Potential for reduction of burden and local elimination of malaria by reducing *Plasmodium falciparum* malaria transmission: a mathematical modelling study

Jamie T Griffin, Samir Bhatt, Marianne E Sinka, Peter W Gething, Michael Lynch, Edith Patouillard, Erin Shutes, Robert D Newman, Pedro Alonso, Richard E Cibulskis, Azra C Ghani

Summary

Background Rapid declines in malaria prevalence, cases, and deaths have been achieved globally during the past 15 years because of improved access to first-line treatment and vector control. We aimed to assess the intervention coverage needed to achieve further gains over the next 15 years.

Methods We used a mathematical model of the transmission of *Plasmodium falciparum* malaria to explore the potential effect on case incidence and malaria mortality rates from 2015 to 2030 of five different intervention scenarios: remaining at the intervention coverage levels of 2011–13 (Sustain), for which coverage comprises vector control and access to treatment; two scenarios of increased coverage to 80% (Accelerate 1) and 90% (Accelerate 2), with a switch from quinine to injectable artesunate for management of severe disease and seasonal malaria chemoprevention where recommended for both Accelerate scenarios, and rectal artesunate for pre-referral treatment at the community level added to Accelerate 2; a near-term innovation scenario (Innovate), which included longer-lasting insecticidal nets and expansion of seasonal malaria chemoprevention; and a reduction in coverage to 2006–08 levels (Reverse). We did the model simulations at the first administrative level (ie, state or province) for the 80 countries with sustained stable malaria transmission in 2010, accounting for variations in baseline endemicity, seasonality in transmission, vector species, and existing intervention coverage. To calculate the cases and deaths averted, we compared the total number of each under the five scenarios between 2015 and 2030 with the predicted number in 2015, accounting for population growth.

Findings With an increase to 80% coverage, we predicted a reduction in case incidence of 21% (95% credible intervals [CrI] 19–29) and a reduction in mortality rates of 40% (27–61) by 2030 compared with 2015 levels. Acceleration to 90% coverage and expansion of treatment at the community level was predicted to reduce case incidence by 59% (CrI 56–64) and mortality rates by 74% (67–82); with additional near-term innovation, incidence was predicted to decline by 74% (70–77) and mortality rates by 81% (76–87). These scenarios were predicted to lead to local elimination in 13 countries under the Accelerate 1 scenario, 20 under Accelerate 2, and 22 under Innovate by 2030, reducing the proportion of the population living in at-risk areas by 36% if elimination is defined at the first administrative unit. However, failing to maintain coverage levels of 2011–13 is predicted to raise case incidence by 76% (CrI 71–80) and mortality rates by 46% (39–51) by 2020.

Interpretation Our findings show that decreases in malaria transmission and burden can be accelerated over the next 15 years if the coverage of key interventions is increased.

Funding UK Medical Research Council, UK Department for International Development, the Bill & Melinda Gates Foundation, the Swiss Development Agency, and the US Agency for International Development.

Copyright © Griffin et al. Open Access article distributed under the terms of CC BY. 2015. World Health Organization; licensee Elsevier. This is an Open Access article published without any waiver of WHO's privileges and immunities under international law, convention, or agreement. This article should not be reproduced for use in association with the promotion of commercial products, services, or any legal entity. There should be no suggestion that WHO endorses any specific organisation or products. The use of the WHO logo is not permitted. This notice should be preserved along with the Article's original URL.

Lancet Infect Dis 2016; 16: 465–72

Published Online January 19, 2016 http://dx.doi.org/10.1016/S1473-3099(15)00423-5

See Comment page 393

Medical Research Council Centre for Outbreak Analysis and Modelling, Imperial College London, London, UK (J T Griffin PhD, Prof A C Ghani PhD); **School of Mathematical Sciences, Queen Mary University of London, London, UK** (J T Griffin); **Global Malaria Programme, World Health Organization, Geneva, Switzerland** (M Lynch MD, E Patouillard PhD, E Shutes MPH, R D Newman MD, Prof P Alonso MD, R E Cibulskis PhD); **Spatial Ecology and Epidemiology Group, Department of Zoology, University of Oxford, Oxford, UK** (S Bhatt DPhil, M E Sinka PhD, P W Gething PhD); **Swiss Tropical and Public Health Institute, Basel, Switzerland** (E Patouillard); **and Universität Basel, Basel, Switzerland** (E Patouillard)

Correspondence to: Prof Azra C Ghani, Medical Research Council Centre for Outbreak Analysis and Modelling, Department of Infectious Disease Epidemiology, Imperial College London, London W2 1PG, UK **a.ghani@imperial.ac.uk**

