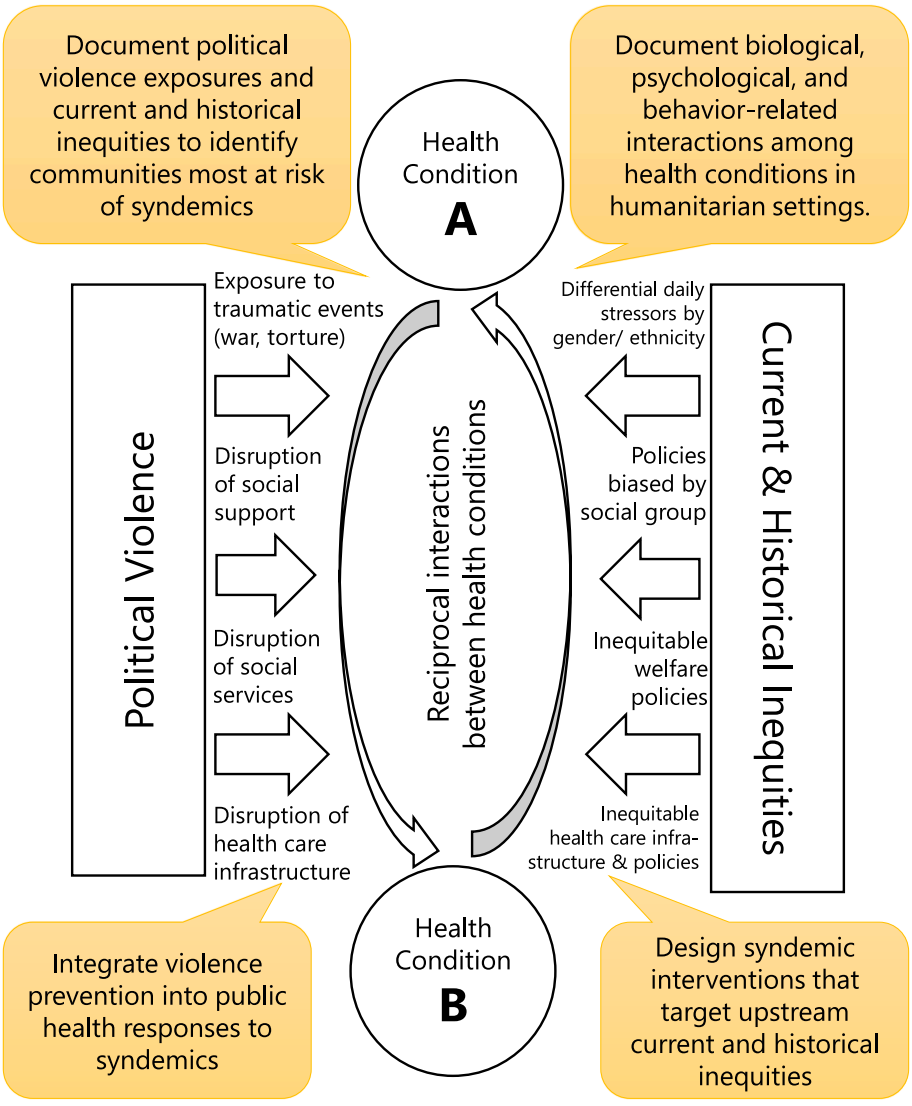

Fig. 4. Model for responding to syndemics in humanitarian settings.

and physical violence, and experiences of trauma and displacement could identify sites with particular vulnerability. Localized documentation of human rights violations is typically done in complex humanitarian emergencies, e.g., INSEC in Nepal during its civil war (INSEC, 2005) or Human Rights Watch reports in Ethiopia (Human Rights Watch, 2018), but mapping activities as part of these research initiatives are rarely overlaid on health data to reveal patterns of morbidity and mortality.

