Malaria eradication: benefits, future scenarios & feasibility

A report of the Strategic Advisory Group on Malaria Eradication

World Health Organization

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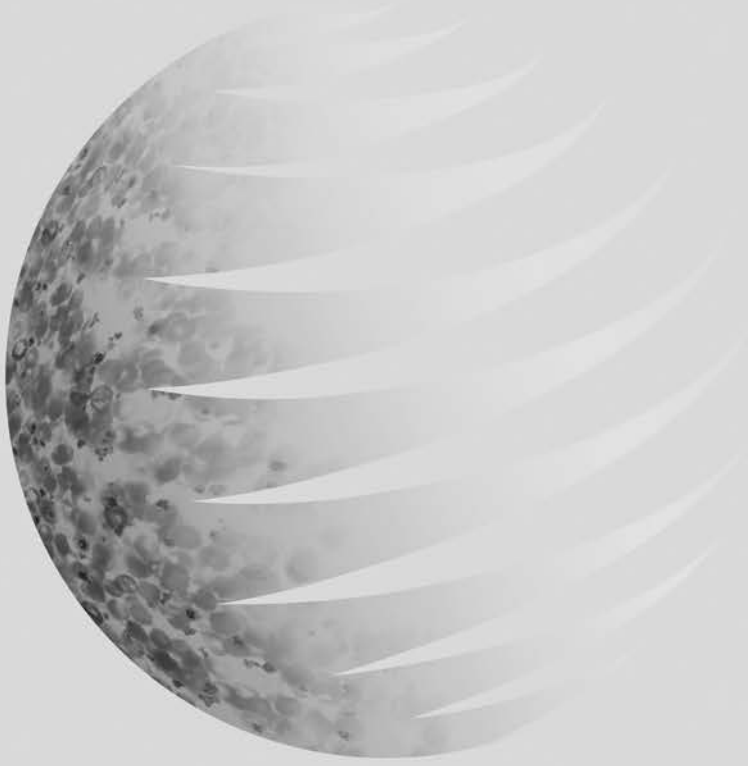

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The past leads us forward . . .

“Malaria control should not be a campaign, it should be a policy, a long-term program. It cannot be accomplished or maintained by spasmodic effort. It requires the adoption of a practicable program, the reasonable continuity of which will be sustained for a long term of years.”

Mark F. Boyd (1939)

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Foreword

From 2000 to 2015, many countries made tremendous headway in the fight against malaria. Globally, malaria deaths fell by more than 50%. The malaria-specific target of the 2000 Millennium Development Goals – which aimed to halt and reverse global incidence of the disease by 2015 – was attained. Seventeen countries eliminated malaria, and six were certified by WHO as malaria-free. This exceptional progress prompted renewed interest and discussion around one of the ultimate goals in global public health: malaria eradication.

In 2016, at the request of my predecessor, Dr Margaret Chan, WHO established a strategic advisory group tasked with analysing future scenarios for malaria, including the feasibility and expected cost of eradication. Organized into seven different workstreams, this group of eminent leaders and scientists considered a broad set of factors that underpin malaria: biological, technical, financial, socioeconomic, political and environmental. Based on reports and analyses commissioned by the group, they reviewed trends in poverty and population growth, mobility, agricultural development, climate change, urbanization and more.

Fast forward to 2020 and the malaria landscape has changed considerably. On a global scale, progress has levelled off; according to our latest *World malaria report*, no gains were achieved in reducing malaria case incidence over the last five years. Worryingly, malaria is on the rise in many countries with a high burden of the disease. Critical 2020 targets of WHO's *Global technical strategy for malaria 2016–2030* will be missed. The COVID-19 pandemic has complicated the picture for malaria even further.

Last August, WHO published an executive summary of our advisory group's key findings. This book includes a more detailed analysis of their insights and recommendations for reinvigorating the fight against malaria. Key among these is a call for greater investment in the research and innovation of new tools, without which we are unlikely to succeed. Priority is also given to providing affordable, people-centred health services, strengthening surveillance systems and developing strategies that are tailored to local conditions.

WHO continues to unequivocally support the goal of malaria eradication. To achieve this vision, we must deliver on our promises: to increase domestic and international investments in health; reduce malaria in the highest-burden countries; achieve universal health coverage; ensure no child dies from a preventable disease; and leave no one behind in pursuit of health and development goals because they were born poor. By delivering on these promises and investing in the development of transformative new tools, the world can achieve the health-related Sustainable Development Goals and eradicate malaria.

On behalf of WHO, I would like to thank the esteemed members of our advisory group for lending their time, talent and expertise to this important piece of work.

Dr Tedros Adhanom Ghebreyesus

Acknowledgements

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* These five members of the SAGme had to depart before the work of the Group concluded and have therefore not reviewed this manuscript.

Abbreviations

The following abbreviations have been used in this document.

ACT	artemisinin-based combination therapy
AIM	Action and investment to defeat malaria
BCE	before current era
BMGF	Bill & Melinda Gates Foundation
CDC	Centers for Disease Control and Prevention
DDT	dichlorodiphenyltrichlorethane
DFID	(UK) Department for International Development
EB	Executive Board
EPIC	Economic Projections of Illness and Cost
GDP	gross domestic product
GFATM	Global Fund to Fight AIDS, Tuberculosis and Malaria
GMEP	Global Malaria Eradication Programme
GMP	Global Malaria Programme
GPEI	Global Polio Eradication Initiative
GTS	Global technical strategy for malaria 2016–2030
HBHI	High burden to high impact
HRP	histidine-rich protein
IDWSSD	International Drinking Water Supply and Sanitation Decade
IRS	indoor residual spraying
ITN	insecticide-treated net
LULCC	Land use and land cover changes
malERA	Malaria Eradication Research Agenda
MDG	Millennium Development Goal
pc	per capita
***Pf*PR**	*Plasmodium falciparum* parasite rate
PHC	primary health care
PMI	(US) President's Malaria Initiative
RBM	RBM Partnership to End Malaria
RDT	rapid diagnostic test
R&D	research and development
SAGme	Strategic Advisory Group on Malaria Eradication
SDG	Sustainable Development Goal
UHC	Universal Health Coverage
UK	United Kingdom of Great Britain and Northern Ireland
UN	United Nations
USA	United States of America
WHO	World Health Organization
WPV1–3	wild polioviruses 1–3

Executive summary

The Executive Summary of this report was published in August 2019 *(2)*.

Summary and introduction

A world free of malaria is a major goal of global health, unequivocally embraced by the World Health Organization (WHO) soon after its founding in 1948. This aspiration has energized and inspired generations of health workers, malaria experts and global health leaders alike. The WHO's Global Malaria Eradication Programme (GMEP; 1955–1969) was an ambitious attempt to achieve a malaria-free world. While the GMEP led to the elimination of malaria in many countries, it failed to achieve global eradication. Furthermore, the plan was not fully implemented in sub-Saharan Africa where the greatest burden of malaria was found *(3)*. Falling short of eradication led to a sense of defeat, the neglect of malaria control efforts and abandonment of research into new tools and approaches. Malaria came back with a vengeance; millions of deaths followed. It took decades for the world to be ready to fight back against malaria.

Almost 50 years later, the world has once again begun to consider the feasibility of eradicating malaria. Significant declines in the global malaria mortality rate and case incidence between 2000 and 2015 and an increasing number of countries certified as malaria-free have generated renewed enthusiasm for tackling one of the main causes of death and disease in the world. In 2015, the Sixty-eighth World Health Assembly unanimously endorsed the *Global technical strategy for malaria 2016–2030* (GTS) – a bold plan to rid the world of 90% of the burden of death and disease due to malaria and to eliminate this infection from at least 35 more countries by 2030 *(4)*. These ambitious yet achievable targets are considered essential stepping stones on the path to achieving a world free of malaria, the vision that was reaffirmed in the plan.

KEY TERMS

Control: Reduction of disease incidence, prevalence, morbidity or mortality to a locally acceptable level as a result of deliberate efforts. Continued interventions are required to sustain control.

Elimination: Interruption of local transmission (reduction to zero incidence of indigenous cases) of a specified malaria parasite in a defined geographical area as a result of deliberate activities. Continued measures to prevent re-establishment of transmission are required.

Eradication: Permanent reduction to zero of the worldwide incidence of infection caused by human malaria parasites as a result of deliberate activities. Interventions are no longer required once eradication has been achieved.

Source: WHO *(1)*.

In 2016, at the request of the WHO Director-General, a group of scientists and public health experts from around the world were brought together to advise WHO on future scenarios for malaria, including whether eradication was feasible. Over three years, the members of the Strategic Advisory Group on Malaria Eradication (SAGme) analysed trends and reviewed future projections for the factors and determinants that underpin malaria.

Our analysis and discussions reaffirmed that eradication will result in millions of lives saved and a return on investment of billions of dollars. We did not identify biological or environmental barriers to malaria eradication. In addition, our review of models accounting for a variety of global trends in the human and biophysical environment over the next three decades suggests that the world of the future will have much less malaria to contend with. However, even with our most optimistic scenarios and projections, we face an unavoidable fact: using current tools, we will still have 11 million cases of malaria in Africa in 2050. Under these circumstances, it is impossible to set a target date for malaria eradication, to formulate a reliable operational plan for malaria eradication or to give it a price tag.

Our current priority should be to establish the foundation for a successful future eradication effort. At the same time, we need to guard against the risk of failure, as such failure might lead to the waste of huge sums of money, frustrate all those involved (national governments and malaria experts alike), and cause a lack of confidence in the global health community's ability to rid the world of this disease.

We need a renewed drive towards research and development (R&D) on vector control, chemotherapy and vaccines in order to develop the transformative tools and knowledge base necessary for achieving eradication in the highest burden areas. We need political leadership that makes effective and efficient use of increased domestic and international funding. We need bespoke national and subnational strategies guided by improved use of data and stronger delivery systems to provide the appropriate mix of services to all those in need, without financial hardship. We need strengthened cross-border, regional and international cooperation on malaria control and elimination efforts worldwide. When these critical foundations are laid, we believe that the world will be in a much stronger position to make the final and credible push for eradication.

As we complete our work in 2019, we recognize that the world stands at a crossroads in the fight against malaria. Despite huge progress in reducing malaria cases and deaths between 2000 and 2015, in the last five years, we have witnessed the stalling of global progress. The world is not on track to meet the 2020 milestones that will lead us to lower case incidence and mortality by 90% by 2030 (from 2015 levels) *(5)*. Without massive concerted and coordinated action, we are unlikely to meet these targets.

While we are certain that eradication by a specific date is not a promise we can make to the world just yet, there is a clear agenda – beginning with getting back on track to achieve the goals of the GTS – that should immediately be pursued to make eradication possible.

The case for eradication

Malaria is a disease of the most vulnerable: the very young and the poor. Every year, there are about 219 million cases of the disease and more than 400 000 deaths. Children under 5 years of age account for 67% of all malaria deaths, while over 93% of malaria deaths occur in sub-Saharan Africa *(5)*. Eradicating malaria would have the greatest beneficial impact on the world's most vulnerable populations.

As well as saving millions of lives and improving health and health equity, eradication offers a return on investment that would last indefinitely. Endemic countries would no longer suffer from their enormous malaria burden, and countries that had previously eliminated malaria would avoid the risk of re-establishing the disease. The economic case for eradication is strong, so long as the chances of an eradication effort succeeding are high.

The social benefits of eradication can be demonstrated in part by conventional economic statistics. Analysis of data on malaria and gross domestic product (GDP) from 180 countries between 2000 and 2017 shows that each 10% reduction in malaria incidence was associated with an average rise of 0.3% in GDP per capita and faster GDP growth *(6)*. High-burden, low-income countries had higher than average gains. In these countries, the same reduction in malaria incidence was associated with an increase in the level of GDP per capita of nearly 2%. There is no question that eradicating malaria would make the world healthier, more productive and more prosperous.

Malaria eradication would save millions of lives and generate significant economic benefits.

While we do not yet have a way to eliminate the last pockets of malaria transmission, we do have a plan to get 90% of the way there: the GTS. Additional analyses show that scaling up current malaria interventions between 2016 and 2030 to reach 90% of the population in the 29 countries that accounted for 95% of the global burden in 2016 would prevent an additional 2 billion malaria cases and 4 million deaths over that period compared to sustaining current intervention levels. This would be an astonishing humanitarian triumph. Within these 29 countries, the cost of scaling up is projected to be US$ 34 billion, but the economic gain, calculated only with respect to market data and not social benefits, is estimated at US$ 283 billion in total GDP during this period. As the social benefits of these scaled-up

interventions are likely to be even higher, this calculation indicates that malaria control should be strengthened, independent of the decision to eradicate.

Learning from history

We reviewed the history of the GMEP and took away several important lessons:

- Eradication strategies need to account for the hardest places from the outset to avoid failing before launching.
- Eradication cannot be promised too early in order to use it as a resource mobilization strategy or there is a risk of donor and political fatigue when goals are not reached on time.
- National malaria elimination strategies must be designed to fit the country context and retain flexibility to adjust to short- and long-term changes.
- Research and development are critical until eradication is achieved, and even beyond that, to limit any post-eradication risks.
- The outcome of a second malaria eradication attempt will have profound implications not only for malaria but also for other diseases under consideration for eradication.

Rarely do we get a second chance to make something right. Learning from the past malaria eradication effort will help to avoid the same mistakes and will give the world a better chance to achieve the ultimate goal of malaria eradication.

The history of the Global Malaria Eradication Programme (1955–1969) demonstrates that eradication efforts must include the hardest areas from the outset.

Global trends that will affect malaria eradication in Africa

Over the past three years, we have assessed the evolving malaria landscape, considering the biological, technical, financial, socioeconomic, political and environmental factors that affect the disease, particularly in Africa where we know we face the highest burden of malaria in the world. We have examined trends in poverty and population growth, mobility, agricultural use and urbanization that interact with the spread and intensity of malaria. We have considered, among other factors, the roles of climate change, land use change and human migration in determining who will have malaria and where in the future. We refer to these long-term sociodemographic and environmental changes as megatrends.

Our analyses show that megatrends will introduce unpredictability into the distribution of malaria; however, overall, these megatrends are likely to lead to reduced malaria transmission, which will benefit the drive to

eradication. Socioeconomic development is likely to accelerate elimination in many countries of Africa by improving housing conditions, nutrition, education, and access to preventive and curative health care. Climate change will affect malaria transmission by altering temperature, humidity and rainfall, potentially shifting the geography and seasonality of transmission. Changes in land use, particularly expansion of agriculture, will bring about further changes in malaria distribution in ways that are difficult to predict.

The combined effect of megatrends in Africa is likely to benefit the eradication effort.

Population growth and the movement of populations from rural to urban settings will also affect malaria transmission. The global population of 7.7 billion in 2019 is set to grow to 9.7 billion by 2050, by which time more than two thirds of the world's population is likely to live in cities *(7, 8)*. Most of the growth projected in the next 20 years will occur in sub-Saharan Africa and Asia. Urbanization has typically reduced malaria transmission due to increasing living standards, destruction of mosquito breeding sites and improved access to health care. However, with urban areas expected to grow at unprecedented rates in conjunction with equally important new population dynamics of short- and longer-term peri-urban migration, the historical association between urban migration and rising living standards may break down.

While there is significant variation in the potential impact of changing human and biophysical environments on malaria in time and space, the analytical framework we used suggests that the world will have much less malaria in 30 years than it does now. Even under the most optimistic scenario, however, with current tools and approaches fully implemented everywhere, our analyses do not show that malaria eradication can be achieved within the next several decades. The model that we reviewed showed 11 million malaria cases remaining in Africa in 2050, even after maximizing current interventions (insecticide-treated mosquito nets (ITNs), artemisinin-based combination therapies (ACTs) and indoor residual spraying (IRS)). The areas left behind in that future scenario are the parts of Africa where malaria is currently the most entrenched.

Potential threats to eradication

The world has only ever eradicated two diseases: smallpox and rinderpest (cattle plague). Polio and dracunculiasis (Guinea worm disease) are in the last stages of long eradication campaigns, but success is not yet guaranteed. Eradication efforts are complex undertakings, and unexpected roadblocks or deviations can threaten at each turn in the road. Malaria is no different. We evaluated several potential threats to malaria eradication, using lessons learned from the GMEP and other eradication efforts to

inform our analyses, but we recognize that new threats we have not considered might someday occur.

Potential biological threats to malaria eradication include the development of insecticide and antimalarial drug resistance, vector population dynamics and altered vector behaviour. For example, *Anopheles* vectors might adapt to breeding in polluted water, and mosquito vector species newly introduced to Africa, such as *An. stephensi*, could spread more widely into urban settings.

Potential threats are risks to monitor and manage, but they do not render eradication impossible.

Financial threats include lack of sufficient and continued commitment from countries and international donors, insufficient political commitment and failure to engage opinion leaders, political leaders, and the private sector. Drawing from the ongoing efforts to eradicate polio, we considered the impact of complex emergencies, including epidemics. Recent developments in the eradication of dracunculiasis also pointed to the need to evaluate the potential for non-human primate malaria to generate sustained transmission among humans.

We concluded that although complex emergencies are likely to cause disruptions of progress towards elimination and eradication, these effects, which tend to be time-limited, can be overcome and should not deter the world from attempting to eradicate malaria. The effects of these serious events can be mitigated by robust and resilient health systems with strong surveillance capacity and emergency preparedness plans. Malaria risk should be included in the broader global and local discussions regarding disaster risk reduction and response.

The existence of a non-human reservoir of infection has always been considered a major barrier to eradication of any disease. Transmission of simian malaria to humans has been described in several parts of the world, with the highest numbers of cases recently observed in Malaysia. So far, there has been no clear evidence of sustained human–mosquito–human transmission among any of the simian malaria species.

Continued surveillance and research are vital to gain a deeper understanding of the zoonotic reservoirs and vectors involved. Additionally, clear control strategies for simian malaria should be implemented to reduce the risk of parasites becoming more transmissible between humans and the mosquito vector. The existence of non-human malaria species is a concern, but not a reason to reconsider the malaria eradication agenda at this stage. Rather, this is a risk to be monitored and managed.

A pragmatic way forward

We clearly need to get the world back on track to achieve the important public health goals that are on the pathway to eradication, and then to cover the last mile to eradication at that time. Based on our analyses, we do not believe that this is the time to push for an eradication date. We must not set the world up for another failed malaria eradication effort that could derail attempts to achieve our vision for decades.

With a clear strategy and better estimate of the likely duration of effort to be maintained over the last mile, particularly in high-burden countries, it will be possible to estimate both the costs of global eradication and the vast economic and social benefits that can be attained. To avoid repeating mistakes of the previous malaria eradication campaign, estimated costs should be calculated only when a final plan has been determined and details of requirements are clear enough for a full cost calculation to be undertaken. To move ahead without this is to risk donor fatigue at funding an effort that has spiralling costs.

When a clear strategy to eradicate malaria can be articulated, a full calculation of the likely costs of eradication can be undertaken.

Getting back on the path to eradication

The promise of a malaria-free world has driven great progress, and we have come a long way since 2000. The rapid decline in malaria mortality from 2000 to 2015 can truly be described as a triumph of modern public health. While the number of malaria cases declined globally by 22% (from 271 million to 212 million), deaths due to malaria decreased by a remarkable 50% (from 864 000 to 429 000) *(9)*. Similarly encouraging is the increasing number of countries that have eliminated malaria. Since 2010, 10 countries have been certified as malaria-free, a notable achievement given that, between 1987 and 2007, no country was certified as having eliminated malaria. In 2016, WHO identified 21 countries with the potential to achieve zero indigenous cases of malaria by 2020 and formed the E-2020 initiative *(10)*. China, the most populous country in the world, and El Salvador, one of the smallest, both interrupted malaria transmission in 2017 and are on track to be certified as malaria-free by 2021. Including these two countries, at least 10 countries are on track to have zero cases in 2020, meeting the elimination goal of the GTS.

These achievements are tributes to the outstanding performance of the public health workforces of countries throughout the world, assisted by the contributions of national partners and international donors and organizations. While socioeconomic development and implementation of

other life-saving interventions such as immunizations must be credited with substantially reducing morbidity and mortality in general, millions of lives have been saved through the implementation of effective methods to prevent and treat malaria.

Getting back on track to meet global goals for reductions in malaria cases and deaths is a critical step on the path to eradication.

Despite the success in reducing malaria burden between 2000 and 2015, progress in malaria control overall has since stalled, with malaria incidence and mortality relatively unchanged since 2015 *(11)*. Of great concern to us all is that the world is significantly off track to be able to meet the target of a 90% decrease in malaria incidence and mortality by 2030, as articulated in the GTS. This is probably the most important and urgent threat to realizing our vision of a malaria-free world.

In response to the worsening malaria situation, WHO and the RBM Partnership to End Malaria have catalysed the country-led "High burden to high impact" (HBHI) approach, providing a renewed focus on making a durable impact in countries with the highest burden of malaria and getting back on track to achieve the 2030 targets of the GTS *(12)*. The country-owned and country-led approach will initially focus on getting the 11 highest burden countries back on track, 10 of which are in Africa.

By adopting the HBHI approach, countries will establish an enabling environment for increasing and maximizing the use of resources for malaria impact. Four mutually reinforcing response elements feed into tangible actions and concrete outcomes:

- political will translated into better use of resources and action
- information used more strategically
- technical guidance improved
- response efforts better coordinated.

The approach will be rolled out to all malarious countries in Africa as we progress towards a malaria-free continent.

What should a successful approach to malaria eradication look like?

A logical way to approach eradication is to focus on burden reduction and sequential elimination in malaria-endemic countries and regions. To

help countries reduce malaria burden, eliminate malaria from within their borders and then push towards the end goal of eradication, we call for focused effort in four areas.

1. Research and development for new tools

One of the highest priorities is a renewed R&D agenda that improves the knowledge base and products without which eradication will not be achieved. Over the last decade, a large, collaborative effort (the Malaria Eradication Research Agenda (malERA)) has produced consensus on the tools, strategies and enabling technologies that need to be developed. Effectively, malERA has become a blueprint for the R&D community. The current tools for vector control – principally ITNs and IRS – are old and imperfect and do not attack outdoor biting. Therefore, continued R&D is a high priority for identifying novel interventions to reduce mosquito biting in areas with the greatest underlying environmental suitability for transmission. R&D is also needed to develop improved vaccines and better insecticides, to identify markers of drug resistance, and to develop new genetic technologies that can alter mosquitoes' ability to transmit the parasite. Basic research should exploit advances in molecular biology and continue the discovery of the new tools, including drugs and insecticides, that will be required to push towards eradication.

We call for better tools and approaches; universal access to affordable, quality, people-centred health services; flexible, rapid and reliable surveillance and response systems; effective, tailored subnational, regional and national elimination strategies; and direct engagement of communities in local elimination efforts.

As demonstrated in campaigns against polio and smallpox, implementation science is required until the very end of the programme for adapting strategies to suit local conditions or assessing new tools.

2. Access to affordable, quality, people-centred health care and services

To eliminate malaria and prevent the re-establishment of transmission, a country will require strong political commitment and investment in Universal Health Coverage (UHC), with a well-functioning primary health care (PHC) system at its base. Health system quality is strongly correlated with malaria progress across the spectrum of malaria endemicity. A strong governance framework will need to bring together health systems infrastructure, service delivery, civil society and communities.

Global funding for malaria has remained relatively stagnant since 2010. Increases in domestic financing need to be complemented by increases in international financing.

3. Surveillance and response

A reliable, rapid and accurate surveillance and response system will be fundamental for dealing with changes in transmission likely to result from the global megatrends of urbanization, climate change and population growth. A multisectoral approach to development in urban settings and elsewhere should require the inclusion of malaria in all policies in order to ensure that risks for malaria transmission can be alleviated or prevented in relevant areas of housing, road building, land use planning, and general urban design.

4. Subnational, national and regional strategies

Interrupting transmission and preventing the re-establishment of malaria can only be achieved if there are national and subnational strategies tailored to local conditions. Strategies are needed to accurately define populations at risk, ensure that populations at risk are covered with effective interventions to prevent infections, and guarantee that all malaria patients get the care needed in a timely and comprehensive fashion. This will require the provision of safe and effective services to all those in need, without them incurring any financial hardship. Achieving this will require the extension of strategies beyond malaria by integrating them within the broader health system in order to ensure close-to-community networks of people-centred primary care services. Additionally, eradicating malaria will require inclusion of other sectors, including the private health care sector, agriculture, tourism, military and police, in a multisectoral approach to include malaria eradication aspects in all policies.

At the regional or subregional level, there is a need for strategies that approach malaria holistically, ensuring that malaria interventions do not stop at international borders but extend throughout areas at risk. Bilateral and multilateral cooperation will be essential to working across borders.

Other important enabling factors

In pushing towards a malaria-free world, the role of communities is essential. Developing field-tested approaches to improving community engagement will be vital. Eradicating malaria will require a combination of top-down, expert-led approaches with those that are bottom-up and community-driven. Public institutions will have to earn the trust of their populations by co-planning and adapting malaria interventions and elimination strategies, co-monitoring the quality of programme services and interventions, and co-evaluating achievements and lessons learned. Communities need to be given the opportunity to play a central role in the establishment and management of quality, people-centred and resilient health services.

Staying on target for eradication

Eradication must remain the global vision. This goal can only be achieved through the reduction of the global burden of malaria and progressive

elimination of malaria in countries and regions, as laid out in the GTS. It is therefore an absolute priority to bring progress towards the milestones of the GTS rapidly back on target in order to drive down the mortality and morbidity of malaria. New initiatives to support the GTS goals, such as the HBHI approach and further innovative research, must be pursued aggressively. Crucially, however, even if the ambitious targets of the GTS are achieved, there will still be much more to be done, with an estimated 32 million cases remaining in 55 endemic countries in 2030 (Noor A, WHO, unpublished data, 2019).

Reinforcing the Global technical strategy for malaria 2016–2030 *with a dynamic series of rolling five- and 10-year plans will establish the platform from which a successful eradication effort can be launched.*

Getting back on track to achieve the milestones and goals of the GTS is not an alternative to eradication, but an essential step towards eradication. The gaps (including tailored national and subnational strategies, increased national and international funding, capacity-building and surveillance systems) between the actions taking place at country level and the requirements for successful implementation of the GTS must be bridged as a matter of urgency. The communities at risk need to be the central focus of these efforts. We must harness the opportunities presented by global developments, such as the United Nations (UN) Sustainable Development Goals (SDGs) and the WHO push for PHC and UHC, both of which ensure people-centred, equitable care, in order to further advance towards a world without malaria *(14, 15)*.

We recommend reinforcing the GTS with a dynamic series of rolling five-year and 10-year plans leading out of the critical 2025 and 2030 targets, which we need to get back on track to achieve. These rolling plans should have clear targets and be subject to rigorous review in order to enable responsive modifications to strategy guided by an evolving risk-assessment and decision-making framework for eradication. With such a high-profile, renewed and sustained effort, we will establish the platform from which a successful and time-limited eradication effort can be launched.[1]

1 This report contains the view of the majority of the SAGme members. One member disagreed with the conclusion that a time-bound commitment to malaria eradication was premature.

Report of the WHO Strategic Advisory Group on Malaria Eradication

Introduction

The world has long hoped for the eradication of malaria, one of the most ancient and pernicious infections of humans that is responsible for more than 200 million cases and 400 000 deaths annually. Between 2000 and 2015, exceptional progress was made against the disease, raising aspirations for achieving eradication of malaria for the first time since the end of the Global Malaria Eradication Programme (GMEP) in 1969. In 2015, the World Health Assembly adopted the *Global technical strategy for malaria 2016–2030* (GTS) and endorsed the vision of a world free of malaria *(4)*. The GTS was developed to help countries reduce the human suffering caused by malaria by setting ambitious but feasible goals to reduce malaria morbidity and mortality by 90% and increase the number of malaria-free countries by 2030 (Fig. 1). World Health Organization (WHO) Member States agreed to strengthen health systems, combat drug and insecticide resistance, and intensify efforts to scale up malaria prevention and control to protect everyone at risk.

In 2016, WHO Director-General Dr Margaret Chan convened the Strategic Advisory Group on Malaria Eradication (SAGme) to consider future scenarios for malaria, including the feasibility of eradication *(16)*. The SAGme was originally composed of 13 members,[2] all scientists or public health experts, who met five times between 2016 and 2019 (see Annex 1). The objectives of the SAGme were to identify the key questions; design and oversee the working groups to address these questions; commission specific analyses; consider the findings; debate the conclusions; and develop recommendations for the WHO Director-General.

To support the SAGme, seven working groups were established (Box 1), each led by one or more SAGme members and supported by WHO staff. Working groups drew on five of the WHO Collaborating Centres for malaria to provide technical analyses, and commissioned working papers to address specific questions and evidence gaps, as needed. The working papers are listed in Annex 2 and form the basis for the sections of this report. Findings from each of the working groups were presented and discussed at each of the SAGme meetings *(17)*, which were attended by WHO Collaborating Centres and many other representatives of partner organizations. The working papers and discussions during the SAGme meetings, along with published reports and articles on topics that were already well covered in the scientific literature, informed SAGme's final conclusions and recommendations.

2 Four original members departed before the conclusion of the SAGme, and two more were added to the original list.

Fig. 1. Key elements and goals of the *Global technical strategy for malaria 2016–2030*

Source: WHO *(3)*

Box 1. Seven work packages designed by the WHO SAGme 2016–2019

WORKING GROUPS
1. Potential economic benefits of malaria elimination and eradication
2. Lessons learned from previous or current eradication efforts
3. Megatrends that will affect future scenarios for malaria
4. Characterizing the areas likely to be the last to eliminate
5. Health systems readiness for malaria elimination and eradication
6. Community engagement for malaria elimination and eradication
7. Mitigating potential threats to malaria eradication

At the initial meeting in 2016, recognizing the importance of the renewed discussion around malaria eradication, the SAGme advised WHO to clarify its position on the goal of malaria eradication. The SAGme participated in the drafting of a document that was presented to the WHO Executive Board (EB) in May 2017 *(18)*. The document explicitly stated that WHO considers the vision of a malaria-free world, as specified in the GTS, to be equivalent to malaria eradication, a goal that WHO unequivocally supports. The document submitted to the EB provided a history of malaria eradication efforts, described the current situation and clarified the importance of the GTS in the effort to achieve malaria eradication. Finally, the document introduced the SAGme's objectives and method of work and committed the Secretariat to reporting back to the EB once the SAGme had completed its work.