2. *Identify opportunities for upstream community-based and political interventions during and after humanitarian crises to mitigate the drivers of health differentials.* If public health practitioners exclusively focus on health outcomes, the drivers of health disparities will remain in place. Therefore, interventions should mitigate local and regional contributors to these differences. This can be local initiatives such as the Nepal example, in which discrimination was tackled at the school and community level. This can and should also include further upstream efforts such as trying to mitigate the encampment of or stressful migrations of displaced persons crises and the origins of other humanitarian emergencies, but it may also include local upstream targets like, in the Somali Region of Ethiopia, ensuring safe elections, peaceful transfers of power, the provision of medical care to displaced persons, and community-based primary healthcare in underserved and politically insecure locations. Interventions can also address violence related to law enforcement and security personnel in humanitarian emergencies to improve health (Boazak et al., 2020; Kohrt et al., 2015; Weine et al., 2020). Representativeness of local leadership should be documented. In regions where the community control of post-emergency resources is dominated by one ethnic or religious group, or where women are not equally represented in humanitarian response activities, and when humanitarian responses fail to meet the needs of people on the move, these sociopolitical factors will likely contribute to poorer health outcomes even if basic medical supplies and services are distributed. The mapping of the relative representativeness of local and regional coordinating bodies can be used to intervene at the level of planning and coordinating committees. A successful intervention may not change the total amount of health resources needed but may change how they are allocated. Pre-humanitarian emergency local indicators related to factors such as voting rights and female literacy may also be good indicators of settings where the greatest comorbidities may arise (c. f., Kohrt et al., 2010a). If women and ethnic minority groups are represented in health, education, and livelihood planning post-emergency, this may lead to more inclusive and salutogenic response strategies.
3. *Collaborative approaches are needed to transform structures, institutions, and processes to respond at the level of social, political, and economic*

determinants with upstream and political interventions. Only through these collaborations will it be possible to effectively address the first two recommendations above. In Nepal, the program would not have been successful without partnering with local groups advocating for rights of women, low-caste groups, and ethnic minorities. In Ethiopia, the de-escalation of the conflict in the Somali Region and the use of traditional methods of conflict resolution with Somali elders helped people return to their homes, re-establish connections with community-based health workers, and get control of their diets and medication regimens within a few months. Given that syndemic understandings cannot be developed without accounting for historical and current inequities and the nature of the political violence at hand, solutions cannot be achieved without working in partnership with the communities that constitute these institutions, structures, and social relations.

5. Conclusion

Humanitarian interventions risk being less effective when siloed by single medical conditions with a narrow focus on responding to acute infectious disease outbreaks and distributions of material goods like vaccines and food aid. There are increasing efforts through mechanism such as cluster systems to improve communication of health programs with sectors of protection, security, education, and economic livelihoods, as well as initiatives in political reforms and peace and reconciliation. However, from a health perspective there has been a dearth of theoretical frameworks to understand how these domains interact. Syndemic theory provides one way of conceptualizing these relationships and designing interventions to respond. When considering how to respond to chronic social injustice this also raises questions about the scope of neutrality. Maintaining neutrality in conflict settings and focusing narrowly on the efficient provision of basic life-saving goods and services has been an operational tactic for nongovernmental humanitarian organizations to maintain access to populations in need (IFRC, 2020; Slim, 2015). And yet, in practice, this principle also either ignores or stands in the way of relief operations' necessary engagement with the political roots of complex emergencies, and their necessary partnerships with local aid groups, governmental agencies, politicians, and advocates (Ali and Murphy, 2020; Benton and Atshan, 2016; Kihato and Landau, 2017). One way forward to reducing the fragmentation of relief work, human rights work, and political action might be to embrace use of theoretical models that can address both multi-morbidity and the social, economic, and political structures that shape risk factors and health. Applying syndemic theory to humanitarian emergencies, in situations like we describe here, can therefore foster re-thinking and expanding the objectives, mechanisms, and focus of emergency responses.

Credit statement

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References

Adhikari, RP, Kohrt, BA, Luitel, NP, Upadhaya, N, Gurung, D, Jordans, MJD, 2014. Protective and risk factors of psychosocial wellbeing related to the reintegration of former child soldiers in Nepal. Journal of Mental Health and Psychosocial Support in Conflict Affected Areas 12 (3), 367–378.

Albala-Bertrand, J.-M., 2000. Responses to complex humanitarian emergencies and natural disasters: an analytical comparison. Third World Q. 21, 215–227.

Alhalal, E., Ford-Gilboe, M., Wong, C., AlBuhairan, F., 2018. Factors mediating the impacts of child abuse and intimate partner violence on chronic pain: a cross-sectional study. BMC Wom. Health 18, 160.

Ali, Degan, Murphy, Marie-Rose Romain, 2020. Black Lives Matter is also a reckoning for foreign aid and international NGOs. Open Democracy (19 July). https://www.opendemocracy.net/en/transformation/black-lives-matter-also-reckoning-foreign-aid-and-international-ngos/.

Benton, A., Atshan, S.e., 2016. "Even War Has Rules": on Medical Neutrality and Legitimate Non-violence. Springer.