Between the initial meeting of the SAGme in 2016 and the third meeting in November 2017, signs of a troubling trend in malaria incidence and mortality were noted. The *World malaria report 2018* confirmed that the world was off track to achieve the GTS morbidity and mortality targets for 2020, although the goals related to elimination and prevention of re-establishment remained achievable *(11)*. WHO and RBM catalysed a country-led approach to jumpstart efforts to reduce malaria burden in the 10 countries in Africa with the highest number of malaria cases and in India, which together accounted for more than 70% of the global malaria burden *(12)*. Under these more sobering conditions, the SAGme continued its work, albeit with a sharpened focus on what was needed in the near term to achieve goals in the longer term.

Although progress in malaria control has levelled off since 2015, this SAGme report strongly reaffirms WHO's vision since 1955 of a world free of malaria. This report defines the public health, economic and social equity case for malaria eradication and describes future scenarios for malaria given current and future interventions and global environmental, demographic and social trends. It identifies the areas where malaria is likely to be eliminated last and characterizes the factors that drive transmission in those places. Threats to eradication are enumerated and analysed in order to identify mitigation approaches. Finally, recognizing the importance of the GTS targets as critical milestones on the pathway to eradication, this report outlines the approaches that will need to be adopted to achieve the GTS targets for 2030 and lay the foundation for an eventual time-limited malaria eradication campaign.

The case for malaria eradication

History and burden of malaria

Malaria is a life-threatening infection caused by parasites of the genus *Plasmodium* and transmitted between humans through the bite of an infective *Anopheles* spp. mosquito. In areas of moderate to high transmission, young children experience the highest incidence of infection, with partial immunity developing along with exposure and age. In 2018, there were an estimated 228 million cases and 405 000 deaths due to malaria, with 93% of the cases occurring in sub-Saharan Africa and 67% of the deaths occurring among children under 5 years of age *(5)*. In 2017, malaria was estimated to be responsible for 6.6% and 7.4% of deaths in children under 5 years and 5–14 years, respectively *(19)*. The consequences of malaria during pregnancy include maternal anaemia, preterm birth and low birthweight, all of which are risk factors for neonatal and infant mortality *(20)*. Malaria has always been a disease of poverty, associated with lower socioeconomic status, food insecurity, poor housing and lack of medical care *(21)*. Malaria is also a disease of the environment, associated with tropical areas where mosquito survival is high, breeding sites are plentiful, and temperatures are suitable both for mosquito and parasite development.

Malaria is one of the most ancient diseases of humans: as far back as 2700 BCE, the Chinese Nei Ching (the Canon of Medicine) described recurrent fevers with signs and symptoms similar to malaria, while malaria antigens have been detected in Egyptian mummies dating to 3200 BCE *(22, 23)*. Malaria has played an important role in human history, contributing to the fall of Rome and altering the course of

several wars. The human genome itself has been directly shaped by malaria through selection for certain traits that have given carriers a slight survival advantage; the prevalence and distribution of several haemoglobinopathies, including sickle cell anaemia, are almost entirely due to selection pressure from malaria *(24)*.

Given the burden and history of malaria, it is not surprising that malaria eradication has remained an important aim of global public health for almost a hundred years. WHO launched the GMEP in 1955 after the residual insecticide dichlorodiphenyltrichlorethane (DDT), first used during the Second World War, appeared to be the transformative tool that heralded the global eradication of malaria. The GMEP was initiated in part because of the important opportunity presented by DDT to reduce malaria transmission, but also, somewhat contradictorily, because of fear that resistance of the mosquito vectors to DDT would soon render the insecticide ineffective and eradication impossible. However, the GMEP's strategy and likelihood of success was questioned after it was discovered that DDT was not effective everywhere and malaria re-emerged in some areas after long malaria-free periods. Funding for the GMEP was eventually withdrawn, and the programme was effectively ended in 1969 *(3)*. While the GMEP helped to eliminate malaria from many regions of the world, it failed in its principal objective of global malaria eradication.

Decades of vastly reduced malaria control efforts and massive resurgences followed the end of the GMEP. WHO and other major agencies reduced their support for malaria operations in favour of general health programmes. Resistance to DDT and chloroquine, a first-line malaria treatment, spread because of weak malaria control programmes. These trends continued until the global health community finally recognized that new tools and strategies were required *(3)*.

Malaria control was reinvigorated in the early 1990s as a result of the Global Ministerial Conference on Malaria held in Amsterdam in 1992 and the adoption of the new WHO *Global strategy for malaria control* launched in 1993 *(25)*. New tools were developed and insecticide-treated mosquito nets (ITNs) became the backbone of malaria control efforts, spearheaded by WHO. In addition, the development of artemisinin-based combination therapies (ACTs) to treat malaria more effectively and new easy-to-use point-of-care diagnostics (rapid diagnostic tests (RDTs)) enabled an unprecedented expansion of malaria prevention, diagnosis and treatment.

Building on the foundations of the *Accelerated implementation of malaria control in Africa*, in May 1998, the WHO Director-General, in conjunction with the WHO Regional Office for Africa, the World Bank, and the governments of the United States of America (USA), United Kingdom of Great Britain and Northern Ireland (UK), and France, initiated a new effort to control malaria. This new initiative emphasized the value of partnership,

evidence-based action, political mobilization, and participation of civil society, and evolved into the Roll Back Malaria Partnership (later renamed the RBM Partnership to End Malaria) *(26, 27)*.

The African Summit on Roll Back Malaria, held in Abuja, Nigeria in April 2000, was a pivotal moment for malaria *(28)*. The Summit was attended by 44 of 50 malaria-endemic countries in Africa, with 19 delegations led by heads of state and the remaining delegations by senior government officials. The Summit was also attended by senior officials from WHO, the World Bank, the United Nations Children's Fund (UNICEF) and the United Nations Development Programme (UNDP), as well as other key partners. The delegates signed a declaration that committed them to halving the malaria mortality for Africa's population by 2010. This involved implementing the strategies and activities of the RBM initiative, including ensuring that at least 60% of the population at risk was covered by malaria prevention and treatment.

Several new institutions became involved in malaria prevention and control in the late 1990s and early 2000s, contributing importantly to the scale-up of malaria interventions. Significant energy in the malaria community led to accelerated research and development (R&D), new forms of collaboration and new funding mechanisms. Ministers of health, particularly those in the African region, ensured that the development of a global financing fund included malaria. The launch of the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM; https://theglobalfund.org/en/) in 2002 and the US President's Malaria Initiative (PMI; https://www.pmi.gov) in 2005 fundamentally changed the landscape for malaria prevention and control, contributing to a massive increase in the resources available to intensify malaria control efforts throughout most malaria-affected countries. Finally, the Bill & Melinda Gates Foundation (BMGF; https://www.gatesfoundation.org), formed in 2000, has invested substantial financial resources in research and control efforts and played a catalytic role in malaria control and elimination.

Within a broader global context, the UN Millennium Development Goals (MDGs) identified malaria as a serious public health and development challenge, and set time-bound targets to halt and reduce the incidence of malaria by 2015 *(29)*. The Sustainable Development Goals (SDGs), which represent a broad set of interdependent goals, call for progress to be made in malaria control and elimination in support of achieving Universal Health Coverage (UHC) *(14)*.

In the first decades of the 21st century, there has been unprecedented impact on malaria control through the combination of increased resources, improved interventions and broader efforts to improve global health. In 2000, the number of global malaria cases was estimated to be 271 million (range 202–304 million), with most cases occurring in Africa

(90%) and South-East Asia (7%) *(9)*. Between 2000 and 2015, however, malaria cases declined by 22% to 212 million, while deaths due to malaria decreased by 50% from 864 000 to 429 000 *(9)*.

At the Malaria Forum in Seattle in October 2007, Melinda Gates and her husband, Microsoft Chairman Bill Gates, inspired by the enthusiastic efforts underway to control malaria and reduce the substantial toll of malaria on resource-limited countries, called for the global eradication of malaria. Although agreement that a global eradication effort could succeed was not universal, the proposal of such an ambitious and inspiring goal by a well-respected, innovative and wealthy donor challenged international organizations, development agencies, nongovernmental institutions and national governments of malaria-endemic countries to accelerate their malaria agendas. At the Malaria Forum, WHO Director-General Dr Margaret Chan embraced the goal of eradicating malaria, stating, "We have to make it work in the interest of humanity. I, for one, pledge WHO's commitment to move forward with all of you" *(30)*.

In May 2015, the World Health Assembly endorsed the GTS, which reaffirmed the vision of a malaria-free world. The GTS was designed to operate within the SDG framework, taking advantage of cross-cutting opportunities, such as the focus on achieving UHC and addressing antimicrobial resistance and other health priorities outlined in the SDGs *(4)*. The GTS set ambitious but realistic goals: 90% reductions in both global morbidity and mortality from malaria by 2030 compared to the 2015 baseline, and elimination of malaria in 35 countries where it was transmitted in 2015 (Fig. 1). The GTS estimated that annual funding would need to increase to US$ 6.4 billion by 2020 from the US$ 2.7 billion spent in 2015 to meet the 2020 morbidity, mortality and elimination milestones.

To complement the GTS and position malaria within the wider development agenda, RBM developed *Action and investment to defeat malaria 2016–2030* (AIM) in coordination with WHO *(31)*. AIM illustrated the benefits of eliminating malaria in terms of creating healthier, more equitable and more prosperous societies, and built the investment case for malaria. Two other recent documents have been developed to advocate for malaria eradication: *From aspiration to action – What will it take to end malaria*, written jointly by Bill Gates and Ray Chambers, the UN Special Envoy for Financing the Health Millennium Development Goals and for Malaria *(32)*, and *Malaria eradication within a generation: ambitious, achievable, and necessary*, a report of the Lancet Commission on Malaria Eradication *(33)*. The former document seeks to spark a renewed discussion on the determinants and feasibility of eradicating malaria by 2040 through new strategies, tools and financing, while the latter considers the feasibility and affordability of malaria eradication by 2050.

Despite the significant improvements in malaria control between 2000 and 2015, progress stagnated between 2015 and 2018, with the number of cases and deaths plateauing *(5)*. Fifteen countries in sub-Saharan Africa plus India account for almost 80% of malaria cases, while seven countries (Burkina Faso, Democratic Republic of the Congo, India, Niger, Nigeria, Sierra Leone and the United Republic of Tanzania) are responsible for about 53% of all global malaria deaths. The amount invested in malaria control and elimination in 2018 was US$ 2.7 billion – far short of the US$ 6.8 billion estimated to be needed in 2018 to reach the 2020 GTS targets *(4, 5)*. Notwithstanding the large expenditures and tremendous efforts underway by a multitude of malaria-endemic countries, donors, multilateral agencies and nongovernmental organizations, significant gaps remain in the prevention, diagnosis and treatment of malaria *(5)*.

In response to the lack of progress towards the GTS morbidity and mortality targets, at the Seventy-first World Health Assembly in May 2018, WHO Director-General Dr Tedros Adhanom Ghebreyesus called for an aggressive new approach. “High burden to high impact” (HBHI) is a country-led response, catalysed by WHO and RBM, to reignite the pace of progress in the global fight against malaria *(12)*.

The HBHI approach is guided by a few key principles. It is:

- country-owned, country-led, and aligned with the GTS, the health-related SDGs, national health goals, strategies and priorities;
- focused on high-burden settings;
- able to demonstrate impact, with an intensified approach to reducing mortality while ensuring progress is on track to reach the GTS targets for reducing malaria cases;
- characterized by packages of malaria interventions, optimally delivered through appropriate channels, including a strong foundation of primary health care (PHC).

The HBHI approach has started with the 10 countries in Africa that have the highest burden of malaria, and with India. By November 2019, the HBHI approach had been initiated in Burkina Faso, Cameroon, Democratic Republic of the Congo, Ghana, India, Mozambique, Niger, Nigeria and Uganda. The remaining countries, Mali and the United Republic of Tanzania, are expected to hold their national consultation meetings by the end of the first quarter of 2020.

Economic impact of malaria

In addition to the health burden on individuals and populations, malaria has significant negative consequences for national economies. There is a close mutual relationship between poverty and health: ill health reduces the productivity and incomes of people and nations, and poverty harms health through poor nutrition, decreased educational opportunities, poor housing

and reduced access to health care. The associations between health and poverty create a mutual reinforcement cycle that is difficult to break.

Children, who are the most affected by malaria, are likely to learn less at school because they are often absent or unable to concentrate at school because they are unwell *(34, 35)*. Working-age populations in malaria-endemic areas may be less productive at work, either because they are ill from malaria or caring for sick children; this lower productivity in turn reduces current and future earnings and savings *(36-38)*. Furthermore, if individuals expect to live a shorter life, their savings and investment in human capital, such as developing skills, knowledge and experience, will likely be less *(39-41)*. Increased domestic spending, including government and household expenditures, in health care may also reduce investment opportunities in physical and human capital and decrease foreign investment attractiveness.

In 2001, Jeffrey Sachs and John Gallup compared the income of malaria-endemic countries with the income of non-endemic countries at different points in time during the period 1965–1995 *(42)*. They found that malaria-endemic countries had per capita income levels that were 70% lower than those of non-endemic countries, holding other factors constant. They also found that a 10% reduction in their malaria exposure index[3] was associated with a 0.26 percentage point increase in annual per capita income growth rates during the study period.[4]

This analysis revisits the evidence on the economic burden of malaria *(6)*. Using data from 180 countries and controlling for national historical, institutional, geographic and socioeconomic characteristics, as well as for unobserved factors that do not change over time in each country, a 10% reduction in malaria case incidence was associated with a nearly 0.3% increase in the level of per capita income over the period 2000–2017. Assuming that the associations between the level of income and its determinants, including malaria incidence and other factors, remain constant over time, a 100% reduction in malaria case incidence (equivalent to elimination of malaria within a country) would be associated with an average per capita income increase of nearly 3%.

Based on this analysis, the economies of low-income countries and those with the highest incidence of malaria will benefit more from malaria elimination than will higher income and lower incidence countries. In the group of countries with the lowest income in 2017, malaria elimination would be associated with an increase in national per capita income of nearly 16% (Fig. 2).

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3 Gallup and Sachs's malaria exposure index was defined as the product of the land area subject to malaria and the fraction of malaria cases attributable to *Plasmodium falciparum* malaria.

4 National per capita income levels measured as GDP per capita (GDPpc).

In countries in the highest malaria incidence group, elimination would be associated with an increase in per capita income of nearly 20% (Fig. 3). In general, the poorer countries also had the highest incidence of malaria.

Fig. 2. Distribution of gains from malaria elimination by 2017 World Bank income group

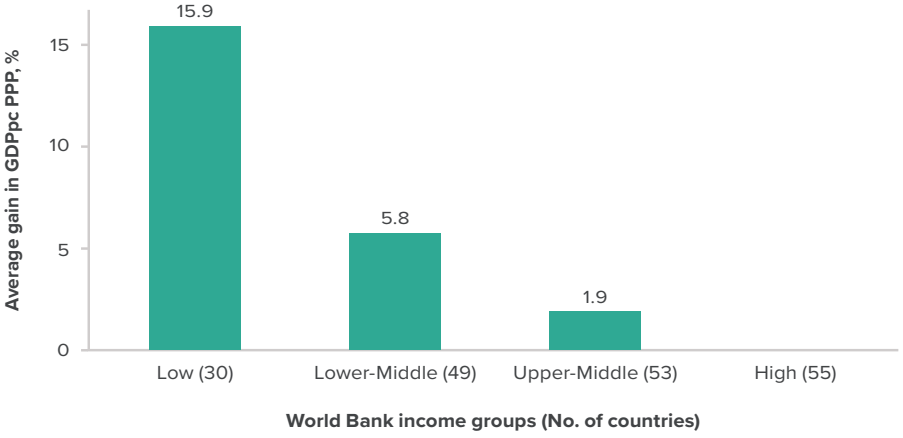
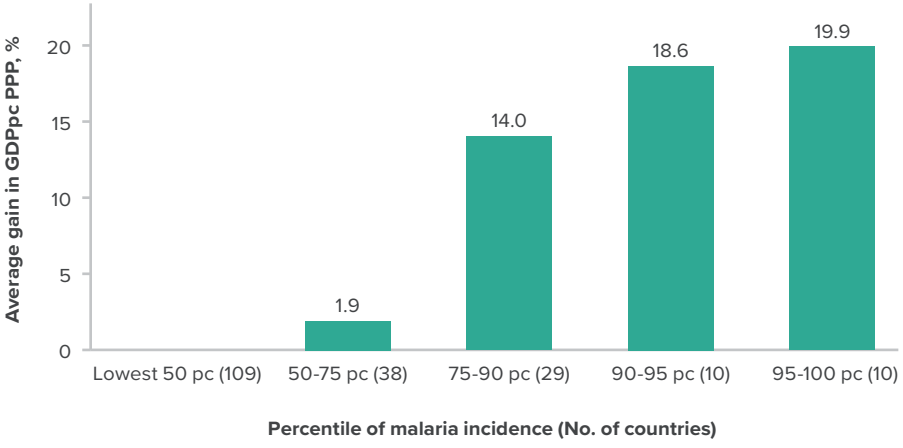


Fig. 3. Distribution of gains from malaria elimination by 2017 malaria incidence percentile



Results from this analysis show a weaker association between national income and malaria incidence than that suggested in the Gallup and Sachs study. This difference is likely in part due to the reduction in the marginal benefits of malaria control resulting from increases in interventions since 2000, as well as differences in the methods and data used.

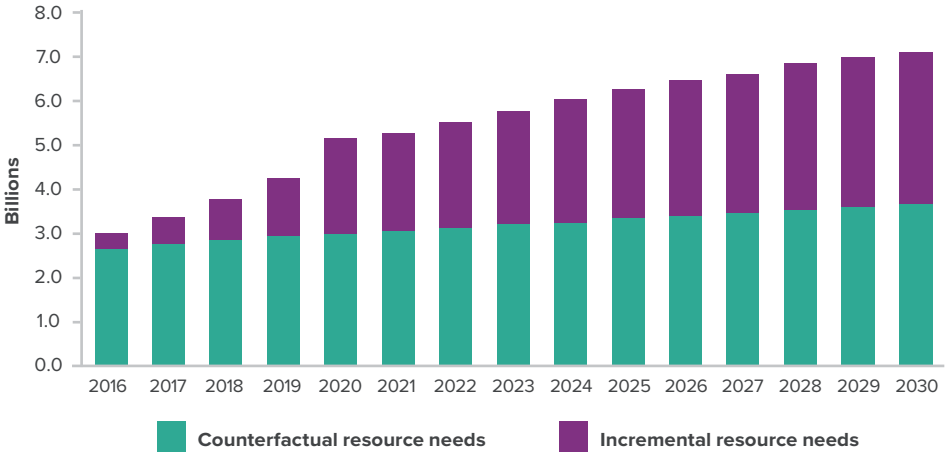
Another study commissioned by the SAGme looked at the potential impact of large reductions in malaria incidence on economic outcomes over the period 2016–2030. The study considered the channels through which increasing investments in malaria control and the associated reductions in incidence and mortality affect labour supply and physical capital accumulation, and what difference changes in these two production factors make in terms of national and per capita income. Investing in malaria control interventions contributes to reduced disease morbidity and associated mortality. A reduction in malaria morbidity can improve the productivity of the labour force by reducing the number of work days lost to illness or days lost to caring for a sick child or relative. Associated savings in health care spending from averting malaria cases is hypothesized to increase capital accumulation. Malaria control and elimination interventions could, however, negatively affect capital accumulation, as they require investments that could have been saved or put to alternative use. Finally, a decline in mortality from malaria would eventually increase the size of the labour force when children whose premature deaths were averted become adults.

The study modelled these different interactions using the WHO tool for Economic Projections of Illness and Cost (EPIC) *(43)*. The analysis focused on the 29 malaria-endemic countries that together accounted for 95% of global malaria cases and deaths in 2016. Of these 29 countries, 19 were categorized as low-income and 10 as lower middle-income countries. The aggregated income of these 29 countries was US$ 3 930 billion in 2016 (with individual countries ranging from US$ 1.9 billion – US$ 2 360 billion) *(9)*. The study modelled the impact on economic growth of investing in the progressive scale-up of intervention coverage to 90% compared to maintaining 2015 coverage levels. Total resource needs to either maintain or scale up intervention coverage over the study period in the 29 selected countries was estimated following the methodology described in Patouillard et al. *(44)*.

To maintain intervention coverage at 2015 levels, the total resource needs were estimated to increase from around US$ 2.7 billion per year in 2016 (<1% of aggregated GDP) to US$ 3.7 billion per year in 2030, for a total investment of US$ 47 billion over the period 2016–2030.

By contrast, scaling up interventions to 90% by 2030 increased resource needs from around US$ 3 billion per year in 2016 to US$ 7.1 billion per year in 2030, for a total investment of US$ 81.2 billion over that period (Fig. 4). The additional total investment needed between 2016 and 2030 to scale up interventions to 90% coverage from 2015 coverage levels would therefore be US$ 34.2 billion.

Fig. 4. Estimated resource needs to sustain intervention coverage at 2015 levels and incremental resource needs to scale up coverage to 90% by 2030



The impact of a 90% increase in intervention coverage on malaria incidence and mortality compared to the base scenario was estimated using a dynamic mathematical model of malaria transmission *(45)*. Scaling up interventions to 90% coverage by 2030 would avert 2 billion malaria cases and 4 million deaths in the 29 selected countries. The effect of this decline in malaria on aggregated national incomes would be a 0.17% gain (equivalent to US$ 283 billion) over the period 2016–2030. Similar results were found with respect to per capita income. Given the relatively short analytical timeframe (14 years), most (97%) of the gains in national income come from reductions in malaria case incidence, which in turn decrease the amount spent on malaria treatment and increase productivity due to fewer working days lost to illness. The relative contribution of reductions in malaria mortality to the size of the labour force would increase over the period 2016–2030 (from 1.2% to 4.7%), with children whose deaths were averted in 2016 entering the labour force around 2026; the effect of averted deaths in terms of increasing the labour force is expected to grow beyond 2030.

These analyses provide valuable information for evaluating the case for eradication. Ultimately, however, any decision to launch a time-limited eradication campaign should be based on a cost–benefit analysis that takes into account the probability that eradication will succeed; the additional costs of eliminating malaria in individual countries over and above the baseline of control for those countries; the increase in well-being for those individuals who, were it not for eradication, would have been either stricken with malaria or harmed by having to take actions to avoid becoming infected; and post-eradication risks. Such an analysis should also take into account related concerns, such as the social inequities derived from a disease that disproportionately affects the most vulnerable populations and the substantial burden malaria places on the health system. More generally, economic analysis of the decision to launch a time-limited eradication campaign should be comprehensive as to all effects on all members of the societies affected by the decision.

Learning from eradication campaigns

Disease eradication is an audacious undertaking that is more complex and more difficult than almost any other human endeavour, even landing a person on the moon. The complexity of eradication efforts arises from the need for cooperation of communities and countries around the world, across language and cultural barriers, to implement context-specific strategies in a wide variety of changing epidemiological, environmental and sociological environments. In part because of these challenges, smallpox is the only human disease to have successfully been eradicated. Eradication is achieved only when every country has eliminated disease transmission within its borders. Eradication, therefore, depends on all affected countries undertaking individual elimination efforts, although success is likely to be achieved more rapidly if neighbouring countries move together towards elimination. As a country's willingness to participate in a collective effort is likely to depend on the belief that all other countries will participate and that the ultimate goal will be achieved, eradication also requires significant global and regional coordination.

Currently, polio and dracunculiasis (Guinea worm disease) are slated for eradication, but both diseases have consistently missed target dates and still face significant challenges *(46, 47)*. Malaria differs importantly from smallpox, polio and dracunculiasis in terms of the biology of the infectious organism, life cycles, natural history, modes of transmission, ease of diagnosis, and number and types of interventions. To gain insights into malaria eradication, past campaign efforts to eradicate malaria, smallpox, dracunculiasis and polio

were reviewed to understand what has worked and what challenges have been encountered in terms of the technical, political, operational, financial, administrative and strategic aspects of these programmes. Key questions are summarized in Box 2.

Box 2. Key questions of eradication campaigns

1. Launch conditions: How many cases of disease were reported in the years leading up to the launch of the eradication campaign? What was the level of agreement among experts as to the likely success of the campaign? Was there a clear strategy to achieve eradication?
2. International coordination and financing: How was the global eradication programme coordinated and funded?
3. World Health Organization: What role did WHO play in the eradication programme?
4. Political support: How was high-level political buy-in encouraged and maintained?
5. Community engagement: How did programmes engage and mobilize communities to actively participate in elimination and eradication efforts?
6. Health systems: To what extent were eradication efforts integrated into the national health system? Has the eradication effort benefited the health system and vice versa?
7. Surveillance: What aspects of surveillance were critical to achieving reductions in disease incidence?
8. Research and innovation: Did the eradication programmes see research and development as central to the eradication effort? How important was innovation to the success of the effort?

Malaria

In 1955, the World Health Assembly decided to make malaria eradication a direct short-term goal rather than a long-term vision. There was significant disagreement within the global health community at the time (as there is now) regarding both the approach to malaria control and the feasibility of global malaria eradication. Those who supported eradication in 1955 presented several arguments to attempt to overcome objections to the programme. First, supporters looked to local elimination of malaria in one setting (Sardinia) as evidence that

eradication[5] would be possible in other settings and even globally. Second, proponents of eradication made the economic argument that it would save costs in the long run when control efforts were no longer required. Third, supporters described control programmes as unsustainable for financial and other reasons, because of the need to continually combat the development of resistance. In particular, the increase in resistance to DDT was cited as justification for initiating an eradication campaign before "development of resistance to insecticides in anopheline vector species materializes" *(48)*. Finally, the implications of the decision to start a global eradication campaign and the difficulties of achieving eradication, including raising the financial resources needed to see the programme through to completion, were downplayed at the decisive World Health Assembly in 1955 *(49-51)*.

The challenges of malaria eradication and possible unintended consequences of a global campaign carried high risk, and critics anticipated the various problems that the campaign eventually suffered. At the time of the launch of the GMEP in 1955, no clear implementation strategy had been developed and no pathway had been described. Africa, the continent with the greatest burden of disease, was initially not included in the programme. There was an overreliance on a single intervention, namely DDT, even though it was unclear as to whether spraying with DDT could achieve the goals of the campaign in all settings, particularly with the spectre of insecticide resistance looming. Once an eradication strategy had been developed, the potential obstacles were still downplayed, and the impression was maintained that eradication could be achieved within a circumscribed timeframe and budget *(52)*.

The GMEP involved a highly rigid and inflexible one-size-fits-all approach that was expected to succeed primarily by spraying DDT in a uniform manner. The strategy was flawed by not responding to local realities or diverse vectors; neglecting the most difficult areas, most notably sub-Saharan Africa; relying on a single technology; and underestimating the social and behavioural determinants of success. The strategy also failed to recognize the lack of trained staff, was not sufficiently evidence-based, and probably could never have succeeded in the most difficult areas, even outside of Africa. The campaign was generally ill-prepared for unexpected challenges, did not include sufficient ongoing research, and could not deal with repeatedly prolonged schedules or exploding costs. In addition, WHO did not support essential adaptation of guidance to local circumstances and there was no systematic approach to allow for

5 During the GMEP, the term **eradication** was also used to refer to the effort to reduce malaria transmission to zero within national boundaries, a concept that is currently defined as **elimination** *(1)*.

institutional learning and large-scale revisions at the global or local level. Despite these flaws and variable levels of implementation of the strategy, some countries did achieve success with this approach.

Regardless of countries' capacity and will, the earmarking of funds for malaria eradication made it appear financially attractive to embrace the goal *(53)*. Several countries were accused of merely re-labelling their control programmes or only half-heartedly pursuing eradication to gain access to malaria eradication funds. While this earmarking of funds added a persuasive dimension to the normative documents of WHO, it did not always secure the desired results.

Unfortunately, the perspectives, roles and contributions of affected countries and populations were continuously overlooked in the policies developed around the GMEP. As a consequence, decisions made at the global level did not necessarily overlap with local needs and priorities and were poorly communicated. Furthermore, voices at the subnational level found it particularly challenging to be heard at the global level, especially as global funding structures often incentivized governments to embrace policies that national programmes did not fully support. This not only made it more difficult to take the views of local populations into consideration, but it also posed a challenge for implementation *(54)*. Many of the negative consequences of the eradication campaign occurred not so much in the course of its lifetime, but during and after its conclusion and transition to different goals.

Despite elimination in some countries and improved control elsewhere, the desired global result was not achieved. Increasing resistance to DDT and chloroquine, lack of progress and a decline of voluntary funding, in particular at the global level, led to the eventual abandonment of the time-limited goal of eradication in 1969 *(53-55)*. Eradication was retained as a vision by WHO, but the strategy adopted by the World Health Assembly in 1969 was less ambitious in scope.

The new global strategy adopted by the World Health Assembly in 1969 was praised for its more flexible approach to malaria. But, flexibility brought its own implementation challenges. First, the new strategy was often not understood by national programmes, nor were the precise implications of the change in global strategy properly communicated. Second, the necessary changes in each country's actions could not be monitored or evaluated against a common frame of reference *(55, 56)*. There are good epidemiological, social, cultural and political reasons for allowing the local context to determine an elimination strategy, but effectively designing and implementing flexible strategies actually requires more resources and capacities, both at the national and at the global level, than do highly rigid approaches.

Not only were the resources available for malaria reduced and the new strategy misunderstood, but also it became evident that the anticipation of eradication and an end to malaria had led to a neglect of research on malaria and of education in malariology. As some would later observe, and as Lewis Hackett had jokingly foreseen in 1948,[6] the eradication campaign had eradicated the malariologist *(57-59)*. In light of these issues, it is not surprising that there were recurrent complaints that the strategy proposed in 1969 was not properly implemented *(60)*.[7]

There is no doubt that the GMEP had its successes and positive consequences. However, achieving success in malaria control and elimination might have been achieved without a global eradication campaign. After the initial euphoria from the launch and early successes of the GMEP faded, there was a long period of neglect and, in some countries, the malaria burden increased. The failure of the GMEP became a cloud hanging over the idea of eradication campaigns in general, but the successful smallpox eradication campaign that followed breathed new life into the concept of disease eradication *(61)*.

Smallpox

The Intensified Smallpox Eradication Programme was launched in 1966 and ended in 1977, with the world declared free of smallpox in 1980. In 1967, near the beginning of the Programme, there were approximately 100 000 smallpox cases worldwide *(62)*.

The WHO director of the smallpox eradication campaign, Donald A. Henderson, stated that, "For a global programme against a disease to be undertaken, universal political commitment is necessary"*(63)*. However, support for smallpox eradication was far from universal until after eradication had been achieved. For example, even within WHO, there were a variety of opinions on whether smallpox eradication could be achieved, many negative views having been influenced by the recent failure of the GMEP *(64)*. The programme continued largely because of the support of the USA and Soviet Union.

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6 In an address at a congress on tropical medicine and malaria, Hackett commented on the successes of Fred Soper and others against malaria in the following manner: "And Dr Soper may even now be preparing for his next big campaign, to eradicate malariologists" *(57)*.

7 For example, resolution WHA31.45 states explicitly that it is regrettable that "most of the recommendations in resolution WHA22.39 adopted by the Twenty-Second World Health Assembly when it re-examined the global strategy for malaria eradication, and in subsequent resolutions of the Executive Board and Health Assembly, have not been adequately implemented" *(60)*.

Coordination across countries and synchronization of eradication efforts was essential to avoid smallpox infections being reintroduced from country to country. WHO led the international coordination effort with strong backing from the USA and Soviet Union. Annual conferences and the World Health Assembly were used as vehicles to support coordination efforts. However, smallpox eradication was not a top-down, centrally managed programme, as the GMEP had been. Instead, smallpox eradication was the result of a collection of individual national programmes solving problems in their own way *(64)*. Community support was considered critical to allowing entrance of the vaccinators, and community leaders were recruited as advocates. What is more, the political will to increase domestic budgets was generally not needed, as the approach involved using existing resources and budgets more efficiently.

In addition to coordinating the efforts and sharing the lessons learned across countries, WHO provided field epidemiologists to advise programme managers in country and administrators to help manage logistics. WHO staff who were working with national and local ministries of health actively assisted programmes in adapting global guidance according to the specific situation in the country. At times, WHO staff deployed at country level played a transformative role, such as when William Foege and colleagues evaluated the surveillance-containment approach in Nigeria and began promoting the strategy at a global level *(65)*.

The smallpox eradication effort was neither completely independent of the national health system nor completely integrated. WHO advocated an approach that enabled the smallpox eradication programme to retain clear objectives, evaluation systems and management structures, while benefiting from the coverage and services available in the routine health system *(64)*. This approach allowed for improved surveillance capacity and vaccine programmes to be developed and retained by a strengthened, well-led health system; at the same time, it allowed for creative, problem-solving staff to tailor solutions to overcome obstacles and challenges in implementation. Community support for vaccination activities was also critical to success and community leaders played an important advocacy and liaison role.

Ongoing research played a major role in the successful eradication of smallpox. The programme began as a mass vaccination campaign but ended with an innovative ring vaccination approach designed to contain transmission by rapidly vaccinating all individuals who encountered a smallpox case *(64)*. This significant reorientation of the programme's central intervention was the result of an emphasis on problem-solving R&D throughout the eradication programme. Other R&D innovations, such as a heat-resistant vaccine, the jet injector and then its replacement, the bifurcated needle, were critical to the success of the programme.

The shift in strategy from mass to ring vaccination depended on a high-quality and sensitive surveillance system to identify the index cases. Surveillance was not a passive activity but the starting point for an urgent response built on existing systems. Networks of agents were deployed to visit all health units to ensure regular and complete reporting. Community members were enlisted to act as community surveillance agents, and reports from active case finding were integrated into routine reporting instead of being collected through a parallel system. The greatest boost to surveillance came from containment teams' rapid response to the report of an index case, which validated the importance of reporting cases.

The success of smallpox eradication was in doubt until the very last case. The WHO director of smallpox eradication considered that success would require luck as much as careful planning. However, the problem-solving, country-led approach adopted by those working towards smallpox eradication was critical to its success. In light of this success, such an approach is highly relevant for malaria eradication strategies.

Dracunculiasis (Guinea worm disease)

Dracunculiasis, a self-limiting disease transmitted exclusively by water through the oral route alone, was proposed for eradication as a potential indicator of the achievement of the goals of the International Drinking Water Supply and Sanitation Decade (IDWSSD, 1981–1990) *(66)*. In 1986, the World Health Assembly's adoption of resolution WHA39.21 acknowledged the special opportunity afforded by the IDWSSD for combating dracunculiasis *(67)*. In 1991, when there were approximately 400 000 reported cases globally, a further World Health Assembly resolution called for eradication by 1995, but this goal was not achieved. In fact, the date for global eradication has been postponed several times. In 2004, the ministers of health at the World Health Assembly resolved to eradicate dracunculiasis by 2009. When that date was not met, the global initiative determined to interrupt transmission as soon as possible, but without a defined target date *(68)*. The last mile of dracunculiasis eradication is proving to be more challenging than anticipated. There were more new human cases of dracunculiasis in 2019 (n=53) than 2018 (n=28) *(69)*. Furthermore, the identification of dogs in the transmission cycle in some countries poses an existential threat to dracunculiasis eradication *(70)*.

Global leadership for dracunculiasis eradication has largely come from outside WHO, initially from the US Centers for Disease Control and Prevention (CDC), which was designated as the WHO Collaborating Centre for Research, Training and Eradication of Dracunculiasis in 1984. The CDC was given the responsibility for monitoring progress towards eradication and for providing technical assistance to countries *(71)*. The CDC began

to collaborate closely with The Carter Center in 1986. The Carter Center provided direct technical assistance to countries eliminating dracunculiasis, placing international staff at subnational level to assist with institutional capacity building and to provide extra support for implementation and monitoring of interventions. WHO has played a surveillance role in areas free from disease and in countries at the pre-certification stage; WHO also oversees the process to certify countries free of dracunculiasis *(72)*.

From the beginning, funding was an issue for the dracunculiasis eradication effort. WHO lacked sufficient resources to perform its mandated surveillance and coordination functions, and other agencies similarly faced funding challenges. In 2008, The Carter Center and WHO jointly approached the BMGF and the UK's Department for International Development (DFID), which led to financial pledges from both *(72)*. Recently, The Carter Center has launched a US$ 40 million fundraising campaign, which will aim to raise an additional US$ 20 million to be matched with funding from The Carter Center Challenge Fund *(73)*.

Since 1987, an Interagency Coordinating Group for Dracunculiasis Eradication has held quarterly or semiannual meetings *(71)*. These meetings are seen as critical to ensuring coordination among partners and maintaining momentum towards eradication. National programmes also hold their own annual review meetings together with key stakeholder organizations.

Although the eradication of dracunculiasis was originally conceived as a sub-goal and indicator of the success of WHO's IDWSSD, political will for eradication was achieved in large part through the personal, high-level contacts of former US President Jimmy Carter, who agreed to lead the eradication campaign through his Center. President Carter encouraged the heads of state of Ghana, Mali, Nigeria and Uganda to explicitly support the elimination of dracunculiasis in their countries. He also helped to negotiate a four-month cease-fire during the Sudan civil war in 1995; this cease-fire breathed new life into the dracunculiasis elimination efforts in Sudan that had been stalled by civil strife *(74)*.

The first priority of dracunculiasis elimination programmes was to establish active surveillance across the country using networks of village health workers to conduct surveillance and health education *(75)*. Passive surveillance for dracunculiasis was inadequate at the onset of the eradication campaign, detecting less than 3% of all cases, and initially most programmes did not know the nationwide distribution of the disease *(75)*. Active surveillance efforts illuminated the extent of transmission and allowed rapid progress in interrupting transmission in many countries. When active surveillance systems for dracunculiasis could not be sustained, programmes suffered setbacks, including resurgences of transmission in areas previously thought to be free of disease *(72)*.

A common aspect of most national dracunculiasis elimination programmes is the integration of the programme within, or in close collaboration with, the health care system. While the national programme provides overall strategic guidance and monitoring and evaluation, interventions are implemented through the PHC system. This has not always resulted in optimal implementation and is sometimes seen as being in direct opposition to the goals of disease elimination, which require an additional sense of urgency *(67, 76)*.

The dracunculiasis eradication strategy has evolved over time through a problem-solving approach. The main intervention implemented at the beginning of the eradication effort was to provide clean water. However, when this proved too challenging in many contexts, the use of cloth water filters was evaluated and then introduced. Cloth filters were followed by nylon water filters, which were found to be more effective, and eventually filter straws *(74)*. In more recent years, the use of case containment during worm emergence and protection of water sources have proved effective *(77)*.

Although occasional *Dracunculus medinensis* (the causative agent of dracunculiasis) infections in dogs had been reported as early as the 1950s, reappearance of the disease in Chad in 2010 (10 years after the last case had been reported) was caused by infections in dogs. The canine infections were serving as a reservoir for human infections *(70, 78, 79)*. Investigators are now examining the possibility that intermediate hosts such as fish and frogs may also play a role in transmission. New control efforts are targeting infections in dogs in the hopes that eradication can still be achieved *(68)*. The dracunculiasis eradication programme demonstrates the potential to leverage political leaders with significant clout as champions for eradication, and the need to maintain vigilance to promptly identify and address any new potential threats to eradication that may arise.

Polio

The Global Polio Eradication Initiative (GPEI) was launched in 1988 with the aim of completely eradicating wild polioviruses by the year 2000 *(80)*. Thirty-two years later, this goal has not been achieved, although the reported number of wild-type polio cases has diminished dramatically – from 350 000 in 1988 to 33 in 2018; the number of endemic countries has also declined from 125 to two. Most of the advance against polio took place in the first 15 years of the programme, during which time there was an overall 99% decline in disease burden *(81)*. The GPEI was launched against the background of the successful eradication of smallpox, which led to the establishment of the WHO Expanded Programme on Immunization in 1974. Once it was understood that polio resulted from the transmission of three different types of viruses, each with unique characteristics, one serotype (wild poliovirus type 2, WPV2) was declared

eradicated in 1999 and a second one (WPV3) in 2019 *(82)*. However, achieving eradication of the third wild poliovirus (WPV1) has proven to be much more difficult than expected.

As with malaria, smallpox and dracunculiasis, initial support for polio eradication was not universal. Many experts argued that other diseases caused greater mortality and would be easier to eradicate. In fact, one of the earliest and most influential critics of the GPEI was Donald A. Henderson, former director of the smallpox eradication programme at WHO, who questioned the very feasibility of eradicating polioviruses *(83)*. Some scholars have since argued that the decision to eradicate polio had "more to do with the ideology of a small number of powerful and well-placed players in global public health who were dedicated to the concept of so called eradication as perhaps the major tool for international public health" *(84)*. These eradicationists thought that polio could be easily eradicated and thus would keep the concept of eradication alive *(84)*. In the end, polio was prioritized for eradication more because of feasibility compared to other infectious diseases, including measles and yaws, than because of disease burden. Demonstration of polio elimination in seven countries, epidemiological modelling showing the potential impact of activities, early engagement, and funds made available by Rotary International for polio eradication were influential in generating support for this goal *(85, 86)*.

Compared with the smallpox eradication programme, coordination of polio eradication efforts has been more challenging in the international context of greater political independence in the post-Cold War period. The World Health Assembly resolution that established the GPEI determined a WHO-led, headquarters model, with a WHO coordinator reporting directly to the WHO Director-General. Key partners were originally WHO, UNICEF, the US CDC and Rotary International. Later, BMGF and Gavi, the Vaccine Alliance, were added to the group. By 2019, the GPEI had a complex structure that included several governments, agencies and funders. The initiative has given rise to a number of evolving committees, including an independent monitoring board established in 2012.

Every review of the lessons learned from the history of polio eradication points to the critical importance of building and maintaining a capacity for basic and translational research, innovation and epidemiological studies. This capacity has provided solid evidence to establish and redirect strategies as required. Some reviews have noted, however, that truly game-changing innovations have become available only very late in the programme, similar to what was seen in the later stages of smallpox eradication *(83, 87)*.

In the early days of the GPEI, applied research projects driven by programme setbacks and operational gaps enabled improvements in logistics and supply (including cold-chain technology such as vaccine vial

monitors), diagnostics, tools for monitoring and evaluation, laboratory methodology, and surveillance techniques for acute flaccid paralysis *(88)*. Research has been critical, for instance, in assessing the effectiveness of vaccines in the context of persistence of wild polioviruses despite the best possible vaccination campaigns. Such research has demonstrated the role of compromised immune responses in vaccinated children due to infection with other enteroviruses or chronic diarrhoea *(83, 87)*. The development of rapid sequencing methods has enabled researchers to determine the origin of the infective virus and thus identify outbreaks associated with vaccine-derived poliovirus.

One of the key lessons dating from the onset of the GPEI is the critical role of high-quality, real-time active surveillance (and response) to quantify the burden of disease, monitor progress, actively search for the last infected cases and any reintroductions, and support documentation of interruption of transmission. The GPEI directly supports a surveillance infrastructure that includes large networks of surveillance officers, systems for specimen collection and transport to participating laboratories, standardized and quality-controlled laboratory testing, and data management and analysis systems to enable rapid, data-driven outbreak response. In some countries, the GPEI surveillance is so much better than the routine national surveillance system that it has been used to detect and contain classic infectious diseases that present as epidemics: yellow fever, cholera, meningitis, Ebola, dengue, Zika and chikungunya *(87, 89)*.

The GPEI faces several critical challenges even as eradication appears tantalizingly close. These include the increasing importance of vaccine-derived polioviruses, which caused 329 cases in 17 countries in 2019 *(90)*, and the continued conflicts in Afghanistan and Pakistan, which have prevented vaccination from reaching critical levels and have even targeted vaccinators for assassination. Other critical lessons from the GPEI include the importance of community engagement, development of trust and the consideration of different social factors in successful eradication efforts; the need for specific strategies for particularly challenging populations such as nomadic groups and populations that repeatedly cross international borders; the importance of managing change; and the challenges of sustaining funding and overall commitment when an eradication effort lasts much longer than originally planned.

Despite controversies, the GPEI has continued, with many other resolutions following the launch in order to reflect both the adaptation to new scenarios and the failure to achieve eradication by 2000. In 2012, the World Health Assembly declared the completion of polio eradication "a programmatic emergency for global health", and one year later it endorsed the *Polio eradication and endgame strategic plan* 2013–2018. The *Polio endgame strategy 2019–2023* was launched in 2019 *(86)*. Achieving polio

eradication is likely to increase enthusiasm for other eradication efforts, including malaria, but it is also likely that while the world continues to miss GPEI's target date, it will be challenging to launch other time-limited disease eradication campaigns.

Global trends and impact on future scenarios for malaria eradication

Although previous and current disease eradication efforts provide many lessons for malaria, the world is changing so rapidly that conditions in the future may little resemble the world in which these programmes operated. Therefore, to better describe future scenarios for malaria, the SAGme considered several fundamental changes to the physical and social environments in coming decades that may affect people's risk of malaria. The objective was to combine forecasting of key megatrends – a term first coined in 1982 by John Naisbitt to describe trends that restructure and redirect people's lives – with their anticipated effects on malaria *(91)* in order to identify populations whose malaria risk may either increase or decrease because of these megatrends. This information could then influence the assessment of the feasibility of eradication over defined timeframes.

This set of analyses, commissioned by the SAGme, focus on those trends whose trajectories are somewhat clear and where it is possible to quantify their likely influence on malaria risk: population growth, urbanization, climate change, land use and land cover changes (LULCC), and migration. Other potentially important megatrends are not considered in detail (e.g., women's empowerment, growing access to information technology, education, changes in political systems and governance structures, indirect effects of climate change) because of the difficulty in forecasting either the extent of the trends themselves or their potential influence on malaria risk.

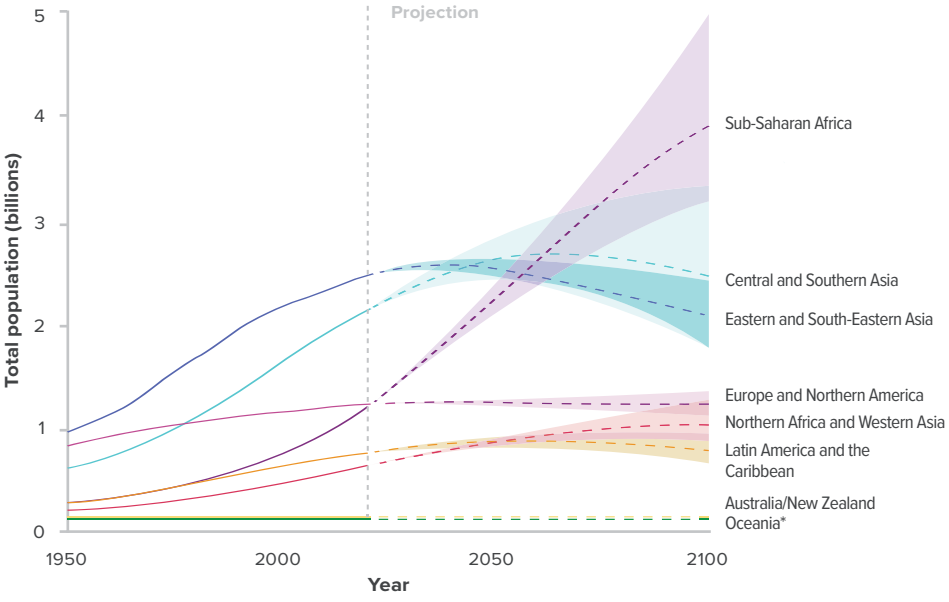
To better understand the likely future scenarios for malaria and the feasibility of eradication over specific timeframes, the current understanding of how malaria risk is mediated by the natural and human environments was first reviewed. This knowledge was then linked to projected changes in those environments (i.e., megatrends) over the coming decades, using plausible trajectories for the megatrends to forecast the extent and intensity of malaria in 2030 and 2050.

The megatrends and their association with malaria risk are described below, followed by a summary of the forecasting and modelling results.

Demographic trends

Global demographic shifts (population growth, declining fertility rates, increased life expectancy) and today's demographic trends vary across the world, as described in detail elsewhere *(7)*. The global population of 7.7 billion in 2019 is set to grow to 9.7 billion by 2050 and 10.9 billion in 2100, with 60% (1.2 billion people) of the population increase by 2050 projected to occur in sub-Saharan Africa (Fig. 5) *(7)*. The rise in the global population will be mostly attributable to population momentum, that is, the large number of children and young adults today who will reach adulthood in future decades will further enlarge the population, even if they have far fewer children than previous generations. As fertility declines and life expectancy increases, the increasing proportion of working-age people who are employed, relative to non-working-age people, could result in a demographic dividend for countries whose children and youth are provided today with education, health services and opportunities for productive engagement in the labour force *(7)*. However, countries without large numbers of children and youth relative to older ages, including Europe, North America and Japan, will have difficulty ensuring a functioning health care system, adequate pensions and social protection.

Fig. 5. Population by sustainable development goal region: estimates, 1950–2020, and medium-variant projection with 95% prediction intervals, 2020–2100



Source: UN, 2019 *(7)*.

These demographic changes focus our attention on Africa, and potentially India, where governments will be challenged to provide services to their rapidly growing populations living in malaria-endemic settings. The better the services are, the greater the resulting demographic dividend and economic benefits will be. In terms of malaria, the growing demographic dividend in Africa and India and the increase in aging and economically inactive populations in many traditional donor countries may alter the balance of donor to domestic investments in malaria.

If malaria control improves as these demographic changes unfold, many young people will grow up without experiencing malaria or developing partial immunity to the disease. Furthermore, individuals will be unfamiliar with malaria as a public health priority, which could make it harder to justify continued investment in national malaria control and increase the risks associated with the failure to do so.

In areas where there is no significant population-level immunity to malaria, if malaria were to return, outbreaks would occur and people of all ages would be vulnerable to severe malaria. With declines in malaria globally, increasing malaria risk in adolescents has already been documented. Minimally symptomatic infections in the elderly who have a degree of immunological memory would potentially provide an ongoing reservoir of infection *(92)*. Studies with long-term migrants from endemic to non-endemic settings have shown that adults from malaria-endemic areas who have acquired a high degree of immunity to malaria will also become vulnerable to disease and possibly death due to prolonged periods without exposure. This would place such individuals at increased risk of morbidity and mortality in the case of malaria reintroduction *(93, 94)*. However, an analysis of countries that have successfully eliminated malaria found very few resurgences, suggesting that reductions in immunity after elimination and increased capacity of health systems combine to stabilize and sustain the state of elimination *(95)*.

Urbanization

The world's urban areas grew by 1 billion persons between 2000 and 2014, with 55% (4.2 billion persons) of the world's population living in urban areas in 2018 *(8)*. As much as 90% of the urban growth in the next 20 years will occur in African and Asian countries. By 2030, 60% of the world's population will likely live in cities, with 68% projected by 2050.

Malaria vectors are generally less plentiful, and the prevalence of infection is generally lower, in urban compared to rural areas, although there is marked heterogeneity *(96-98)*. Urban areas may be at lower risk because potential mosquito breeding sites are removed as infrastructure is built and improved, and housing conditions may be of a higher standard than in rural areas, thereby reducing human–vector contact. However,

infection risk may vary significantly over small areas, compounded by socioeconomic factors *(99)*. Areas of high population densities and low resources, such as slums and informal settlements, may offer favourable grounds for the spread of malaria. Other risk factors include constructed urban breeding sites, such as urban agriculture, tyre tracks and ditches *(100-102)*. Mitigation of malaria risk can be addressed with longer term forward planning to ensure appropriate housing and sanitary engineering that takes into account the risk of vector-borne disease.

Higher population densities in cities can facilitate access to health care providers; however, this situation also clusters people around certain risks and generates intense inequities that leave some without access to basic services *(103)*. Rapid urban population growth can also outpace the capacity of services *(104)*. Invariably, the urban poor face the greatest hardships, often living in slums and informal settlements characterized by substandard housing, overcrowding, lack of access to safe water and sanitation, and lack of secure tenure. The impact of poor access to health care is compounded by frequent travel to rural areas with higher malaria endemicity to visit family or tend to farms. Approximately 60% of sub-Saharan Africa's urban population, one third of the population in urban Asia and one fifth in urban Latin America live in slums *(105)*. These subpopulations may fall outside of the sampling frame in population surveys and end up excluded from population data. This affects the delivery of equitable services and ultimately the realization of national and global targets for health and development *(106)*.

Climate change

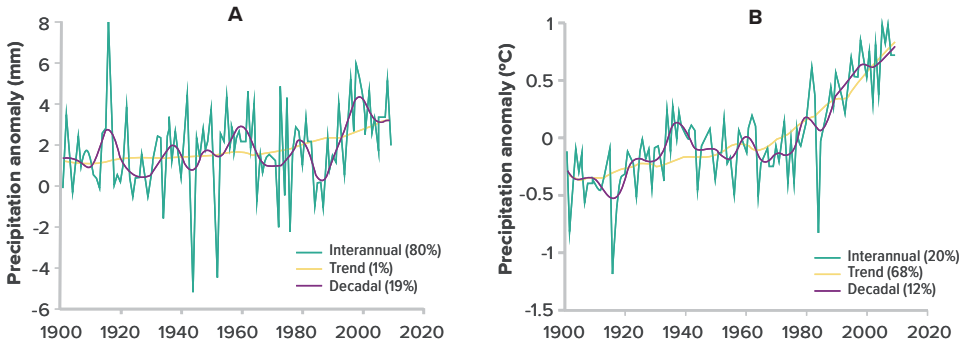
Global population growth and prosperity increase the demand for and consumption of natural resources such as land, water, energy, minerals and food. The resulting anthropogenic emissions of greenhouse gases (carbon dioxide, methane, nitrous oxide) have resulted in approximately 1.0°C higher temperatures currently compared with pre-industrial levels. The Intergovernmental Panel on Climate Change projects that current growth rates will add a further 1.5°C between 2030 and 2050, and the Earth's temperature may even increase by 3.7°C to 4.8°C by the end of the 21st century *(107)*.

Malaria has always been understood to be a climate-sensitive disease, with transmission historically associated with summer months in temperate zones and humid lowlands in tropical regions. Climate can influence malaria directly by affecting transmission dynamics through vector and parasite development, or indirectly through various pathways, for example, by affecting the many socioeconomic factors that combine to determine malaria risk in the real world *(108)*. Unusual weather conditions have often precipitated deadly epidemics.

Three variables – temperature, precipitation and humidity – are known to have a direct effect on malaria transmission *(109)*. The risk of malaria infection and the stability and seasonal patterns of disease transmission are determined by vector abundance, the duration of the extrinsic incubation period (the time between a mosquito being infected and becoming infective), and the survival rate of the vector, combined with the probability of the vector feeding on a susceptible human host. When climate change is considered in isolation, current projections anticipate decreases in malaria in some areas and increases in others, especially at the edges of current transmission zones *(108, 110)*. However, as presented in the section describing the quantitative exploration of malaria trajectories in Africa to 2050, multicausal models suggest that the role of climate change is less important than other factors in terms of influencing where malaria might increase over the ensuing decades.

The climate naturally varies on multiple timescales (Fig. 6), from daily weather and seasonal cycles to fluctuations occurring from year to year (interannual variability) and over longer cycles of 10–30 years (multidecadal variability). This natural climate variability has been superimposed on a background of nonlinearly increasing greenhouse gas concentrations in the atmosphere since around the start of the 20th century. This has led to detectable trends in average climate (particularly temperature), as well as changes in the shorter timescales of climate variability such as extreme weather events and seasonality.

Fig. 6. Timescales of variability for global average precipitation (A, mm/day) and temperature (B, °C) anomalies[a]



[a] Raw annual averages are shown in green, fitted decadal cycles in purple and the long-term trend in yellow. See Greene et al., 2011 *(111)* for methodology.

Climate change will not be felt through gradual trends over long periods of time, but primarily through changes in the frequency and intensity of weather and climate shocks, such as heatwaves, storms, floods and

droughts; the characteristics of seasons; and potentially through alterations in climate drivers, such as the El Niño Southern Oscillation. Weather and seasonal forecasts currently offer the most potential for use in decision-making, as climate change projections are too uncertain for many long-term operational decisions, especially at smaller spatial and temporal scales. Forecasting on a decadal timescale is particularly challenging, yet is likely to be the most relevant when planning efforts to eliminate malaria.

Climate variability and change will also affect malaria transmission by impacting malaria control programmes. For example, extreme weather events may disrupt the logistics of vector control and medical supplies, while climate variability may change the optimum timing of measures like indoor residual spraying (IRS). Overlooking underlying climatic variations may result in inadequate timing of efforts to interrupt transmission in a particular setting and an under- or over-estimate of the impact of different control strategies.

Climate change may also influence the vulnerability of populations to malaria, largely through indirect effects on the socioeconomic factors that underpin malaria risk. Climatic shocks may, for example, impact livelihoods and the proper functioning of health systems. Governments may be required to redirect resources at the expense of malaria control. Rising carbon dioxide levels may impact malaria risk independently of changing climate or weather patterns, for example by influencing larval development or by altering the nutritional content of staple crops.

Land use and land cover changes

LULCC are one of the main causes of global environmental change, contributing to one quarter of anthropogenic greenhouse gas emissions *(112)*. Land cover refers to the physical and biological cover of terrestrial surfaces, such as water, soil, vegetation and infrastructure, while land use refers to the human management and activities that modify land surface processes *(113)*. Global changes to human activities that modify land cover are occurring at an unprecedented pace such that human demands have already altered over 75% of the Earth's ice-free land *(114)*. The demographic shifts and urbanization discussed in the previous sections are two contributing factors, along with increasing agricultural expansion, deforestation, and infrastructure expansion, particularly in tropical areas *(115)*. For example, the growing population is expected to require a 70% increase in food production by 2050, greatly increasing the demand for agricultural and pastoral land use *(116)*.

Deforestation remains one of the main contributors to global LULCC. Changes in forest cover are particularly pronounced in tropical areas, where over 80% of new agricultural land was cleared from tropical rainforests between 1980 and 2000 and an estimated 2100 km^2 of forests

were lost per year between 2000 and 2012 *(117, 118)*. In the absence of new forest conservation policies, it is estimated that 289 million hectares (an area the size of India) of tropical forest will be cleared between 2016 and 2050, driven mainly by agricultural expansion *(119)*. This increased agricultural production supports a growing, more urbanized population, necessitating more roads, waterways and other infrastructure.

Among the effects of these anthropogenic LULCC are emergence of zoonotic diseases and changes in the transmission of vector-borne diseases *(120-122)*. Deforestation, urbanization and agricultural expansion affect the distribution of people, animal reservoirs and disease vectors, impacting infectious disease risks *(120, 123, 124)*. These changes have been linked to altered dynamics and geographical distribution of malaria and other vector-borne diseases globally *(125-127)*. LULCC can modify the physical environment and disrupt existing ecosystems, impacting vector and reservoir populations and altering the rate of parasite development; at the same time, LULCC can simultaneously contribute to social and demographic changes, which may either increase or decrease malaria risks *(127)*.