Boazak, M, Yoss, S, Kohrt, BA, Gwaikolo, W, Strode, P, Compton, MT, Cooper, J, 2020. Law enforcement and mental health clinician partnerships in global mental health: outcomes for the Crisis Intervention Team (CIT) model adaptation in Liberia, West Africa. Global Mental Health 7, e2.

Burkle, F.M., 2006. Complex humanitarian emergencies: a review of epidemiological and response models. J. Postgrad. Med. 52, 110.

Carruth, Lauren, 2014. Camel milk, amoxicillin, and a prayer: Medical pluralism and medical humanitarian aid in the Somali Region of Ethiopia. Social Science & Medicine 120, 405–412. https://doi.org/10.1016/j.socscimed.2019.03.026.

Carruth, Lauren, 2016. Peace in the Clinic: Rethinking "'Global Health Diplomacy"' in the Somali Region of Ethiopia. Culture, Medicine & Psychiatry 40, 181–197. https://doi.org/10.1007/s11013-015-9455-6.

Carruth, Lauren, 2018. Kinship, nomadism, and humanitarian aid among Somalis in Ethiopia. Disasters 42 (1), 141–168. https://doi.org/10.1111/disa.12236.

Carruth, Lauren, 2020. Rethinking fatness, rethinking diabetes. American Anthropologist 122 (3), 643–645. https://doi.org/10.1111/aman.13440.

Carruth, Lauren, Jama Ateye, Mohamed, Nassir, Ahmed, Mussa Hosh, Farah, Mendenhall, Emily, 2020. Diabetes in a humanitarian crisis: Atypical clinical presentations and challenges to clinical- and community-based management among Somalis in Ethiopia. Global Public Health 15 (6), 828–839. https://doi.org/10.1080/17441692.2020.1718735.

Carruth, Lauren, Mendenhall, Emily, 2018. Social aetiologies of type 2 diabetes. BMJ 361, k1795. https://doi.org/10.1136/bmj.k1795.

Carruth, Lauren, Mendenhall, Emily, 2019. "Wasting away": Diabetes, food insecurity, and medical insecurity in the Somali Region of Ethiopia. Social Science & Medicine 228, 155–163. https://doi.org/10.1016/j.socscimed.2019.03.026.

Charlson, F., van Ommeren, M., Flaxman, A., Cornett, J., Whiteford, H., Saxena, S., 2019. New WHO prevalence estimates of mental disorders in conflict settings: a systematic review and meta-analysis. Lancet 394, 240–248.

Chen, L.C., Briggs, S.M., Leaning, J., 1999. Humanitarian Crises: the Medical and Public Health Response. Harvard University Press.

Clapham, C., 2018. The Ethiopian developmental state. Third World Q. 39, 1151–1165.

Demographic and Health Survey Program, 2016. Ethiopia: Standard DHS 2016. https://dhsprogram.com/what-we-do/survey/survey-display-478.cfm.

Devermont, J., Temin, J., 2019. Africa's democratic moment: the five leaders who could transform the region. Foreign Aff. 98, 131.

Edkins, J., 1996. Legality with a vengeance: famines and humanitarian relief in'complex emergencies. Millennium 25, 547–575.

Farmer, P., 2003. Pathologies of Power : Health, Human Rights, and the New War on the Poor. University of California Press, Berkeley.

Galtung, J., 1969. Violence, peace, and peace research. J. Peace Res. 6, 167–191.

Galtung, J., 1990. Cultural violence. J. Peace Res. 27, 291–305.

Gravlee, C.C., 2020. Systemic racism, chronic health inequities, and COVID-19: a syndemic in the making? Am. J. Hum. Biol., e23482 n/a.

Hammer, C.C., Brainard, J., Hunter, P.R., 2018. Risk factors and risk factor cascades for communicable disease outbreaks in complex humanitarian emergencies: a qualitative systematic review. BMJ Global Health 3, e000647.

Herbert, H.K., Hyder, A.A., Butchart, A., Norton, R., 2011. Global health: injuries and violence. Infectious Disease Clinics 25, 653–668.

Human Rights Watch, 2018. We Are like the Dead": Torture and Other Human Rights Abuses in Jail, Ogaden, Somali Regional State, Ethiopia. https://www.hrw.org/report/2018/07/04/we-are-dead/torture-and-other-human-rights-abuses-jail-ogaden-somali-regional.