Deforestation and landscape changes can impact the species composition and abundance of vector populations. Ecological changes in soil, sunlight cover, vegetation type, development of water pockets and water temperature can alter breeding conditions for *Anopheles* malaria vectors. Deforestation can reduce shaded water bodies, the preferred breeding habitats of some anopheline species. Alternatively, some *Anopheles* species thrive when there is greater exposure of water bodies to sunlight, significantly increasing larval survivorship, adult productivity, net reproductive fitness, intrinsic growth rate and biting frequency via shortened gonotrophic cycles – all of which increase vectorial capacity *(127)*. Environmental and climatic changes due to deforestation may favour the survival of different *Anopheles* species, enabling sustained seasonal malaria transmission. In some cases, one *Anopheles* species eliminated because of deforestation might be replaced by another *(125)*.

Relationships between malaria transmission and LULCC are highly dependent on the spatial and temporal units of the data being analysed. Land use change is a dynamic process; initial impacts on disease transmission from disruption of existing ecosystems may change over time as transmission reaches new states of equilibrium. Following deforestation, subsequent stages of forest succession and agricultural development may either create new habitats for disease vectors and hosts or lead to overall decreases in malaria burdens *(125)*. Monitoring these changes requires detailed data on human, mosquito and other host distributions relative to habitat types, collected in a consistent method, to fully understand the long-term consequences of these changing environments. Further research is needed to understand the complex effects of LULCC on malaria risks and to develop disease surveillance and control methods appropriate to local contexts and ecologies.

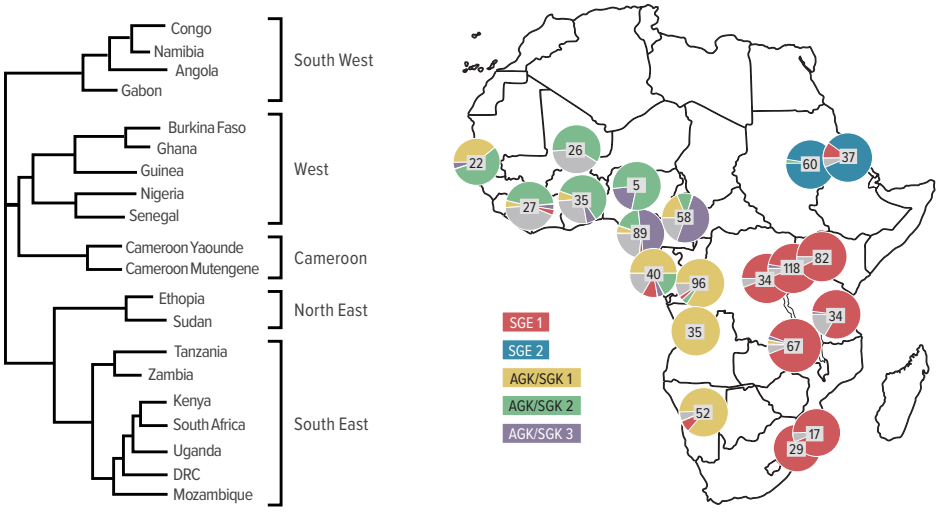
Migration

Human migration is a dynamic and complex trend. In 2017, 258 million international migrants, representing 3.4% of the world's total population, were living outside their country of birth *(128)*. There were 150 million migrant workers in 2015, and by the end of 2017, 68.5 million individuals worldwide who were forcibly displaced due to persecution, conflict, generalized violence and human rights violations. This is almost double the number of forcibly displaced people recorded in 1997 *(128)*. Even though the clear majority of migrants remain within their countries' borders, the movements of the 740 million internal migrants may complicate malaria elimination programmes by increasing the circulation and transportation of parasites and absenting people during mass drug administration, ITN or IRS campaigns *(129)*. In 2017, internally displaced people included some 40 million people fleeing conflict and disaster *(130)*.

It will be important to increase our understanding of the dynamic relations between socioenvironmental circumstances and population migration (both international and internal) in order to ensure successful elimination of malaria from individual countries. For example, the mapping of drug resistance markers in Africa has shown the importance of human migration in the distribution of malaria parasites *(131)*, with the distribution of specific alleles broadly corresponding to economic communities (Fig. 7). This suggests that economic and transport infrastructures may govern parasite movement in Africa by affecting the movement of people *(131)*. Migration flows within malaria-endemic regions are also likely to influence efforts to eliminate malaria. For example, census-derived data are considered a good proxy for subnational migration flows, and an open access archive of estimated internal migration in malaria-endemic countries in Africa, Asia, Latin America and the Caribbean has been developed (Fig. 8) *(132)*. These predicted flows could be used to highlight policy-relevant population dynamics for malaria elimination, although direct molecular surveillance of parasite populations has the potential to provide greater clarity, if adequate capacities can be built and surveillance systems established.

The movement of infected people into areas that have eliminated malaria but remain able to support transmission raises the potential for re-establishment of the disease. Forecasts for migration other than rural to urban and refugee populations in general are unreliable in the short term due to unforeseeable events. The development of new and better approaches to track migration patterns would be extremely helpful.

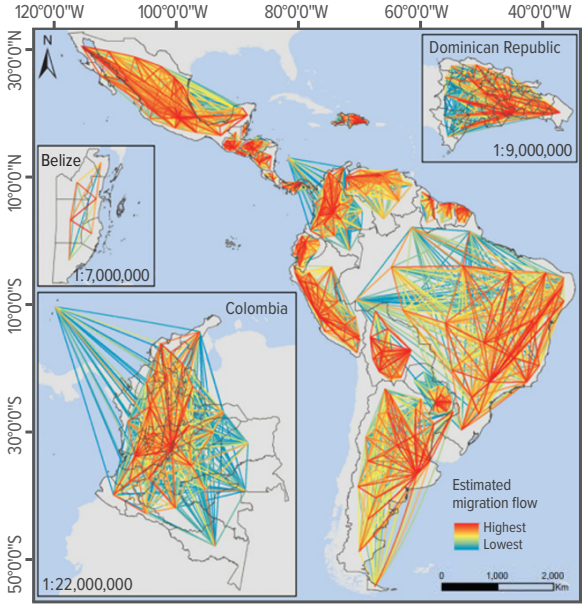
Fig. 7. The African distribution of dhps resistance lineages[a]



[a] Resistance alleles whose flanking microsatellite haplotypes did not conform to a defined major lineage are shown in grey. Sharing of resistance allele lineages among the African populations is shown in a cladogram based on pairwise comparison of allele sharing, which includes all the flanking haplotypes identified. Closely related populations cluster in large geographic regions that supersede national boundaries.

Source: Pearce et al., 2009 *(131)*.

Fig. 8. Census-derived subnational migration data



Source: Sorichetta et al., 2016 *(132)*.

A quantitative exploration of malaria trajectories in Africa to 2050

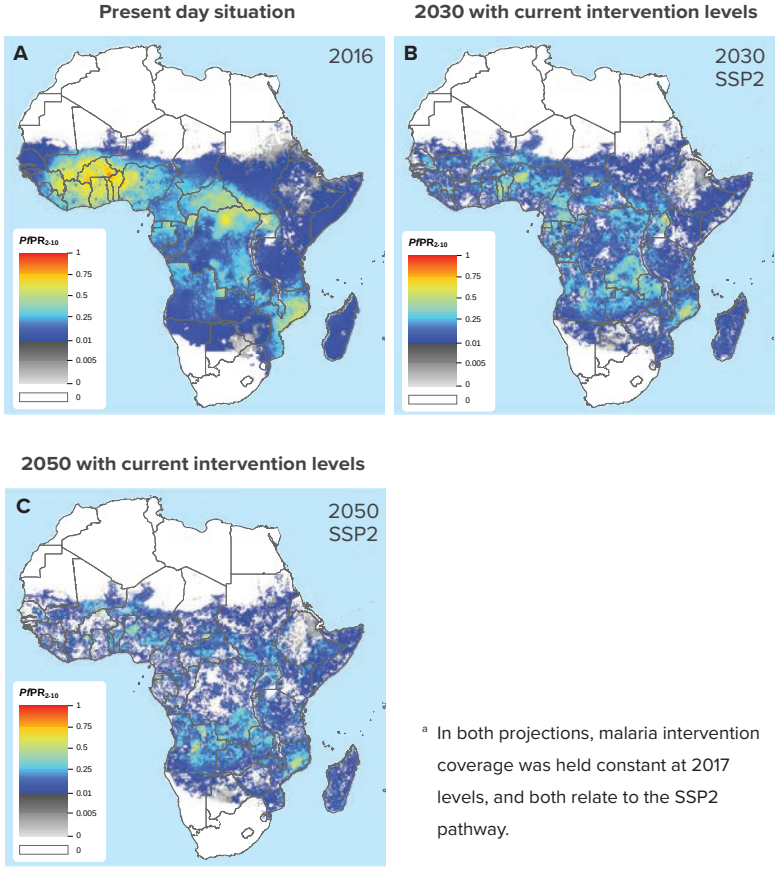
The potential combined future impact of megatrends on malaria in Africa was investigated through the development of an analytical framework that generated maps of malaria risk in Africa for the benchmark years of 2030 and 2050. The analysis was restricted to Africa for two reasons: 90% of the global burden of disease and death due to mortality is in Africa, and the data describing the association between risk of malaria and environmental determinants are less well developed outside of Africa *(5)*. The year 2050 was chosen to represent a notional target date for global eradication, although this choice is somewhat arbitrary, providing a point of reference for analysis rather than a policy-oriented declaration of intent. The year 2030 was included as a key staging-post against which progress towards eventual eradication can be evaluated; it is also the end point of the GTS.

As a starting point, the analysis took our best understanding of malaria risk in Africa in the present day and how that risk is mediated by the natural and human environments. This knowledge was then linked to projected changes in those environments (megatrends) over the coming decades in order to predict the impacts on malaria and implications for eradication. Plausible environmental conditions in 2030 and 2050 were obtained from different scenarios for climate change, as projected by Shared Socioeconomic Pathways. These are internally consistent narratives along with a set of quantified measures of development that describe future scenarios based on different levels of development and energy use *(133)*.[8] Different possibilities for malaria interventions were modelled: **contemporary coverage**, with malaria control in the future maintained at 2017 levels; **scale-up of current tools**, where no new malaria control tools were introduced, but tools currently in widespread use (namely, ITNs, IRS and antimalarial treatment with ACTs) were increased to 80% to represent improved coverage levels; and **innovation of new tools**, which evaluated the possible impact of a variety of new vector control tools, vaccines and drug classes to be used in conjunction with, or to replace, existing interventions.

8 Projections of megatrends in this analysis used the Shared Socioeconomic Pathway 2 (SSP2), referred to as the middle-of-the-road scenario.

Fig. 9 shows predicted endemicity across Africa in 2030 and 2050 under the contemporary coverage scenario wherein interventions are held constant at 2017 levels. The combined effects of the changing environmental factors are predicted to yield significant declines in the *P. falciparum* parasite rate (*Pf*PR) in children 2–10 years old[9] by 2030 and further declines by 2050. By 2050, the *Pf*PR is projected to fall below 10% in most areas experiencing high transmission today (where the standardized *Pf*PR in children 2–10 years old is >30%), while in current low-transmission regions, *Pf*PR will approach zero. Pockets of higher transmission will remain in west and south-east Africa.

Fig. 9. Projected future impact on malaria endemicity of the changing environment. Maps show *P. falciparum* parasite rates (2–10 year olds) for the present day (A), and projected for the years 2030 (B) and 2050 (C)[a]



[a] In both projections, malaria intervention coverage was held constant at 2017 levels, and both relate to the SSP2 pathway.

9 The *P. falciparum* parasite rate in children 2–10 years old ($PfPR_{2\text{-}10}$) is a standardized measure of malaria endemicity *(134)*.

The corresponding level of malaria morbidity associated with these projections is tabulated in full in Table 1. With current intervention levels maintained, annual case incidence is projected to fall from 207 per 1000 persons at risk today to 174 per 1000 in 2030, and to 130 per 1000 by 2050. The declines in incidence rate, however, are largely counteracted by projected growth in the underlying populations at risk, such that the overall number of malaria cases is projected to remain around 200 million in 2030 and 2050, i.e., the same number as in 2017.

Table 1. Projected future incidence rates and cases in Africa in 2030 and 2050 under different intervention scenarios

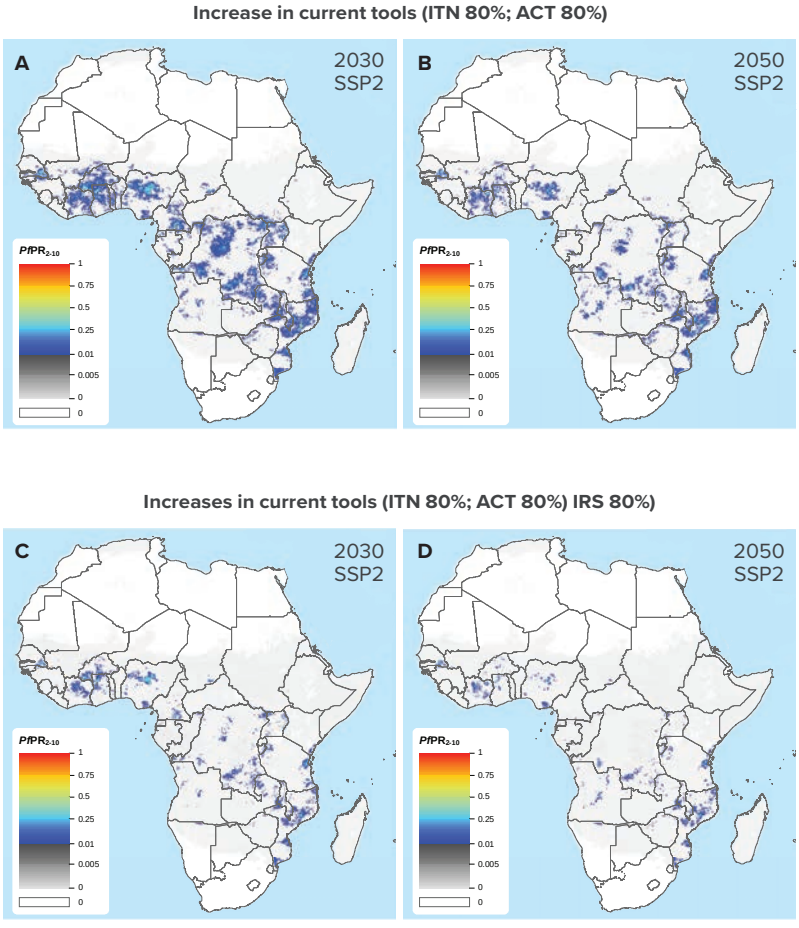
Intervention level	Incidence (cases/1000)			Cases (millions)		
	2017	2030	2050	2017	2030	2050
Current intervention levels	206.7	172.9	130.0	200.54	197.68	202.96
Increase current tools to 80% coverage (ITNs, ACTs)		28.6	17.4		32.74	27.20
Increase current tools to 80% coverage (ITNs, ACTs, IRS)		11.5	7.1		13.10	11.01
Add new tools						
Case management with DHA+PQ[a]		5.0	2.8		5.71	4.38
Monoclonal antibodies		8.6	5.0		9.82	7.77
Pre-erythrocytic vaccine		9.9	5.9		11.28	9.27
Transmission-blocking vaccine		6.2	3.4		7.04	5.32

[a] DHA+PQ=dihydroartemisinin piperaquine, an ACT with a long half-life that increases the prophylactic benefit *(135)*.

Fig. 10 shows the projected effect of changing environmental factors by 2030 and 2050, in addition to the scale-up of existing malaria control tools. Achieving and maintaining effective coverage of both ITNs and ACTs at 80% (Fig. 10A and B) yields further significant declines in *Pf*PR above those due to environmental effects alone. By 2050, the remaining high transmission pockets seen in Fig. 8B have declined to generally less than 5% *Pf*PR and many parts of Africa are at zero. Further addition of IRS at 80% coverage where transmission remains (Fig. 10C and D) leads to elimination from most of the continent, with scattered pockets of *Pf*PR

between 1% and 5% remaining mainly across west and south-east Africa. Table 1 shows the corresponding impacts on morbidity. Under the 80% ITNs, ACTs, IRS scenario, case incidence is projected to fall from 207 per 1000 in 2017 to 7.1 per 1000 by 2050. Despite these declines, the pockets of remaining transmission are projected to still yield some 11 million cases annually in 2050 with population growth taken into account.

Fig. 10. Projected future impact on malaria endemicity of the changing environment and increased coverage of existing malaria control. Maps show *P. falciparum* infection prevalence (2–10 year olds) for the years 2030 (A, C) and 2050 (B, D) under enhanced coverage of existing malaria control tools: 80% ITN and ACT coverage (A, B) and 80% ITN, ACT and IRS coverage (B, D)[a]



[a] All projections relate to the SSP2 pathway.

The additional impact of introducing new malaria control tools along with the scale-up of current tools, and in combination with changing environmental factors by 2030 and 2050, was also projected. Compared to the impact of high coverage with existing tools, the addition of new drug and vaccine-based interventions appears to yield little further reduction in the geographical extent of sustained transmission by 2050. However, further impacts can be seen in morbidity levels (Table 1). Replacing current ACTs with an ACT with a long half-life (DHA-PQ) for case management, for example, is projected to reduce incidence rates in 2050 from 7.1 per 1000 (under 80% coverage of ITN, ACT and IRS) to 2.8 per 1000, although the number of cases would be over 4 million.

The analysis suggests that changing human and biophysical environments will have varied effects on malaria. Overall, however, these changes will have substantial positive impacts that will assist efforts to eradicate the disease over a multiple decade timescale. The models of intervention impact suggest that, in combination with the changing environment, existing control tools could reduce transmission dramatically to small pockets scattered across west, central and south-east Africa. However, such reductions would require intervention coverage to be increased to ambitious levels *(136)*.

Despite the projected large declines, environmental change and maximizing the use of current tools, whether alone or in combination, is not predicted to result in the complete elimination of malaria from Africa. The addition of a variety of innovative new vaccines or drugs would make only modest further impact, likely because the treatment coverage under our base scenario (80% effective treatment with ACTs) is already very high, leaving less scope for further impact with new tools. Innovative vector control, such as attractive targeted sugar baits, was not explored, and it is plausible that tools targeting outdoor biting or larval habitats would be well suited to addressing remaining risk in pockets where outdoor transmission plays an important role, potentially transforming the fight against malaria *(137)*.

This analysis of the impact of megatrends suggests that their overall impact will be positive but heterogeneous across Africa, and insufficient to achieve eradication within a reasonable timeframe.

Eliminating malaria in the hardest places

One of the lessons learned from the GMEP and the current polio eradication campaign is that success in eradication, and the time it will take to achieve eradication, will depend on how quickly malaria is eliminated from the hardest places; it follows, therefore, that areas known to be difficult to eliminate should be targeted as soon as possible. The alternative approach – i.e., to focus initially on the areas of lowest burden, sometimes referred to as shrinking the map – would likely lead to a longer tail of cases, as significant bottlenecks are encountered and addressed only late in the game. Focusing initially only on low-burden areas would also leave millions of people at risk of illness and death from malaria for some time. While some factors, such as armed conflict and terrorism, that will make elimination more difficult cannot be reliably forecasted, other characteristics of places where it will be hard to eliminate can be identified now and used to target areas for earlier intervention. To identify areas likely to be the last to eliminate, future scenarios for malaria were projected based on global megatrends and the scale-up of existing interventions, and the characteristics of the last pockets of malaria were described to inform appropriate strategies.

As shown in the previous section on megatrends, a key determinant of the future trajectory of malaria in a given location is the impact of global socioeconomic and environmental trends. A decomposition analysis was conducted to quantify the distinct effects of different categories of environmental change on malaria. Trends were categorized as: socioeconomic trends (including changes in night-time light brightness, percentage of houses electrified, percentage of housing with modern construction, percentage of housing with impervious surfaces, population density, gross domestic product (pixel level) and percentage of urban population); land cover trends (including changes to the percentage of forested primary land, percentage of non-forested primary land, percentage of managed pasture, percentage of irrigated land and deforestation); vegetation density trends (preferred over measures of precipitation because vegetation density is more closely coupled with malaria transmission); and temperature trends. For each of the four categories, the original geostatistical model used in the megatrends section was run to predict *Pf*PR in 2050, incorporating the projected changes to those environmental characteristics but holding all other factors (i.e., the other three environmental trend categories and malaria control interventions) constant at 2017 levels. This process generated projections for 2050 in which the only drivers of change were the trends within each category. The resulting maps of *Pf*PR in 2050 were then converted into maps

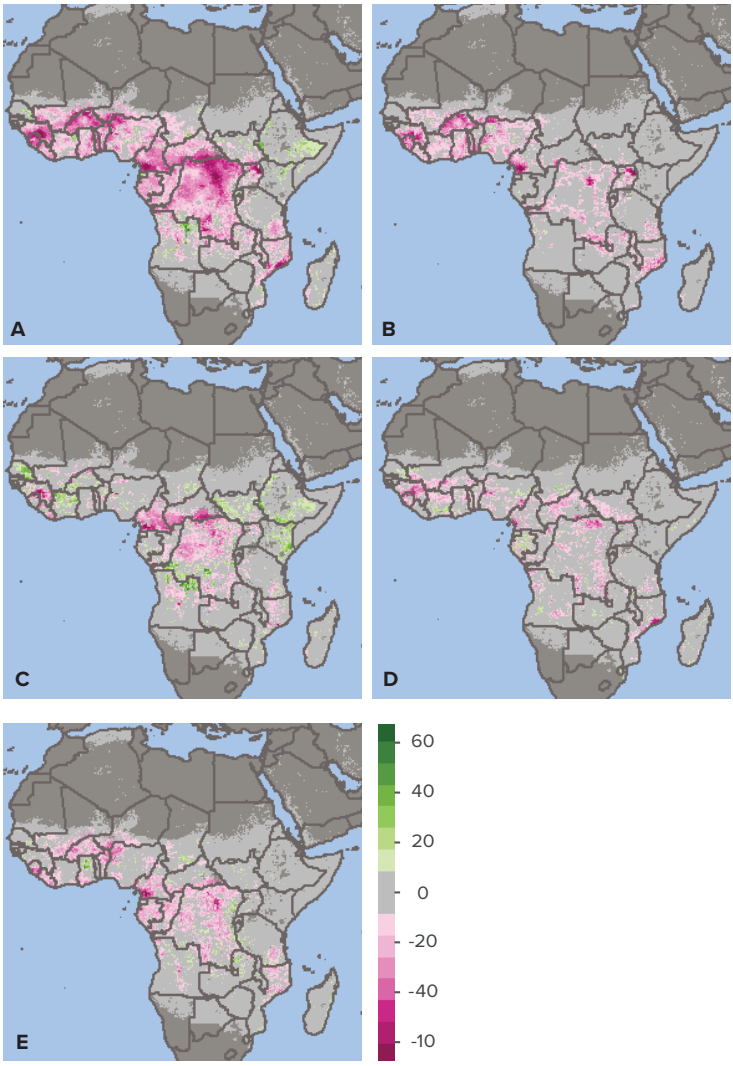
showing the absolute change in *Pf*PR between 2017 and 2050. To further summarize the results, the average value of change was computed for each country and displayed via simple barplots for comparison.

In the analytical framework developed in the section above, three factors combine to determine the level of transmission in 2050 and the projected success of elimination: level of receptivity;[10] combined impact of megatrends; and behavioural characteristics of local *Anopheles* vectors. The level of receptivity, which is defined here as the inherent propensity of each location to support transmission in the absence of any significant malaria control efforts, was approximated in the analysis by using *Pf*PR levels estimated for the year 2000 ($PfPR_{2000}$). The year 2000 was selected on the basis that coverage with ITNs and ACTs was close to zero in that year. $PfPR_{2000}$ is not a perfect proxy for receptivity, as it ignores any IRS activity in that year and the degree of efficacy retained by other (non-ACT) antimalarials at that time. Nevertheless, this value is likely to approximate what conditions would be like if current modern interventions were withdrawn. The behavioural characteristics of locally important *Anopheles* vectors that were included were the fraction of bites that occur indoors (endophagy) and the proportion of bites taken on humans (anthropophily).

Malaria transmission in Africa will be reduced from the impact of megatrends alone, but these effects will be heterogeneous with mean declines in transmission in 32 out of 43 malaria-endemic African countries, but with mean increases in the remaining 11 (Fig. 11A and 12A). The effect is similar when only socioeconomic trends are considered (Fig. 11B and 12B). The effects of changes in land cover are more mixed: areas associated with projected forest loss, particularly around the Congo Basin in northern Democratic Republic of the Congo, Central Africa Republic and Cameroon, are projected to have declining *Pf*PR, whereas substantial areas of Kenya, Ethiopia and South Sudan in east Africa, and Burkina Faso, Côte d'Ivoire and Senegal in west Africa experience increases in *Pf*PR (Fig. 11C and 12C). These increases are likely linked to projected increases in cultivated land, particularly managed pasture, crops and irrigated land. Changes in both vegetation density (Fig. 11D and 12D) and temperature (Fig. 11E and 12E) show an overall but not universal tendency to reduce *Pf*PR, with temperature changes having more geographically heterogeneous effects than other trends.

10 Receptivity is the degree to which an ecosystem in a given area at a given time allows for the transmission of Plasmodium spp. from a human through a vector mosquito to another human.

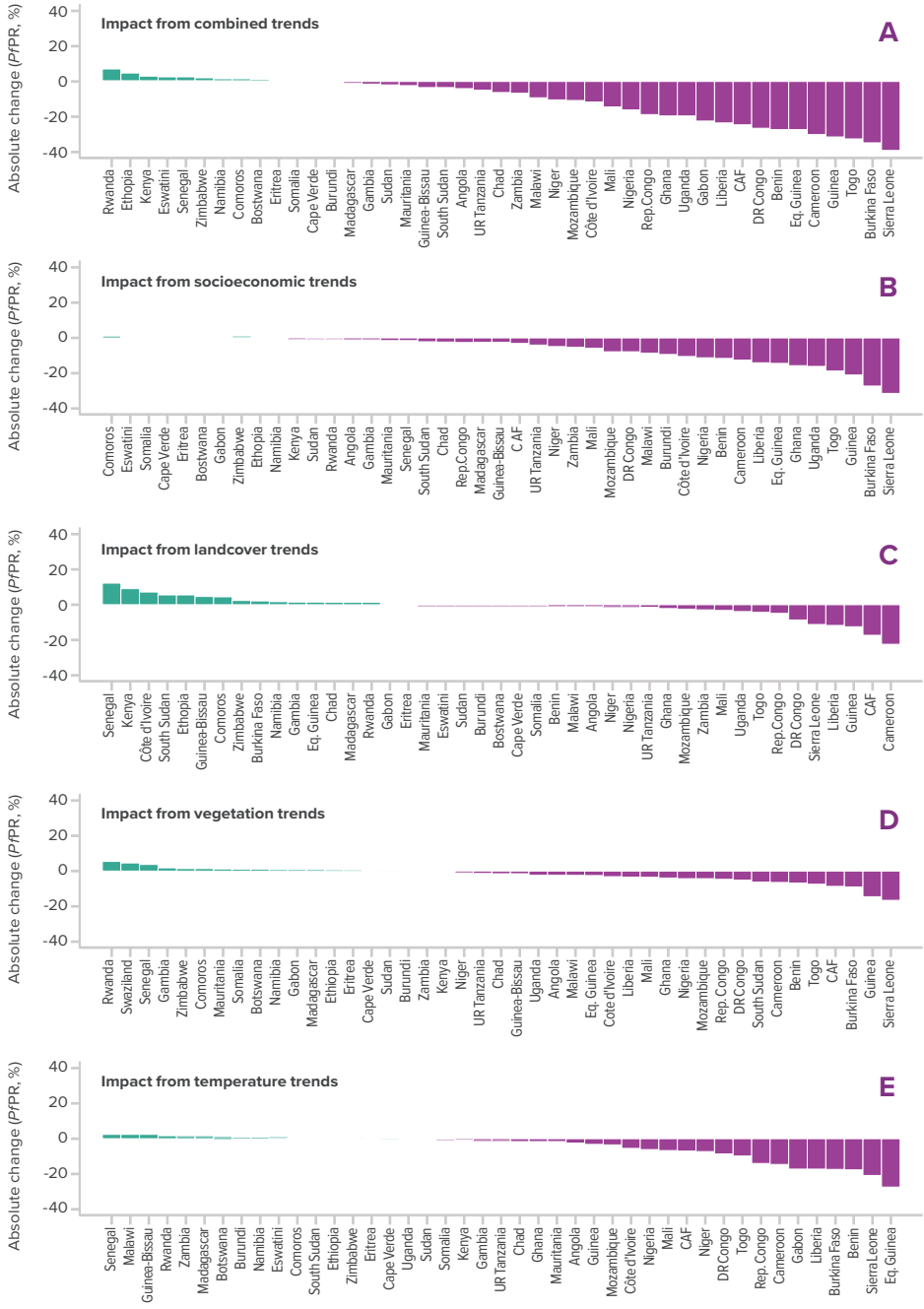
Fig. 11. Projected absolute change in *Pf*PR by 2050 at pixel level. Maps show changes 2017–2050 due to (A) all global environmental trends; (B) only socioeconomic trends; (C) only land cover trends; (D) only vegetation trends; and (E) only temperature trends[a]



[a] All scenarios relate to SSP2 with malaria control maintained at current levels. Dark grey areas were non-endemic in 2017.

To identify factors associated with being harder to eliminate, the characteristics of places that were projected to eliminate by 2050 were compared to those of places where transmission would not be eliminated. The baseline level of receptivity (Fig. 13A) was the factor that most distinguished eliminating and non-eliminating areas, with a mean $PfPR_{2000}$ of 26.1% in eliminating areas compared

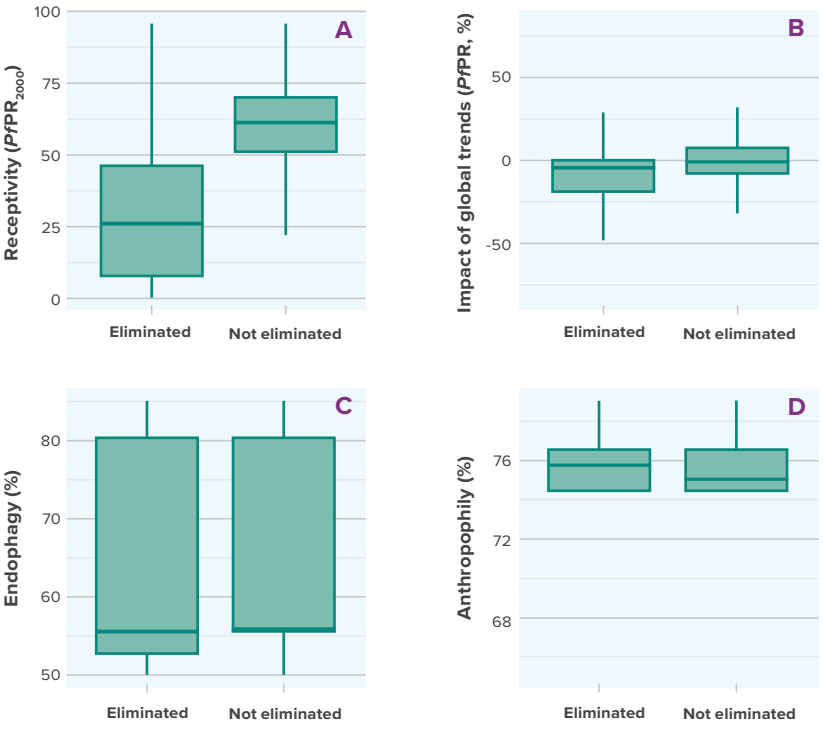
Fig. 12. Projected absolute change in *Pf*PR by 2050 at the national level. Barplots show changes due to (A) all global environmental trends; (B) only socioeconomic trends; (C) only land cover trends; (D) only vegetation trends; and (E) only temperature trends[a]



[a] All scenarios relate to SSP2 and with malaria control maintained at current levels.
DR Congo: Democratic Republic of the Congo; UR Tanzania: United Republic of Tanzania; CAF: Central African Republic

with a mean *Pf*PR$_{2000}$ of 61.1% in non-eliminating areas. The impact of megatrends differed to a lesser degree (Fig. 13B), with mean impact in eliminating areas (-4.2% *Pf*PR between 2017 and 2050) only marginally less than in non-eliminating areas (-0.6%); however, the distribution as a whole was substantially more negative (25th percentile of -19.2% *Pf*PR in eliminating areas versus -8.2% *Pf*PR in non-eliminating areas). There was no clear difference between eliminating and non-eliminating areas in terms of endophagy (Fig. 13C), with an identical mean of 55.6% of bites occurring indoors in eliminating and non-eliminating areas. In terms of anthropophily (Fig. 13D), there was no meaningful difference, with a mean of 76% of bites occurring on humans in eliminating areas versus 75% in non-eliminating areas.

Fig. 13. Boxplots comparing statistical distributions of candidate driving factors in areas projected to eliminate versus those not projected to eliminate by 2050 in a scenario with optimistic intervention coverage[a]. Plots are shown for (A) receptivity[b], (B) magnitude and direction of impact caused by combined global trends excluding changes in malaria control, (C) endophagy[c] and (D) anthropophily[d]



[a] Boxplots show the median (bold line), interquartile range (yellow box) and 2.5th–97.5th percentile (extent of whiskers).
[b] Receptivity was approximated using *Pf*PR in the year 2000.
[c] Endophagy was defined as the estimated percentage of bites by local *Anopheles* occurring indoors.
[d] Anthropophily was defined as the estimated percentage of bites by local *Anopheles* on humans.

Among global environmental trends, the strongest drivers of declining *Pf*PR are likely to be socioeconomic factors, capturing the impacts of urbanization, improved infrastructure, improved housing and so on. These changes result in significant projected declines in many places, but the magnitude of impact will depend both on the current levels of economic development and infrastructure (with countries already farther along this trajectory having less capacity to improve) and their forecasted trajectory of increase to 2050. Projected changes in land cover are likely to have much more varied impacts: While deforestation in the Congo Basin is likely to reduce transmission, intensification of agriculture and irrigation in east and west Africa will have a detrimental impact. These findings highlight the need for vigilance and ongoing surveillance as large-scale changes in land use or land cover occur in Africa in the coming decades. There is also a potential need to develop tailored mitigation strategies to counter the specific mechanisms by which such changes increase malaria risk. Overall, climate impacts are projected to be more modest than the impacts of socioeconomic or land cover changes; nevertheless, climatic changes may be locally significant in many locations. This geographic variability, coupled with the inherent uncertainty of climatic projections, points again to the need for enhanced networks to monitor or predict local climatic changes and their possible implications for malaria elimination, as well as sensitive surveillance systems to capture fluctuations in malaria incidence.

Despite the complexity of untangling the relative importance of receptivity, global trends and local *Anopheles* bionomics in determining whether a location is likely to eliminate or not, the results of the analysis are nevertheless unambiguous. Receptivity, or the level of underlying suitability for transmission, remains by far the biggest factor determining the magnitude of the challenge in reaching elimination. While this relationship is mediated by local variations in the impacts of global trends that effectively alter this receptivity, the analysis suggests that the magnitude of these alterations will not fundamentally change the landscape of risk. Consequently, areas with high receptivity and high burden today remain the likeliest candidates to be the hardest places to eliminate malaria in the future. Perhaps more surprising is the apparent unimportance of levels of endophagy and anthropophily in the local vector population given that the degree to which vectors bite indoors and feed on humans compared to animals is likely to strongly mediate the impact of scaling up contemporary vector control to 80% coverage. This finding may reflect the relatively small variation in these variables across Africa or simply that the magnitude of variation in the overall amount of transmission (driven by receptivity) remains more important than where and on whom bites occur.

Mitigating potential threats to eradication

Eradication efforts are complex undertakings that are likely to face both expected and unanticipated challenges. Known challenges highlighted from the beginning of this report include the lack of human resources and management capacity to overcome bottlenecks along the path to elimination and eradication. Possible biological threats include insecticide and antimalarial drug resistance, parasite mutations that make them more difficult to diagnose, changing vector population dynamics and altered vector behaviour. The existence of non-human primate malaria species, such as *P. knowlesi*, poses a potential existential threat should there be sustained human–mosquito–human transmission of these species. Natural disasters and armed conflicts that disrupt health systems can cause malaria epidemics and reverse progress towards eradication. Other well recognized threats include a lack of, or declining, political will to defeat malaria and insufficient domestic and international financing, particularly as eradication is approached and other diseases are perceived to be more of a priority. The SAGme summarizes several of these key threats below, with particular focus on the potential for non-human primate malaria species and complex emergencies to derail or disrupt eradication attempts.

Biological threats

Resistance of parasites to antimalarial drugs and of mosquitoes to the insecticides used in vector control poses a substantial threat to malaria control, elimination and eradication. Resistance occurs when some organisms develop mutations that favour their survival in the face of interventions while the susceptible organisms are killed off. Natural selection allows the mutated parasites with survival advantage to predominate, generating populations that suffer no or few consequences from the drug or insecticide being deployed *(138)*. From the beginning, resistance to drugs and insecticides has been recognized as a problem for malaria control, and the global malaria community has addressed it in three ways: ensuring a productive pipeline of new interventions using different modes of action; slowing the spread of resistance by managing aspects of the intervention application (e.g., rotation of insecticides and improving treatment compliance); and eliminating the parasite. WHO has developed guidance on insecticide resistance management and on surveillance for antimalarial drug efficacy; hence, the SAGme did not consider these topics in further depth *(139, 140)*.

In addition to developing chemical resistance, the plasticity of mosquito behaviour might affect the effectiveness of interventions or allow mosquitoes to exploit new niches. For example, there is growing evidence

that *An. gambiae* complex mosquitoes have adapted to breeding in polluted water and containers in urban areas *(141, 142)*, and vectors have been shown to shift to outdoor biting following the introduction of ITNs *(143)*. Most worrying for future scenarios of malaria transmission is the potential for efficient malaria vectors to extend their range and invade new areas, which has been seen recently with the detection in Africa of *An. stephensi*, a vector associated with urban malaria transmission in the Indian subcontinent *(144)*. Good entomologic surveillance systems will be needed to monitor insecticide resistance, mosquito distribution and behaviour over time in order to adjust strategies, where possible, in light of these threats.

Similarly, drug resistance poses a challenge to malaria eradication – a challenge that the malaria community has faced for decades. *P. falciparum* resistance to chloroquine developed independently in three to four areas in South-East Asia, the Pacific and South America in the late 1950s and early 1960s, and subsequently spread to all areas of the world *(145)*. Resistance of *P. vivax* to chloroquine has also been found in some regions. Resistance of *P. falciparum* to chloroquine's replacement, sulfadoxine-pyrimethamine, occurred quite quickly, leading to a shift to ACTs in 2001. ACTs contain an artemisinin derivative with short-acting effects paired with one or more complementary compounds that possess a different mechanism of action and are longer acting *(146)*. Most countries changed their national treatment policies to ACTs in the decade following their first recommendation by WHO.

Artemisinin resistance is defined as delayed parasite clearance after treatment with an ACT or artesunate monotherapy. Delayed parasite clearance is only partial resistance. The majority of patients with delayed clearance are still able to clear their infection, except in cases where there is concomitant resistance to the partner drug *(146)*. Resistance to partner drugs is likely to increase treatment failures. Monitoring the drug efficacy of both artemisinin and partner drugs is essential to ensure timely changes in treatment policy and to help detect early changes in the susceptibility of *P. falciparum* to antimalarial drugs.

P. falciparum elimination has been targeted for 2030 in the Greater Mekong Subregion, where artemisinin resistance was first identified, in order to reduce the potential for increased morbidity and mortality from drug resistance. Currently, no country or area of the world is lacking an effective antimalarial treatment. The development of new antimalarials based on drugs other than artemisinin is underway, with the assistance of new procedures that enable more efficient screening of candidate molecules for antimalarial activity *(147)*. Although there will never be an end to the threat of drug resistance as long as malaria parasites persist, mechanisms are in place to provide early warning of treatment failures and new products are in the pipeline to replace failed drugs.

Parasites have also developed mutations that enable them to escape diagnosis by RDTs that detect histidine-rich protein 2 (HRP2) or the related HRP3. These protein targets, which are specific to *P. falciparum*, are strongly expressed by asexual parasites and have multiple copies of the target epitopes per protein. Some 10 years ago, researchers working in the Peruvian Amazon region identified patients infected with *P. falciparum* strains that had acquired deletions in the genes that encode these proteins (*Pf*hrp2 and *Pf*hrp3), rendering them undetectable by HRP2-based RDTs. Since then, many studies have demonstrated the presence of such mutated strains in other countries and regions *(148)*. The frequency and global distribution of this phenomenon is not yet fully understood, but, in a limited number of countries, research has shown that the relative incidence of these deletion mutants is high enough to threaten the usefulness of HRP2-only RDTs *(149)*. WHO is currently developing a global action plan to respond to the problem of HRP2/3 deletions, while RDT manufacturers are working to improve RDTs that detect other antigens.

WHO is actively gathering and compiling real-time data on these biological threats to identify and monitor areas at risk. The Malaria Threats Map is an online, interactive mapping tool that provides a visual overview of recent data and allows customization of displays *(150)*. Data are obtained from reports to WHO by national malaria control programmes and their partners, and from scientific publications. The mapped information is critical to inform appropriate malaria prevention, diagnosis and treatment strategies and to guide the development of new tools.

Threats posed by malaria in non-human primates

Non-human reservoirs of infection present fundamental challenges to eradication, as recently seen with the recognition that dogs may provide a reservoir that is part of the transmission cycle of dracunculiasis in humans. The potential of non-human primate malaria to serve as a source for sustained transmission in humans could pose a similar threat to malaria eradication, as diseases with zoonotic reservoirs are considered impossible to eradicate *(151)*.

Increased human exposure to primate malaria parasites (simian malaria), particularly for populations located in and near forested areas, would present a major threat if parasites were able to adapt and sustain long-term human-to-human transmission. Although primate-to-human transmission is relatively rare, zoonotic malaria parasites – those that are transmitted from an animal population to a human host – could pose a threat to contemporary public health and a challenge to malaria eradication efforts *(152)*. An analysis was undertaken of the threats posed by currently known malaria parasites in non-human primates that

could be transmitted to humans in natural settings. The known primate malaria parasites in apes, Old World monkeys, and New World monkeys were examined; these included *P. knowlesi, P. cynomolgi, P. simium*, and *P. brasilianum* (Table 2).

Table 2. Currently known zoonotic malaria parasites of non-human primates

Parasite	Primate to mosquito to human transmission	Human to mosquito to human transmission
South-East Asia		
P. knowlesi	Yes	No? (potential in vitro)
P. cynomolgi	Yes	Unknown
South America		
P. simium	Yes	Unknown
P. brasilianum	Yes	Unknown
Africa		
Ape *P. vivax*	Yes	Unknown
P. ovale	Unknown	Unknown
P. malariae	Unknown	Unknown

The recorded number of zoonotic malaria cases has been increasing and zoonotic parasites newly identified in humans have sometimes caused epidemics in areas where human malaria had long been eliminated *(153-156)*. Recently in Brazil, outbreaks of what was presumed to be *P. vivax,* which had been eliminated over 50 years earlier, were actually caused by *P. simium*, a simian parasite similar to *P. vivax*. Both parasites pose a significant risk of recurrent infection in the future within and beyond Brazil. Surveillance of New World monkey reservoirs and molecular epidemiological studies to quantify the rates of zoonotic exposure and transmission will be important for malaria control efforts and for understanding the magnitude of this threat across South America.

Similarly, in Malaysia, where human malaria has been eliminated, *P. knowlesi* was responsible for all malaria infections recently reported in rural areas; in 2018, *P. knowlesi* was the cause of more than 4100 cases *(157)*. There is currently no (unequivocal) evidence of sustained human-to-human *P. knowlesi* transmission; however, in vitro experiments highlight the capacity for adaptation to the human host, suggesting that this situation should be monitored closely.

Recent advances in molecular diagnostics and expanded sampling of wild primate populations have shown that the ancient origins of both *P. falciparum* and *P. vivax*, which cause most human malaria infections globally, can be traced to African great apes (i.e., chimpanzees and gorillas). *P. malariae* and *P. ovale* have also been isolated from African great ape hosts, although the directionality of transmission (i.e., ape-to-human or human-to-ape) remains unclear *(158-161)*. Given the taxonomic diversity of malaria hosts, the observation that most (if not all) human malaria parasites originated in our closest evolutionary relatives is striking and has compelled the scientific and public health communities to ask whether primate reservoirs could impede malaria elimination and eradication efforts by acting as a source of recurrent human infection *(155, 162-166)*.

Although it is unlikely that sporadic primate-to-human transmission events can be entirely eliminated, targeted public health efforts can minimize their impact. The consequences of simian malaria in humans need to be understood by stakeholders ranging from local populations to public health officials who can oversee surveillance and the required responses. Such responses include improved diagnosis of simian malaria (including molecular testing where appropriate) and development of clear control strategies for simian malaria that leverage the infrastructure and interventions developed to control human malaria parasites. Coverage of malaria control interventions, particularly surveillance, should be high among populations living near primate hosts harbouring the zoonotic parasite of interest.

The transmission potential of zoonotic malaria could also change. Therefore, continued surveillance and further research on non-human primate malaria is critical for better understanding and thus preventing or mitigating the threat to eradication. Investing in basic science research to evaluate the ecological, epidemiological and molecular drivers of primate malaria zoonoses would help to identify which parasites pose a tangible threat to human populations, how they are distributed geographically, and when seasonal cases are most likely to occur. Resources can then be efficiently allocated to predicted hotspots of exposure.

While primate malaria is not yet a reason to reconsider the feasibility of malaria eradication, it is a threat to be monitored and managed during and following eradication. Efforts to eradicate human malaria should not be derailed by focusing on the potential threat posed by simian malaria. The meaningful engagement of at-risk populations and collaboration with other sectors (such as forestry, mining etc.) will be essential for minimizing the impact of these zoonoses.

Threats posed by complex emergencies

Complex emergencies - encompassing both natural and man-made disasters, epidemics and violent conflicts - have a significant impact on population health and development *(167)*. To investigate how complex emergencies could threaten or delay malaria eradication, three case studies on malaria control and elimination efforts in both past and current conflict and emergency settings were examined to identify challenges, successes and lessons learned *(168)*. The three complex emergencies included violent conflict in Afghanistan; the 2010 earthquake in Haiti; and the 2014–2015 Ebola outbreak in Sierra Leone. Relevant lessons were also drawn from a 2012 series of case studies on countries in the malaria elimination or prevention of re-establishment (POR) programmatic phase.

Despite the diversity of settings, nature and scope of the emergencies, and malaria programme structures and phases, common themes emerged for malaria control and elimination in the three emergency settings (see Table 3).

Table 3. Summary of challenges and lessons learned from the case studies on complex emergencies

Case study location	Elimination goal/ programme phase	Type of complex emergency	Biggest challenges	Primary lessons learned
Afghanistan	Phased elimination by 2030	Violent conflict	• Government access restricted • Ongoing violence reducing health capacity • Heavy reliance on external donors	• Need for flexibility and adaptation to changing circumstances • Community engagement and building trust are essential • Community/ collaboration across all stakeholders is essential
Haiti	Zero transmission by 2020, sustained through 2022	Natural disaster (earthquake)	• Chronic health system weaknesses • Underuse/lack of trust in health system • Heavy reliance on external donors	• Important to maintain vision and commitment to elimination • Rebuilding presents opportunities • Community engagement and building trust are essential
Sierra Leone	Burden reduction	Health emergency (Ebola outbreak)	• Chronic health system weaknesses • Fear, lack of trust in health system • Heavy reliance on external donors	• Community engagement and building trust are critical • Community/ collaboration across all stakeholders is essential

Complex emergencies are likely to disrupt progress towards elimination and eradication, but these can be mitigated and should not deter us from pursuing this goal. Afghanistan, Haiti and Sierra Leone, for example, are all low-income settings with histories of political instability. External funding has generally been used to support routine health systems strengthening, but it has also helped to build malaria programme capacity and improve the coverage of malaria interventions and infrastructure during and after emergency situations. There is a need for flexibility and adaptation to changing circumstances, for example, to address challenges in neighbouring countries receiving refugees, or to go beyond usual practice to consider the use of mass drug administration in the face of epidemic malaria. In these emergency contexts, lack of national ownership and leadership for malaria programme performance and decision-making were seen as major impediments both in terms of routine health system support and in terms of the sustainability of the infrastructure and capacity improvements once post-emergency funding came to an end.

Robust health systems with strong surveillance capacity can help to minimize the impact of complex emergencies. However, in all three countries, weak health systems and limited investment undermined malaria programme operations, even with the support of external funders and partners *(169)*. Emergencies and violent conflict exacerbated systemic problems of underfunding, lack of capacity, poor infrastructure and lack of preparedness, with flow-on effects to other parts of the health system and impacts on neighbouring countries. This underscores the importance of investing in sustainable, robust and resilient health systems, which are complemented by specific emergency preparedness plans to help mitigate the impact of disasters and hasten recovery *(170)*.

Access issues identified in the case studies from Afghanistan, Haiti and Sierra Leone had different causes but similar effects, namely that vulnerable populations did not receive prompt diagnosis or treatment for malaria, and cases were not reported in the national surveillance system. In all three countries, populations living in rural and remote areas had limited access to quality PHC. In Afghanistan, geopolitical circumstances dictated population access to government-run services as a result of sporadic violent attacks that disrupted the delivery of health services or because territory was under the control of anti-government groups. In such cases, services were contracted out to nongovernmental organizations where possible. Even so, in 2017, 164 health facilities were forced to close due to local conflict, affecting 3 million beneficiaries *(171)*. In such instances, malaria programmes had limited information on the malaria burden or epidemics, which made it challenging to launch any targeted and coordinated response.

Social barriers also impacted population access to services. In Haiti and Sierra Leone, significant long-term distrust of the public health system was reinforced by the delivery of poor-quality care *(172-175)*. For example, the malaria programme in Sierra Leone faced many challenges during the Ebola outbreak, most of which could be attributed to conditions that had existed well before the outbreak began. Existing distrust of the health system was amplified by inadequate communication by the government in the early days of the Ebola outbreak, as well as the forcible removal of infected patients from their homes and culturally insensitive burial practices *(176, 177)*. Overall, it was estimated that outpatient attendance at health facilities dropped to just 10% during the outbreak, and patients with malaria symptoms were more likely to seek treatment through the private, informal health sector than in public facilities *(178, 179)*.

In these contexts, the role and importance of community ownership and meaningful engagement efforts between providers of health services and disaster assistance and local communities cannot be underestimated or undervalued. A purposeful and consistent effort to foster trust, such as through community mobilization, educational activities and community-level service delivery, can strengthen programme operations and build strong relationships every step of the way. This will have benefits not only in the context of an emergency but also in the context of routine malaria activities and may help to address some of the health system weaknesses described above *(176, 177, 180)*.

Furthermore, malaria risk should be included in broader global and local discussions regarding disaster risk reduction and response. For example, establishing mechanisms for coordination can support collaboration across many implementing partners and stakeholders. In Afghanistan, a network of partners was key to filling operational gaps and helped to facilitate engagement with communities and communication about malaria risk, particularly among the most vulnerable communities impacted by episodes of violent conflict.

Although complex emergencies are likely to cause disruptions of progress towards elimination and eradication, these effects, which may be time-limited, can be overcome and should not deter the world from attempting to eradicate malaria.

Health systems readiness for malaria elimination

To achieve a world free of malaria, health systems in malaria-endemic countries face a series of highly challenging tasks. They need to accurately define and identify populations at risk, ensure that these populations are covered with effective interventions to prevent and treat infections, and make certain all malaria patients receive quality-assured care rapidly. Interrupting and preventing the re-establishment of malaria transmission can only be achieved if all these requirements are addressed. These requirements imply that in any given epidemiological setting, interventions to reduce disease must be compatible with the structures and functions of the prevailing and developing health and social systems.

Since 2000, several studies have been published on the feasibility of malaria elimination and eradication *(181, 182)*. Most of them have analysed the technical and operational feasibility of interrupting transmission with respect to the ability of countries to create effective national malaria programmes at scale *(183)*. A malaria eradication effort, which involves every malaria-endemic country eliminating transmission within its borders, presents an entirely different proposition. The strength of health systems will likely be a major determinant of the speed at which countries will progress towards malaria elimination, and major investments in health systems may be required to achieve and maintain global malaria eradication.

Measuring the readiness of health systems for any specific intervention or to achieve elimination goals is complex given the multidimensional nature of these systems and the variable importance of these dimensions in different contexts *(184-186)*. Historically, data on health system performance have been limited in terms of both quantity and quality. Over the last 15 years, more information has become available, expanding the ability to characterize and compare health systems across countries and time periods. Existing data were analysed to assess which health system characteristics best predicted progress towards malaria elimination in malaria-endemic countries between 2000 and 2016 in order to determine whether specific aspects of health systems will need to be addressed to achieve elimination.

All available information on health systems was combined in a database and linked to the most recent data on progress in malaria control. A total of 83 health system variables were broadly grouped into six building blocks based on the WHO health systems framework *(184)*. The six building blocks were:

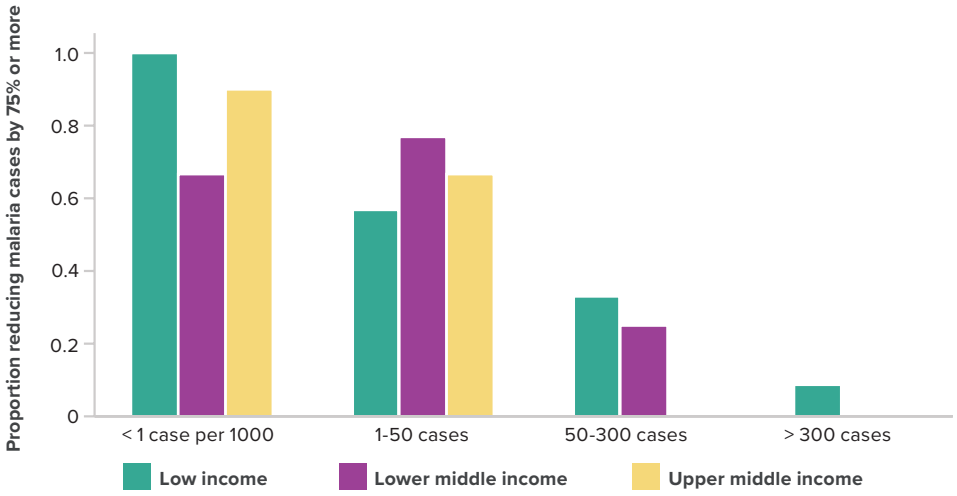
- health system financing
- health service delivery
- access to medicines

- health system workforce and capacity
- governance
- information systems.

Additionally, a total of 35 macroeconomic, demographic and geographic indicators relevant to health systems and malaria control were included as potential covariates. Principal component analysis was conducted to consolidate the available data into core components of health systems. Health systems scores were generated by grouping countries into deciles for each component and summing the deciles across domains for visual comparison among countries. The analysis was performed at the country level across 105 countries with at least one case of malaria after the year 2000.

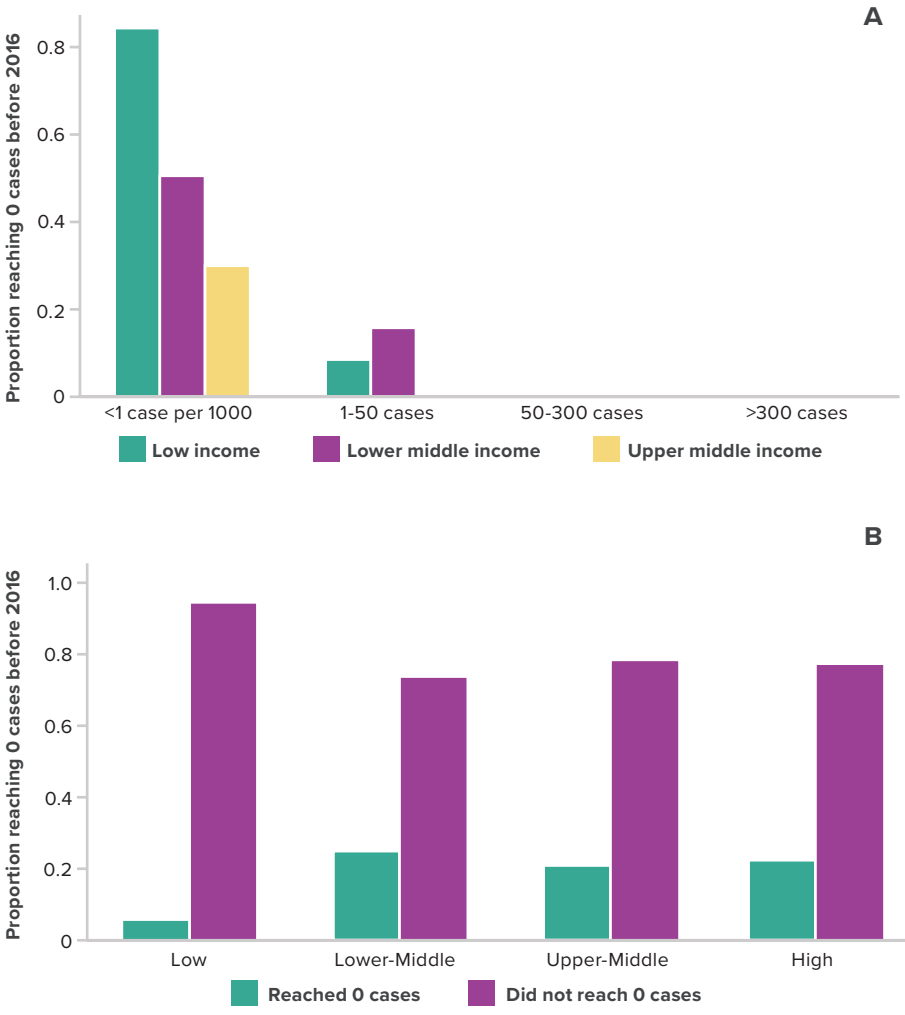
Between 2000 and 2016, several countries reduced their malaria incidence by 75% or more (Fig. 14). Major reductions in malaria cases occurred primarily in areas with relatively low incidence at baseline (i.e., <1 per 1000 population). Only two high-incidence countries (i.e., >300 cases per 1000) succeeded in reaching the 75% target: the Solomon Islands and Guinea Bissau. Seven other countries in the two middle-incidence categories (1–300 cases per 1000 in the year 2000) achieved a 75% reduction in cases: three continental nations (Senegal, Cambodia and Afghanistan) and four island countries (Sao Tome and Principe, Timor-Leste, Comoros and Vanuatu).

Fig. 14. Proportion of countries reducing malaria incidence by 75% or more by baseline incidence and income group, 2000–2016



Of the 105 countries that had cases of malaria between 2000 and 2016, 17 countries eliminated malaria by 2016 (Fig. 15). As expected, most of these countries started with a low number of cases in 2000. Only three countries from the medium-incidence category at baseline eliminated malaria (Paraguay, Sri Lanka and Tajikistan). Of these countries, the highest starting incidence was Sri Lanka with malaria incidence of 13.2 cases per 1000 in 2000. In the low-incidence category, although the low-income group had the greatest proportion of countries that achieved elimination, overall, the low-income group had the fewest countries reaching elimination compared to higher income groups.