IFRC, 2020. The Fundamental Principles of the International Red Cross and Red Crescent Movement, Ref. 4046. International Committee of the Red Cross, Geneva.

INSEC, 2005. Nepal Human Rights Yearbook 2005. Informal Sector Service Centre (INSEC), Kathmandu, Nepal, p. 366.

Integrated Regional Information Network, 2017. Ethiopia Survives its Great Drought, but a Way of Life May Not. http://www.irinnews.org/feature/2016/06/13/ethiopia-survives-its-great-drought-way-life-may-not.

International Organization for Migration, 2019. Humanitarian Needs Overview. https://www.humanitarianresponse.info/sites/www.humanitarianresponse.info/files/2019/03/02_HNO_Summary_030619.pdf.

Jobanputra, K., Boulle, P., Roberts, B., Perel, P., 2016. Three steps to improve Management of Noncommunicable Diseases in humanitarian crises. PLoS Med. 13.

Kaiser, B.N., Haroz, E.E., Kohrt, B.A., Bolton, P.A., Bass, J.K., Hinton, D.E., 2015. "Thinking too much": a systematic review of a common idiom of distress. Soc. Sci. Med. 147, 170–183.
Kaur, G., 2017. Chronic pain in refugee torture survivors. J Glob Health 7, 010303.
Kihato, C.W., Landau, L.B., 2017. Stealth humanitarianism: negotiating politics, precarity and performance management in protecting the urban displaced. J. Refug. Stud. 30, 407–425.
Kliewer, W., Robins, J.L., Borre, A., 2019. Community violence exposure, sleep disruption, and insulin resistance in low-income urban adolescents. Int. J. Behav. Med. 26, 437–442.
Kohrt, BA, Blasingame, E, Compton, MT, Dakana, SF, Dossen, B, Lang, F, Strode, P, Cooper, J, 2015. Adapting the Crisis Intervention Team (CIT) Model of Police–Mental Health Collaboration in a Low-Income, Post-Conflict Country: Curriculum Development in Liberia, West Africa. American Journal of Public Health 105 (3), e73–e80.
Kohrt, BA, Burkey, M, Stuart, EA, Koirala, S, 2015. Alternative approaches for studying humanitarian interventions: propensity score methods to evaluate reintegration packages impact on depression, PTSD, and function impairment among child soldiers in Nepal. Global Mental Health 2. https://doi.org/10.1017/gmh.2015.1013.
Kohrt, BA, Hruschka, DJ, Worthman, CM, Kunz, RD, Baldwin, JL, Upadhaya, N, Acharya, NR, Koirala, S, Thapa, SB, Tol, WA, et al., 2012. Political violence and mental health in Nepal: prospective study. British Journal of Psychiatry 201 (4), 268–275.
Kohrt, BA, Jordans, MJD, Koirala, S, Worthman, CM, 2015. Designing mental health interventions informed by child development and human biology theory: A social ecology intervention for child soldiers in Nepal. Am J Human Biol 27 (1), 27–40.
Kohrt, B.A., Jordans, M.J., Tol, W.A., Luitel, N.P., Maharjan, S.M., Upadhaya, N., 2011. Validation of cross-cultural child mental health and psychosocial research instruments: adapting the Depression Self-Rating Scale and Child PTSD Symptom Scale in Nepal. BMC Psychiatry 11 (1), e127.
Kohrt, BA, Jordans, MJ, Tol, WA, Perera, E, Karki, R, Koirala, S, Upadhaya, N, 2010a. Social ecology of child soldiers: child, family, and community determinants of mental health, psychosocial well-being, and reintegration in Nepal. Transcultural Psychiatry 47 (5), 727–753.
Kohrt, B.A., Jordans, M.J.D., Tol, W.A., Speckman, R.A., Maharjan, S.M., Worthman, C. M., Komproe, I.H., 2008. Comparison of mental health between former child soldiers and children never conscripted by armed groups in Nepal. JAMA 300 (6), 691–702.
Kohrt, B.A., Mistry, A.S., Anand, N., Beecroft, B., Nuwayhid, I., 2019. Health research in humanitarian crises: an urgent global imperative. BMJ Global Health 4 (6), e001870. https://doi.org/10.1136/bmjgh-2019-001870.