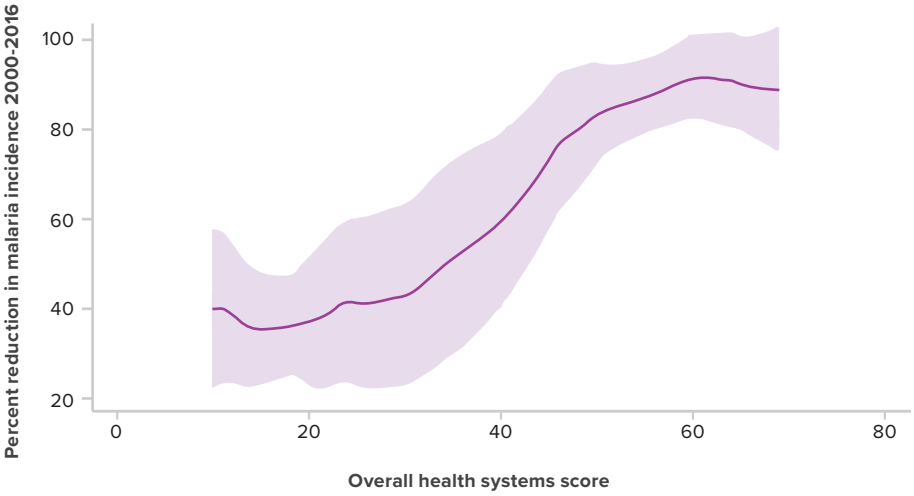
Fig. 15. Proportion of countries eliminating malaria by 2016 by (A) baseline incidence and (B) income group



Health systems scores ranged from 10 in the country with the weakest health system (Chad) to 69 in the country with the strongest health system (Republic of Korea). The three countries with the lowest health systems scores were Chad, South Sudan and Central African Republic, while the highest scoring countries in our dataset were Argentina, Brazil and Republic of Korea.

Health systems scores between 30 and 60 were strongly correlated with progress in malaria control, although the relationship was less strong towards the ends of the scale (Fig. 16).

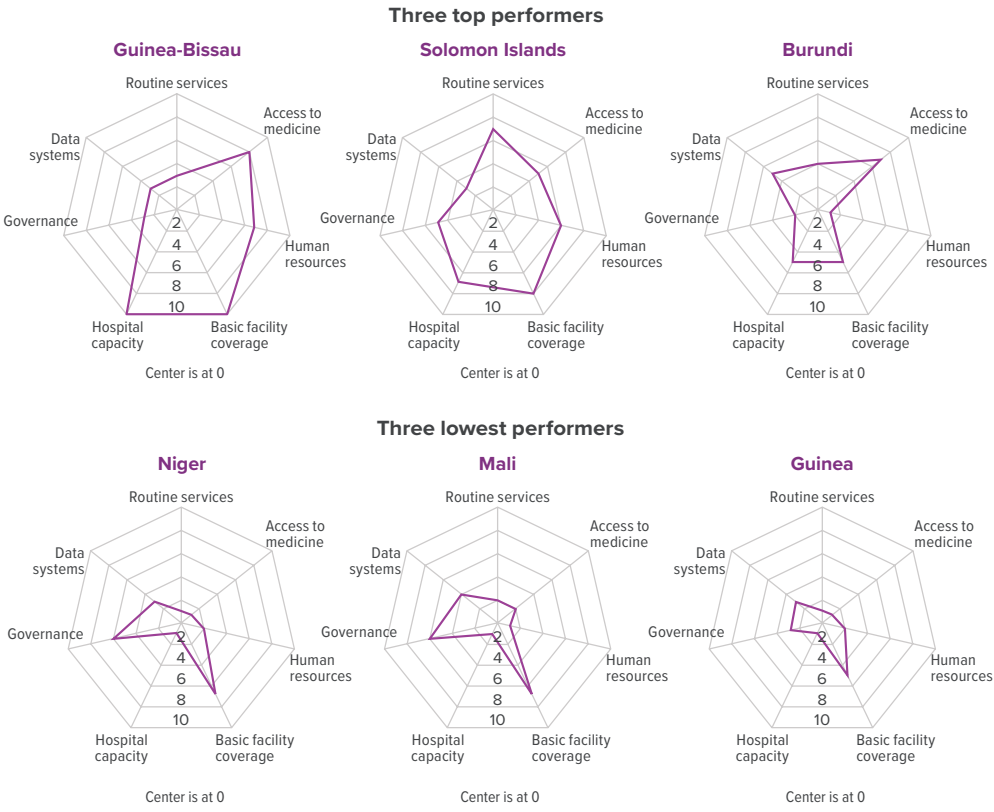
Fig. 16. Health systems score and percent reduction in malaria incidence, 2000–2016[a]



a The graph shows the kernel-weighted local polynomial smoothed relationship between reductions in malaria cases and total health system scores.

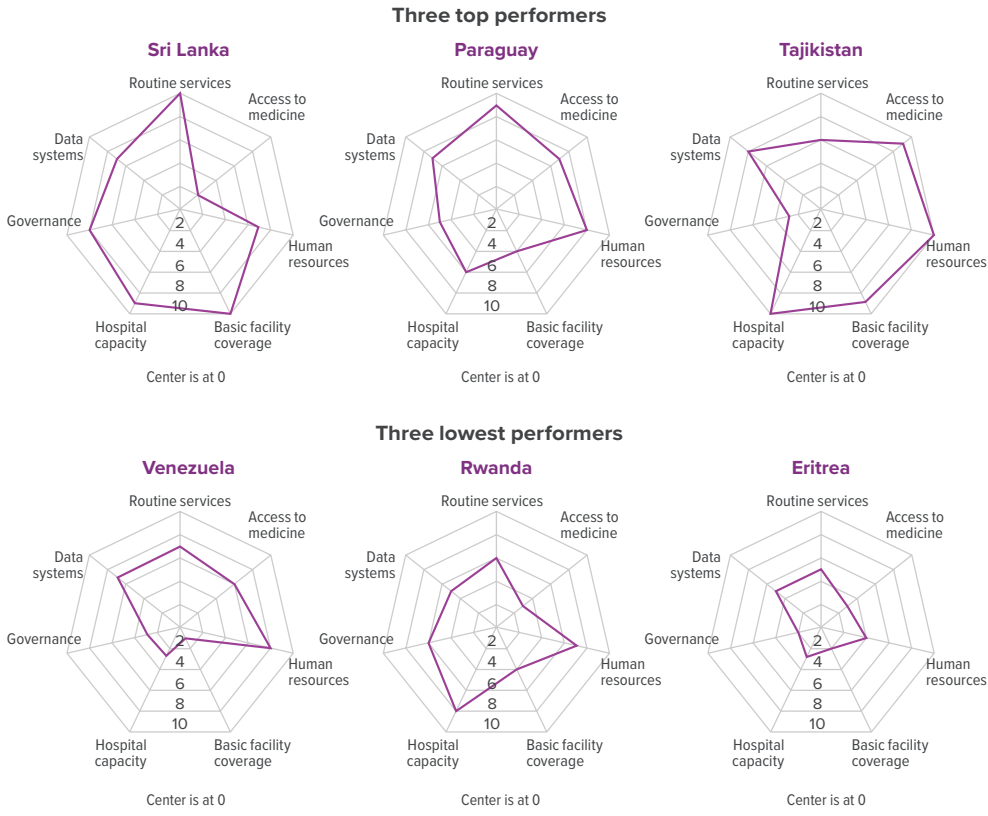
The health systems scores of the countries that experienced the greatest relative reductions in malaria (top performers) compared to those with the lowest reductions (low performers) were markedly different among the high-incidence countries; however, no single domain was consistently associated with high or low reductions in malaria incidence (Fig. 17).

Fig. 17. Health systems scores for highest and lowest performers with respect to relative change in malaria incidence among high-incidence countries, 2000–2016



Among middle-incidence countries, there were some differences between the health systems scores of the highest and lowest performers (Fig. 18). In terms of percent reduction in malaria incidence, the three most successful countries in the entire sample period were Sri Lanka, Tajikistan and Paraguay. All three had an initial incidence of over one case per 1000 and achieved a 100% reduction in malaria incidence between 2000 and 2016; all three had high health systems scores (>45). Among the lowest performers, Rwanda achieved a moderate health systems score overall (39), but experienced a massive increase in malaria incidence after 2012. Venezuela scored well on data systems, staffing and service delivery, but showed major gaps in access to medicines, spatial coverage and governance; the country's overall political and economic situation deteriorated substantially over the five years when there were observed increases in malaria. Eritrea also experienced an increase in cases between 2000 and 2016 and scored poorly on health systems (score of 24).

Fig. 18. Health systems scores for highest and lowest performers with respect to relative change in malaria incidence among middle-incidence countries, 2000–2016



Overall, it was not surprising that stronger health systems were associated on average with greater reductions in malaria incidence during the period 2000–2016. None of the countries that were malaria-endemic in 2000 and achieved zero malaria by 2016 had health systems scores in the two lowest quintiles. However, given the diversity of health systems achieving progress in malaria control and elimination and the fact that some aspects of malaria control programmes often operate outside the PHC system (e.g., ITN and IRS campaigns), this study did not find any specific minimum threshold of health system capacity to achieve progress in malaria control. For example, among low-incidence countries, all countries that eliminated malaria had a health systems score of at least 30; at the same time, Bangladesh had a health systems score of only 19, but still managed to reduce malaria by 94%.

Comparing countries based on the declines in malaria they achieved demonstrates that countries with high incidence at baseline and relatively

weaker health systems were still able to make substantial progress in malaria control, as in the case of Burundi and Bangladesh. In such countries where there were reductions in malaria despite weak systems, key malaria interventions were delivered through vertical processes such as campaigns to overcome inherent health system weaknesses. The large heterogeneity in the characteristics of the health systems in high- and low-performing countries highlights the importance of context-specific and comprehensive malaria and health systems strengthening strategies. This speaks to the need to tailor the strategies of the GTS to the conditions and characteristics of the physical environment, health system and populations at subnational levels.

Community engagement for malaria elimination and eradication

Much can be achieved with effective implementation of interventions led by governments or external partners. However, the history of eradication efforts shows that community engagement in its broadest sense is a key determinant of the speed of progress and achievement of the final goal. Permanently breaking the cycle of disease transmission between parasites, mosquitoes and humans will require careful orchestration of a range of public health responses and interventions that cut across sectors and jurisdictions. Eradication is also dependent on intentional collaborative action by committed communities, key stakeholders and national authorities involved in control and elimination efforts.

Community engagement is a process of continuous relationship-building in which those affected by a problem or issue are central to decision-making and determining appropriate responses. It requires the establishment of trust through early and ongoing communication, as well as mechanisms for coordination and collaboration across many implementing partners and stakeholders. Analysis of malaria responses during complex emergencies (see the previous section on "Threats posed by complex emergencies") has demonstrated the importance of involving communities in all aspects of the planning and implementation of context-specific responses until final certification of malaria elimination is achieved, and potentially beyond as part of prevention of re-establishment. Meaningful engagement with communities should be combined with the power and role of community-based and civil society organizations, not only to support more favourable outcomes for malaria, but also to strengthen demand-driven and people-centred care as an integral component of PHC and UHC *(187, 188)*.

For the purposes of the SAGme, community engagement has been considered in its broadest, most inclusive sense through the full participation of people and their leaders in areas at risk of malaria, including elements of the health system and agencies of relevance to malaria prevention, political commitment, government participation and leadership. Community does not just mean the end-user of services; community also includes members of the health services who have their own skills, experiences and perspectives and who should be meaningfully engaged in the process of planning and implementing the activities they are entrusted with. National and subnational leadership, community ownership, co-planning and ongoing collaboration are integral to the processes essential for success.

Community engagement efforts can range from social mobilization activities with community leaders to health education in the community, to engaging community members in self-care or as community health workers (for example, in support of community diagnosis and IRS), to involving health service personnel in the planning and monitoring of their activities. Importantly, a critical success factor is the meaningful involvement of the community in planning processes, programme implementation, and monitoring and evaluation *(189)*. At its best, community engagement has the potential to strengthen community empowerment and transparency and accountability among all key stakeholders. At its worst, engagement with community has the potential to burden community members with the unintended consequences of consultation fatigue, stress, and financial and time losses *(190, 191)*. Many interventions labelled as community engagement can be characterized as top-down, expert-led efforts designed to achieve behavioural change by informing or persuading community members, rather than by creating a sense of shared decision-making and strategic execution *(192)*. While such interventions may bring community members into contact with a programme, campaign or goal, they are often treated as passive recipients of messaging campaigns rather than as active participants in their own health care.

There is increasing recognition of the need to move beyond traditional mobilization, advocacy and educational approaches to explore ways to build co-production in health care, with a focus on health services, communities and other stakeholders working together to achieve health goals *(193)*. Conditions and opportunities must be created to support the co-production of health in a way that places people at the centre of malaria eradication considerations. In this context, trust and mutual understanding become the drivers for engaging in partnerships and relationships with authenticity, care and purpose. If community engagement in malaria programmes is to be successful, the interests of communities, government programmes and other stakeholders including donors must be identified so that shared goals can be negotiated *(187)*.

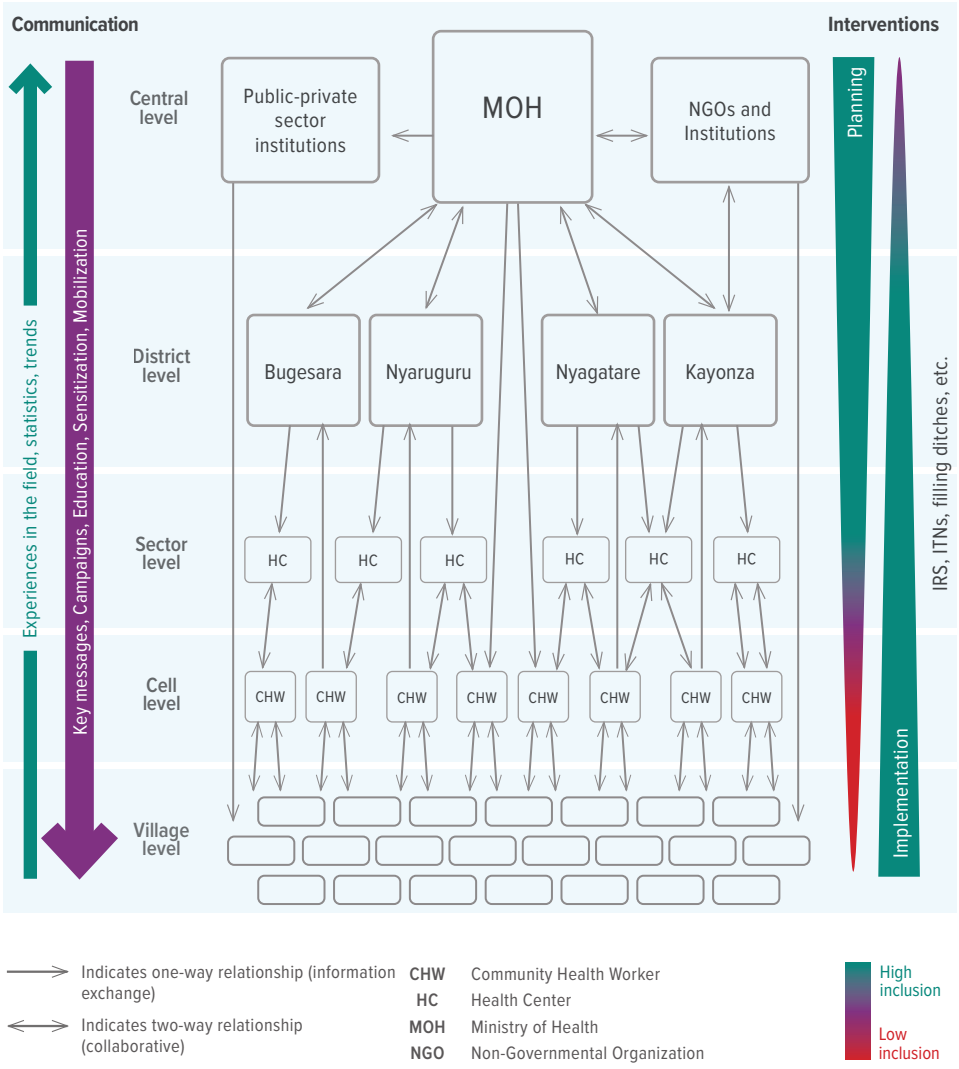
One particularly important part of the broader process of engagement is the interaction between communities at risk of malaria and the health system with which they need to collaborate for a successful outcome. In the absence of a community engagement framework that is specific to malaria, the WHO Community engagement framework for quality, people-centred and resilient health services (CEQ) was introduced and tested with the National Malaria Programme in four districts of Rwanda in 2018 *(194)*. The CEQ uses a combination of inquiry guides with focus groups and relationship mapping to identify community engagement practices in different regions of a country.

The aim of the activity commissioned by the SAGme was to demonstrate how the CEQ could illuminate opportunities for supporting and strengthening collaboration in national malaria programmes and to assess how community engagement could be institutionalized as a way of doing business rather than as an add-on. The CEQ was also used to support Rwanda's efforts to reinvigorate control efforts and return to the trendline of declining malaria morbidity and mortality experienced earlier this century.

The CEQ indeed helped to identify key areas in Rwanda's malaria programme where community engagement and collective action could be supported and further strengthened. The process of mapping relationships revealed a stark disconnect between those who planned the strategy for malaria control and elimination and those who implemented the interventions. This disconnect created situations where those planning strategies and activities were unaware of potential implementation issues that could have been addressed if those who implemented had been more engaged in the planning process (Fig. 19). Related to this issue, there was no mechanism to exchange information across the country, i.e., between districts, and to share potential solutions to bottlenecks and best practices. The assessment identified community health workers as key players in establishing a bridge between the community and the malaria programme. Focusing support on the potential role of community health workers could facilitate greater collaboration between the community and the programme, improving coordination and performance.

The CEQ assessment identified a strong willingness at every level to see increased community involvement in all aspects of malaria control and elimination efforts. This willingness was expressed both by district malaria officers and community members. One example of how the community can be better engaged in malaria control is in the programme for ITN distribution. Many at the local level do not understand the process of ITN distribution because their absence from the acquisition and distribution process has led to a lack of transparency, which in turn fosters the potential for confusion, false theories and resignation among community members. This problem can be remedied by greater inclusion of and collaboration with the malaria programme and community members in all aspects of the ITN distribution process.

Fig. 19. Relationship map between communities and levels of the Ministry of Health in four districts of Rwanda, 2018



Although community engagement is mentioned in almost every document written about malaria eradication efforts, there is a real lack of understanding of how to build community engagement into the fabric of elimination and eradication efforts. The CEQ provides a practical framework for national malaria programmes to identify areas where communities can be integrated into the co-planning, co-implementation and co-evaluation of malaria interventions in order to achieve better outcomes more quickly.

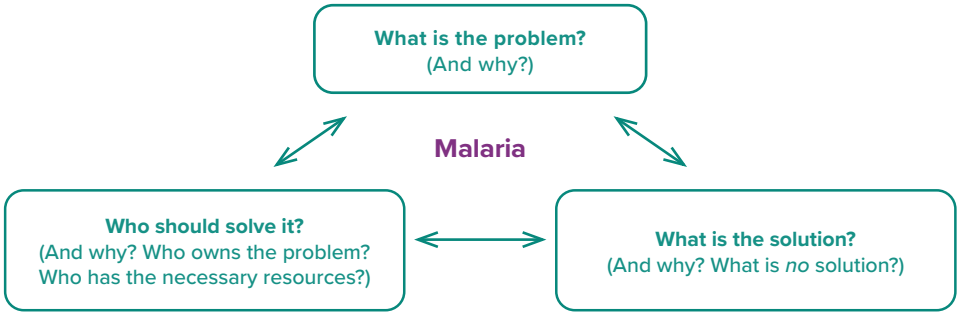
Approaches to global policies to end malaria

Global policies against malaria are developed and implemented in a policy setting whose characteristics must be appreciated when deciding on the way forward. This section looks at how different interpretations of the malaria problem by international organizations, national governments and communities lead to different approaches to influencing global policy-making around malaria control and eradication, and how the leadership and limitations of WHO affect the development and implementation of global malaria policy.

Interpreting and negotiating the malaria problem

Malaria is a complex disease that is marked by what scholars of science and technology studies have called **interpretative flexibility** *(195)*, meaning that different people or groups of people will interpret the malaria problem differently. There are three inter-related questions on which people might potentially disagree. These three questions and common follow-up questions are presented in Fig. 20 *(196)*.

Fig. 20. Inter-related questions that help to identify specific interpretations of the malaria problem



Source: Eckl, 2017 *(196)*.

This interpretative flexibility can be illustrated by observing the several approaches to (or traditions of) malaria control, three of which have been particularly relevant in the history of malaria control. There is an entomological approach in the tradition of Ronald Ross; there is a pharmaceutical approach in the tradition of Robert Koch; and there is a

socio-medical approach in the tradition of Angelo Celli. Although these three approaches are not necessarily incompatible, they can still result in conflicting recommendations when it comes to prioritizing measures against malaria. As a consequence, there has often been disagreement over policies against malaria, with the supporters of individual solutions convinced that theirs is the right answer.

Each approach, with its distinct interpretation of the malaria problem, depends on the cooperation of specific actors and on the availability of specific resources, as described by two of the three questions in Fig. 20: "who should solve the problem", which asks whose cooperation is needed; and "what is the solution", which asks what resources are needed. The issue of whose cooperation is needed is a key consideration when it comes to implementation of policies. A typical challenge has been that the interpretations of the malaria problem at the global level have not captured national, subnational or community interpretations. Similarly, those who focus on malaria have often overlooked the fact that malaria is not a priority for everyone. Finally, each interpretation highlights particular aspects of the malaria problem; while this has the advantage of representing malaria as a more readily intelligible problem, it can easily lead to oversimplification that does not acknowledge alternative interpretations (including the value of alternative solutions) or the overall complexity of malaria.

Exit and voice, demonstration projects, and organizational proliferation

Malaria policy has often been shaped by both voice and exit. **Voice** refers to the use of decision-making fora wherein the supporters of different views argue or campaign for their point in public. **Exit**-based policy-making can take various forms, but the unifying feature is that solutions are pursued independently of those who do not support them; at the same time, there is the hope that success will put pressure on those who did not originally support the solution *(197)*. For example, exit-based policy-making can involve demonstrating the superiority of a solution to (and interpretation of) the malaria problem through demonstration projects or field trials; these are often conducted with a mix of research-related and political goals in mind. A noteworthy case in point is the much-debated Sardinian campaign; the apparent success of this campaign was instrumental in the rise of DDT-based antimalarial policies and in the eventual decision to start a global malaria eradication campaign, even though closer inspection has revealed that Sardinia was not a clear-cut success story *(198)*.

While exit-based policy-making has the potential advantage that policies can be pursued in the absence of consensus, there are two particularly noteworthy recurrent problems with exit-based strategies. First, there is the question of whether successes in one setting can be reproduced in another setting, or, going one step further, whether successes in a circumscribed setting can

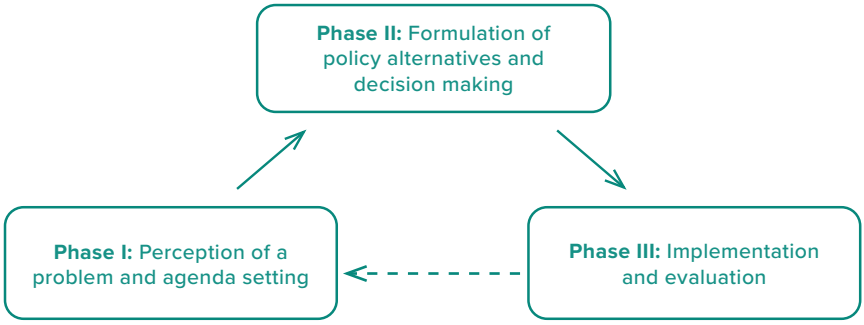
be scaled up to larger areas or even to the global level. Second, exit-based strategies tend to be biased towards solutions that have an easily discernible short-term effect that can then be used to persuade others to support the solution. In the context of malaria control, this has often meant that the sustainability of such solutions has not been properly assessed, nor has the influence of long-term changes on malaria transmission been systematically investigated. These problems are among the factors responsible for the remarkable ups and downs in malaria control, where enthusiasm is followed by pessimism. Moreover, they have led to a neglect of systemic change – both at the level of society and at the level of health systems.

While exit-based policy-making has been relevant throughout the history of malaria control, the proliferation of actors, partnerships and initiatives since the 1990s has given exit-based strategies an even more prominent role. The existence of alternatives to voice-based policy-making has undermined the formal authority of WHO "to act as the directing and co-ordinating authority on international health work" *(199)*. Other organizations may explicitly or implicitly promote different interpretations of the malaria problem than WHO and choose to use exit-based strategies to promote their approach. These developments are not unique to malaria, but represent a challenge in global health governance more broadly. While WHO is certainly a unique organization in the area of global health governance, its leadership has not remained unchallenged and must be continuously reaffirmed *(200)*.

The dramatic structure of the policy process and the challenge of implementation

These developments notwithstanding, voice-based policy-making in central decision-making fora like the World Health Assembly continues to be indispensable. While the general relevance of such decision-making fora has remained undisputed, the dramatic structure of the policy process can easily yield a misleading image of the process as a whole. The process of policy-making can be described in terms of three phases, summarized as perception of a problem (Phase I), decision-making (Phase II), and implementation (Phase III) (Fig. 21). Political practitioners, the media, the public and academia are united in their tendency to overestimate the relevance of one particular phase in the policy process, namely **the decision** in the narrowest sense of the term. In domestic politics, for example, the focus is on decisions that turn bills into law, and in international politics, the focus is on decisions that turn drafts into final agreements, resolutions and so forth. Although the notion that such decisions represent the climax of the policy process is not entirely wrong, this view is still misleading, as it focuses on the end point of Phase II while overlooking the other phases of the process described in Fig. 21.

Fig. 21. The three main phases of the policy process



Source: Eckl, 2017 *(196).*

Most of the decisions that are taken with a view to global health policies, such as World Health Assembly resolutions (the most common output of WHO decision-making), are not legally binding, or if they are, they are binding only for some actors. Disregarding the lack of legal authority of these policies leads to overestimation of the relevance of individual resolutions, while the majority of World Health Assembly resolutions are essentially expressions of a collective will that cannot be enforced upon individual Member States.[11]

Typically, World Health Assembly resolutions address different sets of actors whose behaviour is relevant for implementation. The most common actors that are addressed in World Health Assembly resolutions on global health policies are WHO's Secretariat (usually in the form of the Director-General), Member States, other international organizations and non-state actors. The key point is that most resolutions are binding for WHO but less so for its Member States, let alone for external actors. This point can be illustrated by the specific wording commonly used in resolutions. In adopting the GTS, for example, the Sixty-eighth World Health Assembly **requested** the Director-General, **urged** Member States, and **invited** and **called upon** partners to contribute to the implementation of the strategy *(201)*. In other words, while there is a general tendency to view the decisions themselves as the most important part of the policy process, this tendency is particularly problematic in the context of WHO, which has a long history of relying on non-binding policy instruments and whose

11 The kinds of decisions that the World Health Assembly takes and the rules under which they are taken depend on context. While Article 23 of the WHO Constitution has rarely been invoked, World Health Assembly resolutions on global health policies are commonly of a recommendatory nature for WHO Member States.

governance bodies have no direct formal authority over the various external organizations that have proliferated in the past two decades.

As indicated in the section on the interpretative flexibility of the malaria problem, each solution requires the cooperation of specific actors, but this does not imply that these actors share a common interpretation of the malaria problem. Crucially, since only a subset of the actors whose cooperation will be needed or who feel otherwise affected by the decision have access to international governance bodies and expert committees, all others can raise their voice only in the course of the implementation process. This applies to local populations in particular, as decision-making for malaria has a long history of engaging the local level too late. As divergent interpretations of the malaria problem are confronted in the course of implementation rather than during the decision-making phase, the practical challenge is to not dismiss the ensuing debates on the suitability of interventions as an irritating obstacle to implementation, but rather to embrace such debates as an important and anticipated aspect of global health policy implementation *(202)*.

Present dynamics

It is worth considering the structure of the global health governance architecture and WHO's role within it. WHO's formal authority is likely to remain constrained along the lines discussed above; health will generally remain based on soft law and, as such, WHO's governance bodies can primarily only **encourage** Member States to follow WHO's policies. Despite these limitations, WHO has the core function of providing leadership on matters critical to the health of all people and engaging in partnerships where joint action is needed. Recent statements and actions by WHO indicate that the Organization is ready to strengthen its leadership role in global health; however, the reliance on external donors makes this position more complex. The Director-General Dr Tedros Adhanom Ghebreyesus has called for WHO to be bold and creative in finding and cultivating partnerships to accelerate progress *(203)*. The value of harnessing the combined strength of the global health community and the complementary roles is articulated in the *Global action plan for healthy lives and well-being for all (204)*. WHO will remain central to global malaria agenda-setting and policy-making, but exit-based policies will also continue to play a role.

As discussed above, there is always a thin line between complementarity and competition. The multiple voices coming from different sectors, governments and organizations can, at times, generate tensions around the strategies and approaches for malaria eradication. Given the existing tensions around a grand strategy in the struggle against malaria, it seems that WHO and its Member States can make a valuable contribution by stating clearly where they stand and where they are heading. Considering that the agreed goals and targets of the GTS are already ambitious,

even putting malaria control back on track and following up on existing commitments could make a significant difference. Therefore, it is a good time to take another look at the GTS and RBM strategies to identify what it will take to get back on track to achieving the 2025 and 2030 targets. It will be possible to focus on current challenges and to harness the potential of some of the present dynamics as outlined in this section. Moreover, the vision of eradication remains intact and an incremental approach that builds on the current global strategy provides enough flexibilities for ambitious countries that want to move towards elimination.

A pragmatic, strategic and humanitarian way forward

Malaria eradication has been WHO's vision since at least 1955, and the SAGme has not been presented with any evidence to suggest that this vision should be abandoned. From a conceptual perspective, neither the existing challenges of malaria control nor the existence of zoonotic malaria species yet make it impossible to eradicate human malaria. However, it is more difficult to determine the future trajectories of factors that have an impact on malaria transmission (e.g., megatrends) and the potential for developing new tools to address the areas where the conditions are most suitable for malaria. As a result, it is not possible at this point to formulate a clear strategy with which to achieve the eradication of human malaria, nor is it possible to calculate what malaria eradication is likely to cost. In other words, it is premature to turn the vision of a malaria-free world into a goal with a definite target date.

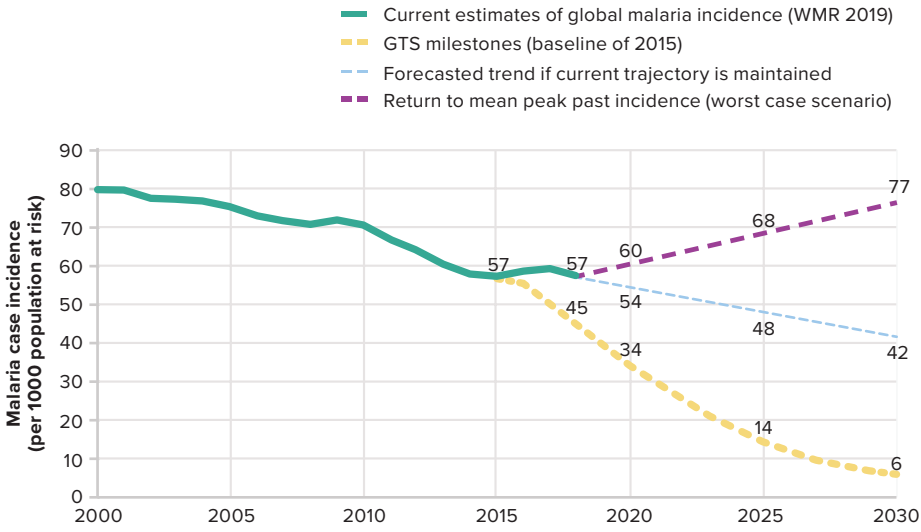
From this perspective, the time and energy of the global malaria and public health community will be well invested by harnessing opportunities and focusing on immediate challenges such as getting back on track to achieve existing global goals for malaria morbidity and mortality and investing in people-centred health systems. An intensified focus on the present situation does not mean that the future should be disregarded, but the lack of clarity regarding long-term projections should not distract from what can be done now. While it has proved challenging to anticipate malaria scenarios for 2030, 2050 or beyond, there are agreed goals, targets and milestones in the GTS that can help to monitor and evaluate current developments and formulate scenarios for the next 10 years.

Getting back on track to meet GTS targets

Malarious countries are increasingly falling into one of two groups. On the one hand, a growing number of countries (49) have fewer than 10 000

cases per year and are therefore nearing elimination *(5)*. The WHO E-2020 initiative, launched in 2016, identified 21 countries with the potential to reach zero cases by 2020, and the world is currently on track to meet the 2020 GTS milestone of elimination in 10 countries that had malaria transmission in 2015 *(205)*. In stark contrast, despite significant progress between 2000 and 2015, the GTS targets for a 40% reduction in malaria mortality rates and incidence by 2020 are likely to be missed by a wide margin (Fig. 22). The global incidence of malaria has remained fairly unchanged since 2015, hovering around 57 cases per 1000 population at risk.

Fig. 22. Comparison of progress in malaria case incidence considering three scenarios: current trajectory maintained (green), GTS targets achieved (yellow) and worst case scenario that is a return to mean peak past incidence in the period 2000–2007 (purple)



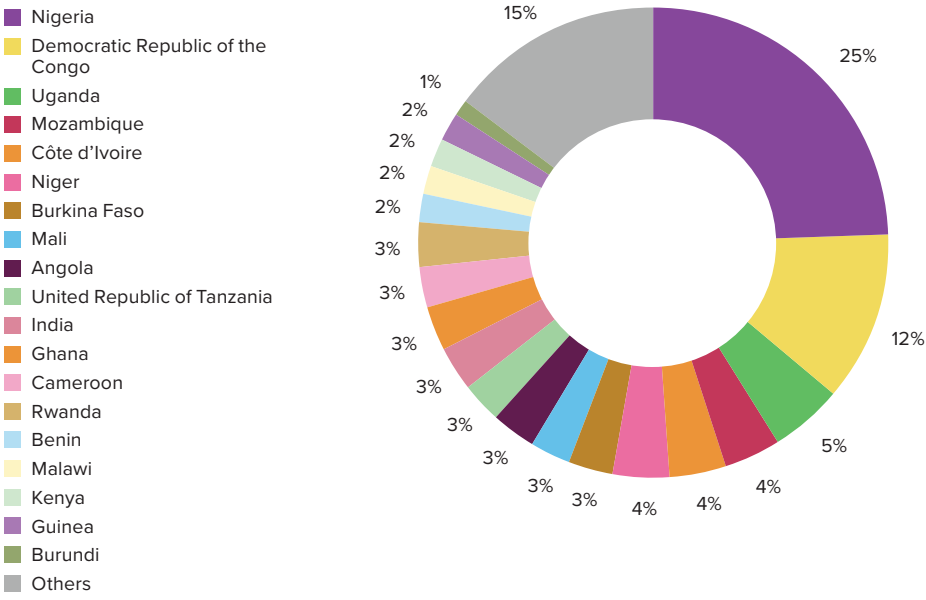
GTS: *Global technical strategy for malaria 2016-2030*; WHO: World Health Organization; WMR: *World Malaria Report*.

Source: WHO, 2019 *(5)*.

The majority of malaria cases and deaths occur in just 11 countries, all but one of which are in sub-Saharan Africa *(5)*. In 2018, around 68% of the estimated case burden and 65% of the estimated deaths globally occurred in 10 countries in sub-Saharan Africa and in India (Fig. 23). Nigeria accounted for the highest proportion of cases globally (25%), followed by Democratic Republic of the Congo (12%), Uganda (5%), Côte d'Ivoire (4%), Mozambique (4%) and Niger (4%). Nigeria, Democratic Republic of the

Congo, United Republic of Tanzania, Niger and Mozambique accounted for 48% of all malaria deaths globally. All told, annually, nearly 152 million cases and 263 000 deaths occur in these 11 high-transmission countries.

Fig. 23. Estimated country share of total malaria cases, 2018



Source: WHO, 2019 *(5)*.

Without more detailed data, it is difficult to identify with certainty why global progress against malaria has stalled. Many factors have undoubtedly contributed to the focal distribution of burden and mortality in these high-burden countries. These include, among others, underlying vectorial capacity; sociodemographic and epidemiologic risk factors; and weak health systems, leading to poor access to care and suboptimal malaria intervention coverage. Coverage gaps could be related to a variety of health system issues, including available financing, commodity shortages, supply chain and delivery challenges, and demand-side issues. Funding for malaria has essentially plateaued since 2010, hovering around US$ 2.5–3.0 billion annually. The expected growth in populations at risk in malaria-endemic countries in sub-Saharan Africa will translate into substantial declines (>25%) in per capita investment for most countries.

In November 2018, WHO and RBM launched the country-led HBHI approach as a mechanism to get the 11 highest burden countries back

on track to achieve the 2025 GTS milestones. The approach, which demonstrates the flexibility of the GTS to react to changing circumstances, has the following four key response elements that work synergistically to improve the current business model:

1. Galvanize national and global political attention to reduce malaria deaths. No one should die from malaria, which is a preventable and treatable illness. A successful technical response relies upon a broader societal shift that integrates the powerful role of affected communities, high-level national political leadership and the complementary role of global advocates. The approach will draw upon and amplify the benefits arising from existing social movements, such as Zero Malaria Starts with Me, and the political opportunities of UHC and PHC to identify and overcome the sociopolitical barriers impeding access to prevention and treatment services for malaria and other health priorities *(206)*.

2. Drive impact in country through strategic use of information. National malaria programmes and technical partners will use a context-specific analytical framework to identify challenges that affect malaria control in areas of high malaria burden. The analytical framework relies on a comprehensive assessment of transmission intensity, the malaria entomological profile, access to services, and other health system and socioeconomic factors that contribute to high mortality and morbidity. The ambition is to generate a very granular picture that can be used to identify the appropriate mix of interventions and a customized health systems response plan for every unique high-burden area in each country.

3. Establish best global guidance, policies and strategies suitable for a broad range of contexts. National and subnational decisions will be guided by global guidance. All available evidence will be analysed to identify the appropriate mix of technical interventions across a broad range of subnational contexts. As part of WHO's core normative functions, the Global Malaria Programme (GMP) will review current WHO guidelines and policy recommendations to take into account different epidemiological and entomological settings, health system characteristics, existing levels of intervention coverage, socioeconomic status and other critical contextual factors. The response will be science-based, data-driven and focused on value for money, prioritizing different packages of interventions for high impact. The approach will continue to be refined based on programme experience and learning.

4. Implement a coordinated country response. Based on the analysis of each country's unique context, ministries of health will work with in-country technical and implementing partners to refine and align their approach for reducing malaria mortality and morbidity in the high-burden target areas. This refined approach will be incorporated into the existing national

malaria response roadmaps and into broader sector planning, budgeting processes and subnational plans.

The HBHI approach is not a funding mechanism, nor is it a separate programme. It is a renewed movement wherein countries are in the driver's seat and enabled, through strong partnership support, to re-energize their fight against malaria. The approach has the following guiding principles. It is:

- country-owned, country-led, and aligned with the GTS, the health-related SDGs, national health goals, strategies and priorities;
- focused on high-burden settings;
- aimed at a demonstrable impact (with an aggressive approach to reducing mortality while ensuring progress is on track to reach the morbidity targets);
- characterized by context-specific packages of malaria interventions, optimally delivered through appropriate channels, including a strong PHC foundation;
- enhanced through a multisectoral approach;
- enabled by a diverse mix of partners, working collaboratively and aligning technical and financial support with locally defined priorities.

By November 2019, the HBHI approach had been initiated in Burkina Faso, Cameroon, Democratic Republic of the Congo, Ghana, India, Mozambique, Niger, Nigeria and Uganda. The remaining countries of Mali and United Republic of Tanzania are expected to hold their national consultation meetings by the end of the first quarter of 2020. The HBHI approach will be supported in all malarious countries in Africa as the continent progresses towards elimination of malaria.

The HBHI approach provides a prime example of a targeted response within the existing GTS. The GTS offers an agreed platform for global malaria control while also providing flexibility. This flexibility can be used to react to unforeseen challenges (such as the stalling of progress after 2015) and to harness current opportunities (such as the development of new tools and increased country leadership). Following such an incremental, flexible approach for achieving the vision of a malaria-free world provides an opportunity to progress towards the ambitious targets that have already been agreed upon, while making fine-grained adjustments where needed.

A successful approach to malaria eradication

As described above, to accelerate progress towards achieving a world free of malaria, a pragmatic, strategic and humanitarian approach should involve supplementing efforts to reduce burden and achieve sequential elimination of malaria in countries and regions, while setting the stage for

an eventual time-limited eradication campaign. The burden reduction goals set out in the GTS of a 90% reduction in malaria incidence and mortality rates by 2030 are clearly on the pathway to eradication. Extra attention to the highest burden areas in the near term will save millions of lives while advancing eradication goals, noting that the areas of highest burden at this time are likely to be the last places to achieve elimination and, therefore, eradication. At the same time, countries currently approaching elimination will benefit from a reduced burden of malaria in their region, as this will enable them to achieve elimination more quickly, promoting regional elimination and eventual eradication.

To achieve malaria eradication, there are six areas that will require focused effort.

1. Reinforcing the GTS

The GTS provides a comprehensive and flexible framework to guide countries in their efforts to accelerate progress towards malaria elimination and a world free of malaria. The target of reducing global malaria incidence and mortality rates by at least 90% by 2030 (from 2015 levels) is an ambitious but critical step towards eradication. The GTS emphasizes the need for universal coverage of core malaria interventions for all populations at risk and highlights the importance of using high-quality surveillance data for decision-making. It also identifies areas where innovative solutions will be essential for attaining the goals of the strategy, and summarizes the estimated global costs of implementation. The GTS was developed in close alignment with RBM's *Action and investment to defeat malaria 2016–2030* in order to ensure shared goals and complementarity *(31)*.

The strategies in the GTS have been largely adopted by countries at the national level but are not yet fully reflected in subnational operational plans. The key pillars of the GTS – universal access to malaria prevention diagnosis and treatment, acceleration of efforts towards elimination and transforming surveillance into a core intervention – must be adapted to local conditions through a process of subnational stratification that defines the populations at risk and considers the variability in environment, populations and health systems present in all countries to define the appropriate mix of interventions. The process of stratification and defining appropriate intervention mixes according to defined criteria and local data results in subnational strategies that can be planned, implemented and monitored towards specific subnational targets, allowing different parts of a country to move towards elimination at different speeds. Countries with a significant burden of malaria will need to start by prioritizing interventions to reduce mortality and clinical cases, but as transmission declines, countries will increasingly implement strategies designed to interrupt and eliminate transmission. Most countries will need assistance with applying the GTS to their local needs; this is an important role that

WHO, RBM, PMI and other agencies can play in supporting the adaptation and implementation of targeted strategies. Organizations financing malaria activities, including the GFATM, PMI and DFID play an important role in helping to translate strategies into fundable activities.

The GTS recognizes the goal of national malaria elimination as another important step towards global eradication. By 2030, the GTS calls for elimination of malaria from 35 out of the 92 countries in which malaria was transmitted in 2015. The world is currently on track to achieve this goal, with more than 10 countries reaching at least one year of zero indigenous malaria cases by 2020 and 39 reporting fewer than 10 000 cases – a somewhat arbitrary threshold that suggests elimination is within reach by 2030 *(5)*. Although countries have generally reached a low level of malaria transmission because of stronger health systems and comprehensive implementation of the GTS strategies, without additional high-level advocacy and programmatic support to cover the last mile, many countries have seen their progress stagnate for several years, or worse, have experienced resurgence. Country-owned efforts to rapidly address bottlenecks in the implementation of elimination activities must continue, as should WHO efforts to promptly certify countries as malaria-free once they meet WHO criteria. In turn, countries that achieve certification can serve as an inspiration to others, providing novel solutions to common problems and presenting realistic examples of what can be achieved even with existing tools.

Regional and subregional approaches to elimination can help to address the problems of malaria along international borders. As many malaria foci cross into neighbouring countries, it will be necessary to ensure that interventions do not stop at borders but extend throughout areas at risk. If interventions are limited to one side, they will only address a fraction of the factors determining malaria transmission and a small proportion of the population at risk. Bilateral and multilateral cooperation will be essential to working across borders, with an emphasis on the need for local-level meetings between health officials on either side to develop relationships and improve communication and coordination.

The SAGme views the strategy and goals of the GTS, already agreed to by the World Health Assembly, as critical to move the world closer to achieving eradication. However, the results from the analyses presented in this report show that other elements should be added to the strategy in order to strengthen the approach, ensure political commitment and increase the financing for malaria. In particular, there should be an increased emphasis on actively engaging communities in malaria control and elimination efforts, strengthening partnerships with PHC and UHC groups, advocating for malaria in all policies, particularly in urban areas, and addressing the potential threats to eradication, as described.

The GTS should be reinforced with a dynamic series of rolling five-year and 10-year plans leading out of the critical 2025 and 2030 targets. These rolling plans should have clear targets and be subject to rigorous review in order to enable responsive modifications to strategy guided by an evolving risk-assessment and decision-making framework for eradication. With such a high-profile renewed and sustained effort, we will establish a platform from which a successful and time-limited eradication effort eventually can be launched.

In addition, WHO should generate renewed commitment to malaria through an updated World Health Assembly resolution. The agreed goals, targets and milestones of the GTS remain ambitious but achievable; as such, they should remain unchanged. Instead, the strategies and resource needs required to get back on track to achieve the 2025 and 2030 targets should be highlighted. WHO should again coordinate with RBM, as originally done with the GTS, in order to ensure that there is a consistent vision structuring high-level political engagement. This will help to ensure commitment and financing for malaria to achieve the goals of the GTS.

2. R&D for new tools

Although the existing imperfect tools that have been applied imperfectly have achieved remarkable impact, there is widespread consensus that the world currently lacks the transformative tools needed to achieve malaria elimination in the highest burden areas *(207, 208)*. One of the highest priorities for achieving a world free of malaria, therefore, is a renewed R&D agenda that improves the knowledge base and products necessary for achieving eradication. Over the last decade, malERA, a large, collaborative effort, has produced consensus on the tools, strategies and enabling technologies that need to be developed *(13)*.

Developing better tools for vector control must be a high priority *(209)*. In particular, areas with high levels of transmission sustained by highly efficient vectors will require radically new interventions to reduce vectorial capacity. In the section on “Eliminating malaria in the hardest places”, the SAGme analysis found that receptivity, or the underlying vectorial capacity of an area, is a prime independent determinant of the likelihood of elimination in the future. malERA has identified a number of potentially transformative approaches to sustainable vector control that require increased attention from the research community. However, there is also a need to increase investments in basic entomological surveillance and research, as new tools will result from better understanding of vector biology. Given the lack of trained entomologists in many malaria-endemic countries, attention must also be paid to increasing training opportunities to facilitate the basic and implementation science agendas.

A related but slightly different vector control issue is the development of new tools that can address vector species that are characterized by

outdoor biting or outdoor resting behaviours. The current core vector control interventions, ITNs and IRS, appear not to be as effective against such mosquitoes as they are against indoor-biting and indoor-resting vectors. New tools could focus on other aspects of mosquito biology, including outdoor feeding and resting, oviposition site preference, mating behaviour or sugar meal selection in order to address residual transmission *(209)*.

malERA also emphasized the critical need to identify tools to mitigate or avoid development of insecticide resistance among vectors so as to preserve the effectiveness of current and future insecticide-based interventions *(209)*. Reducing the risk of resistance involves developing a broader range of insecticides with novel modes of action, as well as developing strategies that minimize the emergence of resistance. Although it is hoped that new tools will use a variety of novel approaches to vector control, insecticide-based interventions are likely to remain the cornerstone of malaria control for several decades at least. This will require continued monitoring of resistance and effectiveness of strategies to reduce the impact of resistance when and where it arises.

Similar to the vector resistance issue, malaria treatment needs new drugs that have high barriers to the development of resistance. Additional important treatment considerations include the identification of drugs that reduce the duration of dosing required, while providing radical cure of all blood- and liver-stage parasites and eliminating mature gametocytes *(210)*.

Malaria caused by *P. vivax* remains a challenging control issue mainly due to the stage of the parasite that persists in the liver (hypnozoite) without causing symptoms but relapses periodically, again rendering the patient both ill and infectious.[12] *P. vivax* is the parasite with the widest geographic distribution, causing 7.5 million cases each year *(5)*. However, the limitations of current diagnostics for blood-stage parasites, lack of diagnostics for liver-stage parasites, and limited options for safe and efficacious treatment of the liver stage pose R&D challenges that are likely to be critical for malaria eradication *(210)*.

R&D is also needed to develop improved vaccines *(210)*. RTS,S/A01, a pre-erythrocytic vaccine, has demonstrated modest efficacy in preventing clinical malaria and is currently undergoing pilot implementation in three African countries *(211)*. However, this vaccine has not been evaluated for prevention of infection and transmission in late-stage clinical trials *(211, 212)*. malERA identified the goal for a pre-erythrocytic vaccine as being the complete prevention of liver-stage infection for at least one transmission

12 *P. ovale* also has an asymptomatic liver stage that causes relapses after the initial infection, but *P. ovale* has a significantly lower incidence of infection than *P. vivax*.

season. As a complementary approach, a blood-stage vaccine that can clear blood-stage infection and limit gametocyte densities could be used to reduce human-to-mosquito transmission. Transmission-blocking vaccines that inhibit parasite transmission from human to mosquito are also being pursued. In addition to further R&D into vaccines, malERA called for more research into monoclonal antibodies to prevent transmission by inhibiting binding of the parasite to liver cells.

Research is needed not only for new tools but also for improving health delivery systems to mitigate intervention effectiveness decay and improve programme efficiency *(213)*. Important areas of research to achieve eradication include approaches to optimally engage community members and community health workers in malaria elimination in collaboration with health systems; optimize the use of new technology; cost-effectively integrate malaria surveillance and response activities into the health system; and develop new tools to measure systems readiness for malaria elimination and prevention of re-establishment at local and subnational levels.

As demonstrated in campaigns against polio and smallpox, implementation science is required until the very end of an eradication programme to ensure that strategies are adapted to suit local conditions and to assess new tools. A recent report has identified the gap between licensure of new products and routine use and scale-up as a significant barrier to the uptake of new technologies *(214)*. As new tools become available, health care systems will be challenged with ensuring that new drugs, diagnostics, vaccines and vector control interventions are appropriate for the context in which they are to be deployed and are delivered appropriately and in time for use at the local level. More funding and focus on implementation science are needed to bridge this gap and to ensure that transformational new tools that receive WHO recommendations are adopted and implemented as quickly as possible.

Research and innovation are critical to improving the quality of cost-effective health products and the availability of health care interventions to those who need them the most. The *Global action plan for healthy lives and well-being for all* presents an opportunity to address key challenges in global research and innovation for health *(204)*. In particular, it calls for improved coordination and alignment of research priorities, and collaboration between global health partners, academia, private sector and product development partnerships in order to maximize respective mandates, capacities and capabilities.

In 2018, US$ 663 million was invested in basic research and product development for malaria, an increase of US$ 18 million from 2017 *(5)*. The gap between the current level of investment and WHO's estimation of annual R&D needs to achieve the GTS targets by 2030 (US$ 673 million)

has been narrowed. However, malaria receives less than 0.25% of the estimated global medical research expenditures, despite accounting for more than 1% of global disability-adjusted life-years due to ill health and 0.8% of global deaths *(215-217)*. The need to increase funding for malaria research is self-evident. The pursuit of transformative new tools and the research needed to get them evaluated, adopted and implemented at scale is likely to be costly, but will be key to unlocking the pathway to malaria eradication.

3. Access to affordable, quality, people-centred health care and services

The SAGme analyses found that health system quality is associated with malaria progress across the spectrum of malaria endemicity. To eliminate malaria and prevent the re-establishment of transmission, a country requires strong political commitment and investment in UHC, with a well-functioning PHC system at its base. UHC is regarded as a cornerstone for sustainable global development, as leaders and communities acknowledge that health is both a human right and essential to economic growth. UHC means that all individuals and communities receive the health care and services they need without suffering financial hardship. For malaria elimination and eradication, achievement of UHC means that individuals and communities will receive the prevention and treatment interventions most appropriate to their context without incurring high costs, in order to reduce the malaria burden and progress towards elimination and eventual eradication.

Malaria elimination and eradication will benefit from improved PHC and the achievement of UHC. This requires the strengthening of health systems in all countries, with robust financing structures at their foundation in order to ensure that financial risks are shared. Improving health care and service coverage also depends on the availability, accessibility and capacity of health workers to deliver quality, people-centred, integrated care. Investments in quality PHC will be key to achieving UHC. PHC ensures that people receive comprehensive care throughout their life, not just for the treatment of a specific problem. For malaria eradication, a strong PHC system should be able to provide the basic, life-saving and transmission-interrupting interventions as part of comprehensive attention to the health of individuals, including recognizing the need to provide treatment for individuals who are found to not have malaria.

Long-term political commitment is critical for scaling up and maintaining effective multisectoral responses to malaria and UHC/PHC. Additional resources, improved management, appropriate technical strategies and community engagement all depend upon intensified political commitment. Typically, government officials are the main targets for building political commitment, but for malaria, attention to a broader range of stakeholders inside and outside government will be needed. The relative importance of other actors will differ between countries but could include members

of parliament, community-based opinion leaders such as traditional or religious leaders, and civil society health advocacy groups. Political commitment to the goals of UHC/PHC and malaria can be influenced by taking advantage of windows of opportunity in the policy process, whether to raise awareness, create a cohesive malaria community or build new alliances.

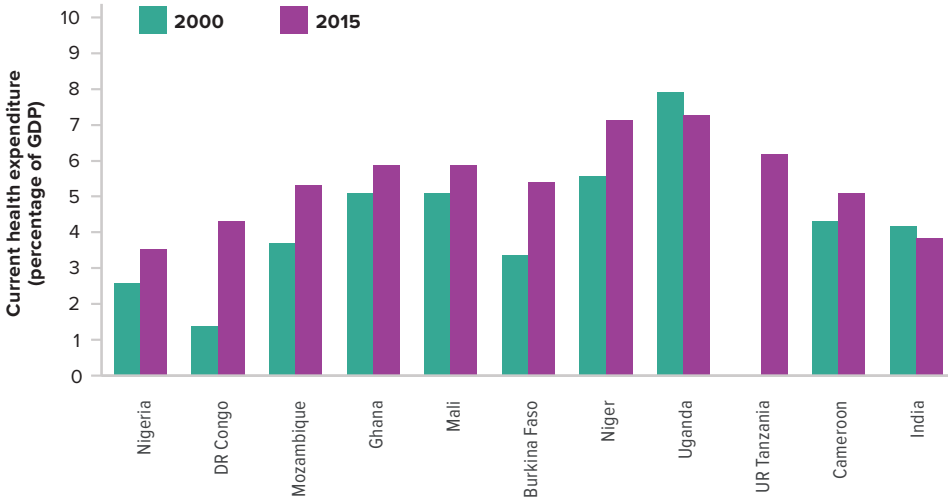
A strong leadership and governance framework will need to bring together health systems infrastructure, service delivery, civil society and communities to deliver UHC, including the components required for malaria elimination. WHO notes that good health systems governance requires that a strategic policy framework be in place, combined with effective oversight, coalition-building, regulation, attention to system design and accountability. The health system as a whole, not just the public system, must be overseen and guided to protect the public interest and improve health status. WHO has developed an action plan for health systems governance to help strengthen the role of government in setting directions for the health sector in a participatory and inclusive process *(218)*.

4. Adequate and sustained financing

Since 2010, global funding for malaria control and elimination has remained relatively stagnant at around US$ 3 billion per year, despite an estimated need of US$ 6.4 billion per year to meet the 2020 GTS targets *(4)*. In 2018, an estimated US$ 2.7 billion was invested in malaria by governments of malaria-endemic countries and international partners – a reduction from the US$ 3.2 billion invested in 2017 *(5)*. Governments of malaria-endemic countries contributed 30% of total funding (US$ 900 million) in 2018, a figure unchanged from 2017. In Abuja, Nigeria in 2001, African heads of state committed to allocating at least 15% of their annual budget to health, but no country has yet reached this target (Fig. 24). In 2019, African Union leaders agreed to increase domestic financing to achieve UHC and make a significant impact on global health, and it is hoped that this commitment will lead to increased domestic funding for malaria *(219)*.

Reviewing financing mechanisms for malaria eradication was beyond the scope of the SAGme but other groups, particularly the GFATM and members of the RBM Partnership, are actively engaged in this area and novel approaches to leveraging both domestic and donor financing are being explored. The Regional Malaria Elimination Initiative in Central America and the Dominican Republic is an example of a blended finance mechanism with private and public funds and results-based payments *(221)*. In-country mechanisms have been established in the Kingdom of Eswatini *(222)* and Zambia (End Malaria Council Zambia; https://www.nmec.org.zm/emc) to mobilize sustainable domestic resources for malaria elimination. However, increases in domestic financing need

Fig. 24. Progress towards the Abuja Declaration target of 15% of GDP expenditure on health among the HBHI target countries



DR Congo: Democratic Republic of the Congo
UR Tanzania: United Republic of Tanzania

Source: WHO Global Health Observatory *(220)*.

to be complemented by increases in international financing and a diversification of funding sources. More than 70% of international financing comes from just three countries: USA, UK and France. USA has provided the most funding for malaria control since the start of the GFATM and the launch of the PMI in 2005; USA accounted for 37.3% of all funding for malaria in 2018 *(5)*. The narrow international funding base for malaria must be expanded for eradication to become a reality.

5. Strengthened surveillance and response

The SAGme analysis of megatrends recognized that while the overall impact of megatrends is likely to favour malaria eradication, local effects will vary considerably. A reliable, rapid and accurate surveillance and response system will be fundamental for detecting and responding to changes in transmission that will result from global changes in urbanization, climate change and population growth. Surveillance systems will need to cover all populations at risk and provide high-quality, specific and essential data in real-time to inform response activities. Surveillance must be complemented by nimble response systems that can react in hours to days to changes in factors that affect malaria transmission in order to interrupt transmission, avert epidemics and prevent the re-establishment of malaria in malaria-free areas.

Data from surveillance systems are also required to improve the prioritization and selection of the appropriate mix of interventions in the local context. Stratification is the process by which local data are used to subdivide countries into areas (strata) with similar characteristics. Maximum impact will be driven by identifying the right mix of interventions, considering the local health system, malaria epidemiology and entomology, ecology and feasibility of implementation. National malaria programmes may need assistance from WHO and other partners to learn how to maximize additional and existing resources, using local data to identify the optimal mix of interventions in subnational areas.

Achieving the goals of the GTS requires that countries analyse needs and implement operational plans accordingly at subnational levels. In addition to using surveillance data for analysis and planning, surveillance data are also needed to monitor and evaluate implementation and progress towards achieving goals that are tailored to local conditions. Countries must be supported to further improve surveillance and response with strong community participation and an adequately resourced health workforce. For surveillance to become an intervention, as described in the GTS, greater resources must be allocated to strengthen and expand existing systems in order to make them fit for elimination and, ultimately, eradication.