Kohrt, BA, Speckman, RA, Kunz, RD, Baldwin, JL, Upadhaya, N, Acharya, NR, Sharma, VD, Nepal, MK, Worthman, CM, 2009. Culture in Psychiatric Epidemiology: Using Ethnography and Multiple Mediator Models to Assess the Relationship of Caste with Depression and Anxiety in Nepal. Annals of Human Biology 36 (3), 261–280.
Kohrt, BA, Tol, WA, Pettigrew, J, Karki, R, 2010b. Children and Revolution: The Mental Health and Psychosocial Wellbeing of Child Soldiers in Nepal's Maoist Army. In: Singer, M, Hodge, GD (Eds.), The War Machine and Global Health. Altamira Press: Rowan & Littlefield Publishers, Inc., Lanham, Maryland, pp. 89–116.
Kohrt, B.A., Worthman, C.M., Adhikari, R.P., Luitel, N.P., Arevalo, J.M.G., Ma, J., McCreath, H., Seeman, T.E., Crimmins, E.M., Cole, S.W., 2016. Psychological resilience and the gene regulatory impact of posttraumatic stress in Nepali child soldiers. Proceedings of the National Academy of Sciences 113 (29), 8156–8161.
Konstam, M.A., Konstam, A.D., 2019. Gun violence and cardiovascular health. Circulation 139, 2499–2501.
Krug, E.G., Mercy, J.A., Dahlberg, L.L., Zwi, A.B., 2002. The world report on violence and health. Lancet 360, 1083–1088.
Lee, C., Tsenkova, V., Carr, D., 2014. Childhood trauma and metabolic syndrome in men and women. Soc. Sci. Med. 105, 122–130.
Lindqvist, D., Wolkowitz, O.M., Mellon, S., Yehuda, R., Flory, J.D., Henn-Haase, C., et al., 2014. Proinflammatory milieu in combat-related PTSD is independent of depression and early life stress. Brain Behav. Immun. 42, 81–88.
Liu, X., Logan, J., Alhusen, J., 2020. Cardiovascular risk and outcomes in women who have experienced intimate partner violence: an integrative review. J. Cardiovasc. Nurs. 35 (4), 400–414.
Macrae, J., Zwi, A., 1994. Famine, Complex Emergencies and International Policy in Africa: an Overview. *War and Hunger: Rethinking international Responses to Complex Emergencies*, pp. 6–36.
Maes, K., 2016. The Lives of Community Health Workers: Local Labor and Global Health in Urban Ethiopia. Taylor & Francis.
Mbanya, J.C.N., Motala, A.A., Sobngwi, E., Assah, F.K., Enoru, S.T., 2010. Diabetes in sub-saharan africa. Lancet 375, 2254–2266.
Mendenhall, E., 2012. Syndemic Suffering: Social Distress, Depression, and Diabetes Among Mexican Immigrant Women. Left Coast Press.
Mendenhall, E., 2019. Rethinking Diabetes: Entanglements with Trauma, Poverty, and HIV. Cornell University Press.
Nesterko, Y., Jäckle, D., Friedrich, M., Holzapfel, L., Glaesmer, H., 2020. Prevalence of post-traumatic stress disorder, depression and somatisation in recently arrived refugees in Germany: an epidemiological study. Epidemiol. Psychiatr. Sci. 29, e40.
Østebø, M.T., Cogburn, M.D., Mandani, A.S., 2018. The silencing of political context in health research in Ethiopia: why it should be a concern. Health Pol. Plann. 33, 258–270.
Peconga, E.k., Høgh Thøgersen, M., 2019. Post-traumatic stress disorder, depression, and anxiety in adult Syrian refugees: what do we know? Scand. J. Publ. Health. https://doi.org/10.1177/1403494819882137.
Poteat, T., Millett, G.A., Nelson, L.E., Beyrer, C., 2020. Understanding COVID-19 risks and vulnerabilities among black communities in America: the lethal force of syndemics. Ann. Epidemiol. 47, 1–3.
ReliefWeb, 2019. Ethiopia: Drought - 2015-2019. Glide: DR-2015-000109-ETH. https://reliefweb.int/disaster/dr-2015-000109-eth.
Rivara, F., Adhia, A., Lyons, V., Massey, A., Mills, B., Morgan, E., et al., 2019. The effects of violence on health. Health Aff. 38, 1622–1629.
Salama, P., Spiegel, P., Talley, L., Waldman, R., 2004. Lessons learned from complex emergencies over past decade. Lancet 364, 1801–1813.
Singer, M., 1996. A dose of drugs, a touch of violence, a case of AIDS: conceptualizing the SAVA syndemic. Free Inq. 24, 99–110.
Slim, H., 2015. Humanitarian Ethics: A Guide to the Morality of Aid in War and Disaster. Oxford University Press.
Smith-Morris, C., 2008. Diabetes Among the Pima: Stories of Survival. University of Arizona Press.
Solomon, H., 2016. Metabolic Living: Food, Fat, and the Absorption of Illness in India. Duke University Press.
Sphere, 2018. The Sphere Handbook 2018. https://spherestandards.org/handbook-2018/.
Stander, V.A., Thomsen, C.J., Highfill-McRoy, R.M., 2014. Etiology of depression comorbidity in combat-related PTSD: a review of the literature. Clin. Psychol. Rev. 34, 87–98.
Toole, M.J., Waldman, R.J., 1997. The public health aspects of complex emergencies and refugee situations. Annu. Rev. Publ. Health 18, 283–312.
Trief, P.M., Ouimette, P., Wade, M., Shanahan, P., Weinstock, R.S., 2006. Post-traumatic stress disorder and diabetes: Co-morbidity and outcomes in a male veterans sample. J. Behav. Med. 29, 411–418.
Tsai, A.C., Venkataramani, A.S., 2016. Syndemics and health disparities: a methodological note. AIDS Behav. 20, 423–430.
Tsai, A.C., 2018. Syndemics: a theory in search of data or data in search of a theory? Soc. Sci. Med. 206, 117–122.
UNICEF, 2018. Ethiopia Humanitarian Situation Report #12 to December 2018. UNICEF Ethiopia. Addis Ababa, Ethiopia. https://www.unicef.org/appeals/files/UNICEF_Ethiopia_Humanitarian_Situation_Report_Dec_2018.pdf.
UNICEF, 2019. Ethiopia Humanitarian Situation Report. https://www.unicef.org/ethiopia/reports/humanitarian-situation-report-september-2019.
UNOCHA, 2018. Ethiopia: Oromia-Somali Conflict-Induced Displacement. Situation Report No. 4. Ethiopia. Addis Ababa, Ethiopia. https://reliefweb.int/sites/reliefweb.int/files/resources/ethiopia_-_oromia_somali_conflict_induced_displacement_june_2018c.pdf.
Vazquez, G., Duval, S., Jacobs Jr., D.R., Silventoinen, K., 2007. Comparison of body mass index, waist circumference, and waist/hip ratio in predicting incident diabetes: a meta-analysis. Epidemiol. Rev. 29, 115–128.
Weine, S, Kohrt, BA, Collins, PY, Cooper, J, Lewis-Fernandez, R, Okpaku, S, Wainberg, ML, 2020. Justice for George Floyd and a reckoning for global mental health. Global Mental Health 7, e22.
Wenzel, T., Kienzler, H., Wollmann, A., 2015. Facing violence - a global challenge. Psychiatr. Clin. 38, 529–542.
Wiedman, D., 2012. Native American embodiment of the chronicities of modernity: reservation food, diabetes, and the metabolic syndrome among the Kiowa, Comanche, and Apache. Med. Anthropol. Q. 26, 595–612.
Willen, S.S., Knipper, M., Abadía-Barrero, C.E., Davidovitch, N., 2017. Syndemic vulnerability and the right to health. Lancet 389, 964–977.
Willman, A., Team, V., 2009. Valuing the Impacts of Domestic Violence: A Review by Sector. *The Costs of Violence*. World Bank, Washington, DC, pp. 57–96.
World Health Organization, 2008. Waist Circumference and Waist-Hip Ratio Report of a WHO Expert Consultation. http://apps.who.int/iris/bitstream/handle/10665/44583/9789241501491_eng.pdf;jsessionid=361573DDBF84B40B572F2B5F0A0FA1FC?sequence=1.
Yodanis, C.L., Godenzi, A., Stanko, E.A., 2000. The benefits of studying costs: a review and agenda for studies on the economic costs of violence against women. Pol. Stud. 21, 263–276.
Zimmet, P.Z., 2017. Diabetes and its drivers: the largest epidemic in human history? Clinical diabetes and endocrinology 3, 1.

Speakers: Leslie Bull, M.A, Luiza Perez, and Nicholas Roberts, M.P.H.
Date: March 29, 2021
Time: 5:00pm to 6:00pm
Title: Panel Discussion: Challenges of Global Health Work

Zoom info: https://weillcornell.zoom.us/j/91691780417 **Meeting ID**: 916 9178 0417 **Passcode**: 149562

Summary: Notes from the field focusing on the challenges and joys doing global health work.