6. Engaging communities

Communities play an essential role in the push towards a malaria-free world. It will be vital to develop field-tested approaches to improve community engagement. Eradicating malaria will require effective leadership that combines technical and community expertise and is driven by effective collaboration at all levels. Public institutions will have to earn the trust of their populations through co-planning and adapting malaria interventions and elimination strategies, co-monitoring the quality of programme services and interventions, and co-evaluating achievements and lessons learned. Integrating community engagement within malaria programmes could be undertaken as part of a larger, collaborative system that recognizes the importance of people-centred care and the value of effective linkages throughout the national, subnational and community levels, including for UHC.

Successful implementation of the GTS will require an approach to engagement with all relevant stakeholders based on collaboration, partnerships, partnership-building and co-creation of plans and management. Nowhere is this more important than with the engagement of affected communities as they prioritize the necessary areas for development and action. As the GTS is adapted to country-specific needs, it is important that community engagement be explicitly articulated to strengthen the technical and operational interlinkages between the

three pillars and two supporting elements of the strategy. The WHO CEQ provides a framework by which national malaria programmes can work in partnership with communities to further strengthen community involvement in co-planning and co-evaluating health systems in order to ensure that such systems are meeting the health needs they are meant to address *(194)*.

Conclusions

Malaria eradication must remain the global vision. The SAGme recommends taking a proactive, strategic, thoughtful and humanitarian approach to achieving eradication by first tackling the immediate challenges posed by a stagnation in progress; re-emphasizing the need for R&D and implementation science; contributing directly to the UHC/PHC agenda to strengthen health systems; ensuring that subnational, national and regional strategies are based on solid, evidence-based recommendations and comprehensive, flexible and accurate surveillance systems; and more directly engaging affected communities in control and elimination efforts. National ownership of the malaria elimination efforts that will lead to global eradication must be the foremost component of this approach. Countries must move under their own direction while being supported and encouraged by WHO and partners to progress as quickly as possible towards elimination and, eventually, eradication. The GTS provides a flexible platform with milestones and targets as reference points that can be used to adjust strategies as conditions change and new tools and approaches become available. Reinforcing the GTS with some key findings from the SAGme analyses will help to lay a strong foundation for eradication.

Ridding the world of a parasite that overwhelmingly affects the poor and vulnerable would be a remarkable step towards global health equity and improved economic conditions in the poorest parts of the world. The SAGme unequivocally supports this goal, and analyses of future scenarios for malaria suggest that eradication is feasible. Exactly when and exactly how we will get there is not yet clear. There is general agreement that the transformative tools that are needed to address the highest burden areas are not yet available, and the uncertainty around when these tools might become available means we cannot yet set a time-bound goal for eradication. Similarly, the different rates of implementation of national strategic plans for malaria elicit significant variation and uncertainty in how quickly malaria incidence will decline. Reconsidering the GTS at periodic intervals will enable recognition of inflection points in the malaria trajectory that could put eradication within sight and trigger the launch of a final and successful time-limited eradication campaign.

To summarize the conclusions of the SAGme, we harken back to the 2001 effort of the WHO Commission on Macroeconomics and Health to understand how investments in health could save hundreds of thousands of lives each year, reduce poverty and spur economic development: “We must dream a bit, not beyond the feasible but to the limits of the feasible, so that we inspire” *(223)*.

Annexes

Annex 1
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Biographical sketches

Marcel Tanner, Chair
Professor Marcel Tanner was the Director of the Swiss Tropical and Public Health Institute (Swiss TPH) from 1997 until 2015, where he emphasized the importance of combining research, teaching and training with their translation into public health action, thereby covering the value chain from innovation to application. He was Professor of Epidemiology, Public Health and Medical Parasitology at the University of Basel and at the Federal Institute of Technology until his retirement in 2017. Since 2016, he has been the President of the Swiss Academy of Sciences.

With over 40 years of experience in research and implementing public health initiatives in low- and middle-income countries, Professor Tanner has devoted his professional life to developing new drugs and vaccines for the elimination of malaria and other poverty-related diseases and to finding new solutions to strengthen health systems in Africa and the Pacific region. He was co-investigator and coordinator of the first malaria vaccine trial in 1992, and, since then, he has participated in several major intervention trials on malaria (iron supplementation, intermittent preventive treatment) and schistosomiasis. His work has also highlighted urbanization, health service utilization and decentralization in health planning and resource allocation with extensive on-the-ground experience in Africa, Asia and Europe.

As a leading expert, he has been an expert advisor and member of various national and international boards and agencies, including WHO, University Hospital Basel, Wellcome Trust, Drugs for Neglected Diseases Initiative, Foundation for Innovative New Diagnostics, International Clinical Epidemiology Network Trust, Gebert-Rüf Foundation, Botnar Foundation and the European & Developing Countries Clinical Trials Partnership. Professor Tanner obtained a PhD in medical biology from the University of Basel and an MPH from the University of London. He has published over 700 research papers as well as numerous book chapters and reviews.

Scott Barrett
Dr Scott Barrett is the Lenfest-Earth Institute Professor of Natural Resource Economics at Columbia University in New York City, with appointments in the School of International and Public Affairs (SIPA) and the Earth Institute. He is also Vice-Dean of SIPA. He is a leading scholar on transnational and global challenges, ranging from climate change to disease eradication. His research focuses on how institutions like customary law and treaties can be used to promote international cooperation.

Before joining Columbia in 2009, he was a Professor at the Johns Hopkins University School of Advanced International Studies in Washington, DC, where he also directed the International Policy Program and the Global

Health and Foreign Policy Initiative. Before that, he taught at the London Business School. He has also been a visiting scholar at École Polytechnique, Harvard, Princeton, Yale, Université de Paris 1 Panthéon-Sorbonne and the Wissenschaftskolleg (Institute for Advanced Study) in Berlin. Among other affiliations, he is a Fellow and former Chairman of the advisory board of the Beijer Institute of Ecological Economics in the Royal Swedish Academy of Sciences. He is the author of numerous journal articles and two books, *Environment and statecraft: the strategy of environmental treaty-making* and *Why cooperate? The incentive to supply global public goods*, both published by Oxford University Press.

Dr Barrett has advised several international organizations, including the United Nations, the World Bank, the Organisation for Economic Co-operation and Development, the European Commission, and the International Task Force on Global Public Goods. He was previously a lead author of the Intergovernmental Panel on Climate Change and a member of the Academic Panel to the Department of Environment in the UK. Dr Barrett received his PhD in Economics from the London School of Economics.

Alex Coutinho

Dr Alex Coutinho is the former Executive Director of Partners in Health in Rwanda, where he partnered with the Government to strengthen health services in three districts that together serve 1 million people. He previously served on the Board of International Partnership for Microbicides from 2003 to 2010, chairing the Board from 2008 to 2010 and from 2019 onwards.

For more than three decades, Dr Coutinho has led large-scale public health programmes in Africa. He spent seven years as Executive Director of the Infectious Diseases Institute at Makerere University in Uganda, where he oversaw prevention, care and treatment research and services for HIV/AIDS, tuberculosis and malaria. Previously, he led The AIDS Support Organisation (TASO), the largest AIDS care and support organization in sub-Saharan Africa, and has served on public and academic sector teams working to strengthen health services and systems in the Kingdom of Eswatini, Rwanda and Nigeria. Dr Coutinho was a founding Board member of the Global Fund to Fight AIDS, Tuberculosis, and Malaria, serving as Vice-Chair of the Global Fund's technical panel for two years, and a former Chair of the Board of Directors of the International AIDS Vaccine Initiative.

Dr Coutinho holds a medical degree and Master's degree in Physiology from Makerere University and an MPH from the University of the Witwatersrand in South Africa.

Richard Feachem
Professor Sir Richard Feachem is Director of the Global Health Group at the University of California San Francisco (UCSF) Institute for Global Health Sciences and Professor of Global Health at both UCSF and the University of California, Berkeley. He is also a Visiting Professor at London University and an Honorary Professor at the University of Queensland.

From 2002 to 2007, he served as founding Executive Director of the Global Fund to Fight AIDS, Tuberculosis and Malaria and Under-Secretary-General of the United Nations. From 1995 to 1999, he was Director of Health, Nutrition and Population at the World Bank. Previously, from 1989 to 1995, he was Dean of the London School of Hygiene and Tropical Medicine.

As a leading expert in public health, he has served as Chairman of the Foundation Council of the Global Forum for Health Research; Treasurer of the International AIDS Vaccine Initiative; Council Member of Voluntary Service Overseas; and on numerous other boards and committees. He was a member of the Commission on Macroeconomics and Health, the Commission on HIV and Governance in Africa, and the Commission on Investing in Health. Most recently, he has served as Chair of the Lancet Commission on Malaria Eradication. Professor Feachem has published extensively on epidemiology, public health and health policy.

Professor Feachem holds a Doctor of Science in Medicine from the University of London, and a PhD in Environmental Health from the University of New South Wales. He is a Fellow of the Royal Academy of Engineering, an Honorary Fellow of the Faculty of Public Health of the Royal College of Physicians and the American Society of Tropical Medicine and Hygiene, and a member of the US National Academy of Medicine. Among other honours, Professor Sir Feachem was knighted by Her Majesty Queen Elizabeth II in 2007.

Nyovani Madise
Professor Nyovani Madise is the Director of Research and Development Policy and Head of the Malawi Office at the African Institute for Development Policy (AFIDEP). Her research focuses on global health issues, particularly untangling the influence of social and economic factors on health in low-income countries. Before joining AFIDEP, she was a Professor of Demography and Social Statistics at the University of Southampton. Professor Madise has previously worked as a Lecturer at the University of Malawi and as a Senior Research Scientist at the African Population and Health Research Center in Kenya.

Professor Madise's current research is on the social determinants of health in the specific areas of maternal and child health, adolescent sexual and

reproductive health, family planning, and food and nutritional security. Most of her work involves advanced statistical analyses of large, nationally representative data. Two new areas of research for her are women's empowerment and interdisciplinary work on the links between population, poverty and the environment. She has over 100 peer-reviewed research publications and sits on several advisory committees of research funders such as DFID, ESRC, Medical Research Council, Research Council Norway and the NWO-WOTRO of the Netherlands. She has previously served on the Wellcome Trust, UK Commonwealth Scholarship Commission, and as a member of the Guttmacher Institute Board. Professor Madise studied mathematics and economics at the University of Malawi and later obtained her Master's and PhD degrees from the University of Southampton.

Lindiwe Makubalo

Dr Lindiwe Makubalo is a South African public health professional who has worked extensively in public health and policy throughout her career. Dr Makubalo has served on several WHO technical and advisory committees and, at a national level, she served on the Medicine Control Council of South Africa. She is currently serving as the South African Health Expert to the WHO and other International Organizations and is based at the South African Mission in Geneva.

Dr Makubalo has led a research unit at the Medical Research Council of South Africa and held the position of Executive Director at the Alliance for Health Policy and Systems Research at WHO Headquarters. She previously served in another sabbatical placement at the WHO TDR where she was responsible for implementation research.

Dr Makubalo holds a PhD from the London School of Hygiene and Tropical Medicine. She served for many years as Cluster Manager responsible for Epidemiology, Research, Health Information Systems and Evaluation at the National Department of Health, as a member of the management team that led the reform of the South African health system in the first post-apartheid administration.

Kevin Marsh

Professor Kevin Marsh is a Senior Advisor at the African Academy of Sciences and Professor of Tropical Medicine at the University of Oxford.

Professor Marsh qualified in medicine at the University of Liverpool in 1978 and, after undertaking specialist training as a physician, he began his research career at the Medical Research Council Unit in The Gambia, working on the immunology of malaria. From 1985 to 1989, he was at the Institute of Molecular Medicine in Oxford and in 1989, with other colleagues, they established a series of research projects on the clinical epidemiology and immunology of malaria at Kilifi on the Kenyan

coast. These subsequently evolved and developed into an international programme (the KEMRI Wellcome Trust Research Programme) involving around 800 staff working across a number of countries in East Africa of which he was Director until August 2014. Professor Marsh has authored or co-authored over 450 publications on different aspects of malaria.

Throughout his career, he has had a particular interest in developing and strengthening research capacity and scientific leadership in Africa. He is currently supporting new initiatives for the acceleration of science in Africa at the African Academy of Sciences. He has been a member or chair of many global health advisory committees, including the WHO Malaria Policy Advisory Committee, which he chaired from its inception in 2012 to 2018.

Cheikh Mbacké

Dr Cheikh Mbacké is a Senior Fellow at the Center for Research on Applied Economics and Finance of Thiès (CREFAT), University of Thiès, Senegal. As Senior Fellow, he helps to mobilize resources to strengthen and sustain the centre and provides mentoring to staff and students at this young research centre. He has helped the centre develop a pan-African research, training and technical assistance agenda on generational economics and the demographic dividend.

Dr Mbacké is a recognized advisor in population and health research and training in sub-Saharan Africa. His advisory work serves various organizations across the world. Since July 2006, he has been Senior Advisor to the Population and Global Development programme of the William and Flora Hewlett Foundation based in California. He sits on the board of directors of numerous institutions, where he brings his experience of more than 30 years in building institutional and individual research capacities.

Previously, Dr Mbacké spent six years at the Sahel Institute in Bamako (1986–1992) and 14 years (1992–2006) at the Rockefeller Foundation where he headed the Foundation's programme for Africa and served as Vice-President for Administration and Regional Programs.

He began his career as a statistician at the National Census Bureau of Senegal in January 1976. Dr Mbacké, a statistician and population scientist by training, holds a BSc in Statistics from the Institute of Statistics and Applied Economics (INSEE) in Paris, an MSc in Demography from the Demographic Training and Research Institute (IFORD) in Yaoundé, Cameroon and a PhD in demography from the University of Pennsylvania in Philadelphia.

Mirta Roses
Dr Mirta Roses Periago is currently a member of the National Academy of Sciences of Buenos Aires. A former Director of PAHO from 2003 to 2013, she currently serves as a senior advisor in global health for Latin American and the Caribbean and sits on several international and national global health committees, such as WHO, the Global Fund Board, the RBM Board and Friends of DNDi.

Before assuming the position of WHO Regional Director for the Americas, she served two terms as Assistant Director of PAHO, from 1995 to 2003, being responsible for the direct supervision of all PAHO/WHO Representative Offices in the Americas, forming part of WHO's Directors of Programme Management Group (DPM) and the Global Programme Management Group (GPMG). She also served for seven years as PAHO/WHO Representative in the Dominican Republic (1988–1992) and Bolivia (1992–1995), developing technical cooperation programmes and gaining vast and successful experience in putting public health at the centre of development priorities.

Her international professional experience includes her work both as coordinator of the Epidemiological Surveillance Unit of the Caribbean Epidemiology Center (CAREC) in Trinidad and Tobago (1984–1986), where she provided service to all the Caribbean countries and as an epidemiologist in the Dominican Republic (1986–1987).

Dr Roses earned her MD from the Universidad Nacional de Córdoba, Argentina in 1969, completing her specialization in tropical medicine at the Universidade Federal de Bahia, Brazil in 1971. Her graduate studies also include a diploma in public health in 1974, a specialization in epidemiology in 1982 at the Escuela de Salud Pública in Buenos Aires, Argentina, and a specialist degree in clinical medicine and epidemiology of infectious diseases at the Universidad de Buenos Aires in 1976.

Philip Welkhoff
Dr Philip Welkhoff is Director for Malaria at the Bill & Melinda Gates Foundation (BMGF), joining in 2018 to lead the Foundation's strategy. Prior to this role, he served as a pro bono external advisor to various programmes, including Agriculture Development and Water, Sanitation & Hygiene.

Previously, he served as Director of Research at the Institute for Disease Modeling (IDM), where he helped develop computer simulations for malaria, polio and other disease transmission dynamics to assist public health professionals and other scientists in planning the eradication of different diseases.

Dr Welkhoff received his PhD from Princeton University in Applied and Computational Mathematics and has dual undergraduate degrees in Mathematics and Aerospace Engineering from the University of Texas, Austin. At Princeton, his work focused on computational neuroscience and biophysics-motivated models of decision-making. Also, while at Princeton, he began working on malaria and mathematical models of disease transmission. Beyond modelling disease eradication, Dr Welkhoff's research interests include technologies for improved public health in the developing world, as well as other global development issues, such as vaccine delivery, developing world nutrition and agriculture, and improved sanitation. He has served on the Board of the Fannie and John Hertz Foundation and serves as a senior interviewer for its graduate fellowship programme.

Xiao-Nong Zhou

Professor Xiao-Nong Zhou is Director of the National Institute of Parasitic Diseases at the Chinese Center for Disease Control and Prevention/ Chinese Center for Tropical Diseases (NIPD-CTDR), and Director for the WHO Collaborating Centre for Tropical Diseases, based in Shanghai, China. He is Chairman of the Sub-committee for Parasitic Diseases of the National Health Standard Committee of China, and is member of the Advisory Committee for the Healthy China Actions, State Council of China. He is a leading expert in the research and control of schistosomiasis and other infectious diseases, with over 30 years' experience in the field.

He obtained his PhD in Biology at the University of Copenhagen, Denmark in 1994, following his MSc in Medical Parasitology from Jiangsu Institute of Parasitic Diseases in China. On his return to China, Professor Zhou established a career in infectious disease research across the fields of ecology, population biology, epidemiology and malacology and worked as a Professor at the National Institute of Parasitic Diseases, where he was appointed Deputy Director in 2001 and Director in 2010.

Professor Zhou has written extensively on parasitology and parasitic diseases and has collaborated with the WHO Western Pacific Regional Programme Review Group on Neglected Tropical Diseases, WHO Scientific and Technical Advisory Committee of Neglected Tropical Diseases, WHO Foodborne Burden Epidemiology Reference Group, and the Scientific and Technical Advisory Committee of the UNICEF/UNDP/World Bank/ WHO Special Programme for Research and Training in Tropical Diseases (TDR). Professor Zhou has been the principal investigator on more than 10 national research projects, as well as several international cooperative projects supported by the WHO-TDR, IDRC (Canada), DANIDA (Denmark), National Institutes of Health (NIH), DFID and BMGF.

Former members

Christopher Elias, 2016–2017
Dr Chris Elias is the President of the Global Development Program at the Bill & Melinda Gates Foundation, where he leads the Foundation's efforts in a diverse range of programme areas aimed at finding new ways to ensure that solutions and products get into the hands of people who need them most.

Didier Fontenille, 2016–2017
Dr Didier Fontenille is a medical entomologist with more than 17 years of experience working on malaria and arboviruses, vector biology, genetics and control in Africa (Madagascar, Senegal and Cameroon). From 2005 to 2014, he directed the Infectious Diseases and Vectors: Ecology, Genetics, Evolution and Control unit (in French *Maladies Infectieuses et Vecteurs : Ecologie, Génétique, Evolution et Contrôle*) at the Institut de Recherche pour le Développement, Centre National de la Recherche Scientifique, Montpellier, France, managing 165 scientists in 11 countries.

Robert Newman, 2016–2017
Dr Robert Newman is the Director of The Aspen Management Partnership for Health, a public–private partnership to improve health systems and outcomes by collaborating with governments to strengthen leadership and management capabilities.

Ana Revenga, ad hoc member, 2016–2017
Dr Ana Revenga is a Senior Fellow in the Global Economy and Development Program at the Brookings Institution and an adjunct lecturer at the Walsh School of Foreign Service at Georgetown University.

Soumya Swaminathan, 2017
Dr Soumya Swaminathan is the Chief Scientific Officer of the WHO. Dr Swaminathan was Secretary to the Government of India for Health Research and Director-General of the Indian Council of Medical Research from 2015 to 2017.

Annex 2
Working groups

Working group 1: Potential economic benefits of malaria elimination and eradication

SAGme members
Scott Barrett (Columbia University, USA)
Richard Feachem (University of California San Francisco, USA)
Ana Revenga (World Bank, USA)

WHO secretariat
Pedro Alonso
Richard Cibulskis
Jeremy Lauer
Edith Patouillard*

Observer participants
Jean-Louis Arcand (The Graduate Institute, Switzerland)
Seoni Han (The Graduate Institute, Switzerland)
Nayantara Sarma (The Graduate Institute, Switzerland)
Pete Winskill (Imperial College, UK)
Scott Filler (Global Fund to Fight AIDS, Tuberculosis and Malaria, Switzerland)

Working group 2: Lessons learned from previous eradication efforts

WHO secretariat
Pedro Alonso
Kim Lindblade*

Observer participants
Justin Cohen (CHAI, USA)
Regina N. Rabinovich (Barcelona Institute for Global Health, Spain; Harvard TH Chan School of Public Health, USA)

Working group 3: Megatrends that will affect future scenarios for malaria

SAGme members
Cheikh Mbacké (University of Thiès, Senegal)
Mirta Roses (Independent, Argentina)
Philip Welkhoff (Bill & Melinda Gates Foundation, USA)
Xiao-Nong Zhou (National Institute of Parasitic Diseases, China)

WHO secretariat
Kim Lindblade
Charlotte Rasmussen
David Schellenberg*

Observer participants
Amelia Bertozzi-Villa (University of Oxford, UK)
Graham Brown (Independent, Australia)
Christopher Drakeley (London School of Hygiene and Tropical Medicine, UK)
Julian Eckl (University of St. Gallen, Switzerland, and University of Hamburg, Germany)
Peter W. Gething (Curtin University, Australia)
Peter McElroy (Centers for Disease Control and Prevention, USA)
Hannah Nissan (Columbia University, USA)
Regina N. Rabinovich (Barcelona Institute for Global Health, Spain; Harvard TH Chan School of Public Health, USA)
Malla Rao (National Institutes of Health, USA)
Laurence Slutsker (PATH, USA)
Madeleine Thomson (Columbia University, USA)

Working group 4: Characterizing the areas likely to be the last to eliminate

SAGme members
Didier Fontenille (Institut de Recherche pour le Développement, France)
Kevin Marsh (African Academy of Sciences, Kenya)
Robert Newman (AMP Health, USA)
Philip Welkhoff (Bill & Melinda Gates Foundation, USA)

WHO secretariat
Kim Lindblade*

Observer participants
Amelia Bertozzi-Villa (University of Oxford, UK)
Ingrid Chen (University of California San Francisco, USA)
Peter W. Gething (Curtin University, Australia)
Laurence Slutsker (PATH, USA)
Regina N. Rabinovich (Barcelona Institute for Global Health, Spain; Harvard TH Chan School of Public Health, USA)

Working group 5: Health systems readiness for malaria elimination and eradication

SAGme members
Alex Coutinho (Independent, Uganda)
Lindiwe Makubalo (South African Permanent Mission to the UN, Switzerland)
Marcel Tanner (Swiss Academy of Sciences, Switzerland)

WHO secretariat
John Aponte
Abdisalan Noor*
Asiya Odugleh-Kolev

Observer participants
Valentina Buj (UNICEF, Geneva)
Ingrid Chen (University of California San Francisco, USA)
Guenther Fink (Swiss Tropical and Public Health Institute, Switzerland)
Maitreyi Sahu (Swiss Tropical and Public Health Institute, Switzerland)
Richard Steketee (President's Malaria Initiative, USA)

Working group 6: Community engagement for malaria elimination and eradication

SAGme members
Alex Coutinho (Independent, Uganda)
Nyovani J. Madise (African Institute for Development Policy, Malawi)

WHO secretariat
Asiya Odugleh-Kolev*
Gunther Baugh
Salim Sadruddin*

Observer participants
Ingrid Chen (University of California San Francisco, USA)
John Parrish-Sprowl (Indiana University, USA)

Working group 7: Mitigating potential threats to malaria eradication

SAGme members
Chris Elias (Bill & Melinda Gates Foundation, USA)
Richard Feachem (University of California San Francisco, USA)
Mirta Roses (Independent, Argentina)
Soumya Swaminathan (Indian Council of Medical Research, India)

WHO secretariat
Charlotte Rasmussen*
Pascal Ringwald

Observer participants
Justin Cohen (CHAI, USA)
Beverly F. (Lee) Hall (National Institutes of Health, USA)
Bruno Moonen (Bill & Melinda Gates Foundation, USA)

Other observer participants without specific working group assignments:

Lawrence Barat (President's Malaria Initiative, USA)
Alexandra Cameron (Unitaid, Switzerland)
Susan Clapham (Department for International Development, UK)
Abdourahmane Diallo (RBM Partnership to End Malaria, Switzerland)
Rachael Hinton (Independent, Switzerland)
Joshua Levens (RBM Partnership to End Malaria, Switzerland)
Lelio Marmora (Unitaid, Switzerland)
Neena Valecha (National Institute of Malaria, India)
Dyann Wirth (Harvard University, USA)

*Indicates the lead WHO staff member.

Working papers

Papers submitted and available at: https://zenodo.org/communities/sagme/

Working group 1: Potential economic benefits of malaria elimination and eradication

Paper 1. Malaria and economic growth: revisiting the evidence
Jean-Louis Arcand (The Graduate Institute, Switzerland)
Richard Cibulskis (WHO, Switzerland)
Edith Patouillard (WHO, Switzerland)
Nayantara Sarma (The Graduate Institute, Switzerland)

A version of this working paper has been published as: Sarma N, Patouillard E, Cibulskis RE, Arcand J-L. Economic burden of malaria: revisiting the evidence. Am J Trop Med Hyg. 2019;101:1405–15.

Paper 2. Projected impact of investing towards universal coverage of malaria control interventions on economic outputs
Seoni Han (The Graduate Institute, Switzerland)
Jean-Louis Arcand (The Graduate Institute, Switzerland)
Jeremy Lauer (WHO, Switzerland)
Edith Patouillard (WHO, Switzerland)

Paper 3. The malaria elimination game
Scott Barrett (Columbia University, USA)

Working group 2: Lessons learned from previous eradication efforts

Paper 1. Lessons from the history of global policies against malaria and aspects of contemporary developments in global health governance
Julian Eckl (University of St. Gallen, Switzerland, and University of Hamburg, Germany)

Paper 2. Lessons for malaria elimination from the eradication of smallpox
Justin Cohen (CHAI, USA)

A version of this working paper has been published as: Cohen JM. "Remarkable solutions to impossible problems": lessons for malaria from the eradication of smallpox. Malar J. 2019;18:323.

Paper 3. Some lessons for malaria eradication from the Global Polio Eradication Initiative

Regina N. Rabinovich (Barcelona Institute for Global Health, Spain; Harvard TH Chan School of Public Health, USA)
Matiana González-Silva (Barcelona Institute for Global Health, Spain)

Paper 4. Lessons learned from the dracunculiasis (Guinea worm disease) eradication programme

Kim Lindblade (WHO, Switzerland)

Working group 3. Megatrends that will affect future scenarios for malaria

Paper 1. Megatrends and populations at risk of malaria

David Schellenberg (WHO, Switzerland)

Paper 2. Pathways to eradication: a quantitative exploration of malaria trajectories in Africa to 2050

Peter W. Gething (Curtin University, Australia)
Amelia Bertozzi-Villa (University of Oxford, UK)
Samir Bhatt (Imperial College, UK)
David Schellenberg (WHO, Switzerland)
Kim Lindblade (WHO, Switzerland)

Paper 3. Factoring climate change into malaria eradication strategy

Hannah Nissan (Columbia University, USA)
Israel Ukawuba (Columbia University, USA)
Madeleine C. Thomson (Columbia University, USA)

Paper 4. Land use and land cover changes: implication for malaria elimination

Adriana V. Diaz (London School of Hygiene and Tropical Medicine, UK)
Christopher Drakeley (London School of Hygiene and Tropical Medicine, UK)
Kimberly Fornace (London School of Hygiene and Tropical Medicine, UK)

Paper 5. History of urban malaria control in Africa: case studies of three contemporary cities

Caroline W. Kabaria (African Population and Health Research Center, Kenya)
David Schellenberg (WHO, Switzerland)

Robert Snow (KEMRI-Wellcome-University of Oxford Collaborative Programme, Kenya)
Abdisalan M. Noor (WHO, Switzerland)

Working group 4. Characterizing the areas likely to be the last to eliminate

Paper 1. The hardest places to eliminate: where, why, and how
Peter W. Gething (Curtin University, Australia)
Amelia Bertozzi-Villa (University of Oxford, UK)
Samir Bhatt (Imperial College, UK)

Working group 5. Health systems readiness for malaria elimination and eradication

Health systems and global progress towards malaria elimination 2000–2016
Maitreyi Sahu (Swiss Tropical and Public Health Institute, Switzerland)
Fabrizio Tediosi (Swiss Tropical and Public Health Institute, Switzerland)
Abdisalan M. Noor (WHO, Switzerland)
John J. Aponte (WHO, Switzerland)
Günther Fink (Swiss Tropical and Public Health Institute, Switzerland)

A version of this working paper has been published as:
Sahu M, Tediosi F, Noor AM, Aponge JJ, Fink G.
Health systems and global progress towards malaria elimination, 2000-2016. Malar J. 2020;19:141.

Working group 6. Community engagement for malaria elimination and eradication

Findings and recommendations from the community engagement work package "A call to support the emergence of quality, people-centered and integrated malaria programs and services"
John Parrish-Sprowl (Indiana University, USA)
Asiya Odugleh-Kolev (WHO, Switzerland)
Salim Sadruddin (WHO, Switzerland)

Working group 7. Mitigating potential threats to malaria eradication

Paper 1. Case study series on malaria in conflicts and emergencies
Gretchen Newby (University of California San Francisco, USA)

Paper 2. Non-human primate reservoirs of zoonotic malaria infection: an underappreciated barrier to malaria eradication?
Erik J. Scully (Harvard University, USA)

Paper 3. Simian malaria: Report on actions to mitigate threat of simian malaria on the road towards malaria eradication
Erik J. Scully (Harvard University, USA)

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