Introduction

Rapid declines in malaria have been achieved globally during the past 15 years because of improved access to treatment and vector control. The estimated proportion of children younger than 5 years at risk from malaria who sleep under a bednet in sub-Saharan Africa has increased from less than 2% in 2005 to 68% (95% CI 61–72) in 2015,[1] and the estimated proportion of patients with confirmed *Plasmodium falciparum* malaria receiving appropriate treatment (artemisinin combination therapy) increased from less than 1% in 2005 to 16% (range 12–22) across countries in 2014.[1,2] This increase

Research in context

Evidence before this study

The previous global strategy for malaria outlined in the Global Malaria Action Plan (2008) set the goals of a 75% reduction in malaria incidence and near-zero deaths by 2015. Substantial progress has been made towards these goals, with an estimated 37% reduction in case incidence and 60% reduction in mortality rates between 2000 and 2015. New goals have now been set as part of WHO's Global Technical Strategy for Malaria 2016–30, endorsed by the World Health Assembly in May, 2015. To inform this goal setting, we reviewed the National Strategic Plans from all malaria-endemic countries and undertook a country-by-country review of previous trends in malaria cases for the 59 countries with sufficiently complete and consistent data. We searched the scientific literature using PubMed with the search terms "projection OR mathematical model" AND "malaria OR falciparum OR plasmodium", for English-language articles published between Jan 1, 2000, and Feb 6, 2015, but did not identify any modelling studies estimating the potential trajectories of *Plasmodium falciparum* malaria at a global level.

Added value of this study

Our modelled scenarios provide an indication of the potential additional benefit of accelerating strategies for prevention and treatment of *P falciparum* malaria over the next 15 years. These provide a consistent estimate across all 80 countries with persisting endemic malaria in 2010 and further provide a link between the necessary coverage and probable effect that cannot be ascertained from National Strategic Plans or case trends alone. The results from this exercise form part of the evidence used to set the goals for the WHO Global Technical Strategy for Malaria 2016–30.

Implications of all the available evidence

The evidence suggests that substantial further gains can be made by increasing existing methods to reduce the burden of malaria and move countries towards malaria elimination over the next 15 years. It also shows that further progress can be made with near-term innovations.

resulted in an estimated reduction in the annual global incidence of malaria of 37% and in malaria-specific mortality rates of 60% between 2000 and 2015.[3] Much of this progress has been in Africa, where transmission of malaria is most intense. Elsewhere, substantial progress has been made towards local elimination, with four countries (Armenia, Morocco, Turkmenistan, and United Arab Emirates) certified as malaria-free, nine entering the prevention of reintroduction phase, and 20 progressing to the pre-elimination or elimination phases.[1]

These gains can be attributed to the renewed political commitment to malaria control and elimination stimulated by the Millennium Development Goals and supported through global and national resource mobilisation. These efforts were aided by the first Global Malaria Action Plan, which was published in 2008 to align stakeholders' efforts to support endemic countries in reducing the burden of malaria.[4] The Global Technical Strategy for Malaria was developed by WHO to provide a vision and goals for malaria for 2016–30 along with a technical strategy for achieving these goals.[3] This strategy is complemented by the Action and Investment to defeat Malaria strategy from the Roll Back Malaria partnership, which guides the implementation and financing of activities to reduce and eliminate malaria.[5]

See Online for appendix

Here we describe the mathematical modelling undertaken as part of the development of the Global Technical Strategy to assess the feasibility of the proposed burden and elimination goals and the intervention coverage needed to achieve these goals, focusing on the 80 countries with persisting stable transmission of *P falciparum* malaria.

Methods

Transmission model

We used a mathematical model of the transmission of *P falciparum* to estimate the effect of different intervention strategies.[6,7] In the model, individuals begin life susceptible to *P falciparum* infection and are exposed to infectious bites at a rate that depends on local mosquito density and infectivity. Newborn infants passively acquire maternal immunity, which decays in the first 6 months of life. After exposure, individuals are susceptible to clinical disease[6] and severe disease[8] and are at risk of death. As they get older, the risk of developing disease declines through acquisition of naturally acquired immunity due to continued exposure. During adolescence, parasitaemia levels fall so that a high proportion of asymptomatic infections become sub-microscopic. Full mosquito-population dynamics were included in the model to capture the effects of vector control in preventing transmission, killing adult female mosquitoes, and the resulting reduction in egg-laying. The model was fitted to data for the relations between rainfall, mosquito abundance, entomological inoculation rate (the rate at which people receive infectious bites), parasite prevalence, clinical disease incidence, severe disease incidence, and death.[6–9] A range of interventions are included[7,9–11] (appendix).

Baseline endemicity

We restricted our analysis to the 80 countries in which *P falciparum* malaria was stably endemic (defined as having non-zero prevalence) in 2010.[12] Estimates of the spatial distribution of the human population were taken from the Global Rural-Urban Mapping Project[13] and overlaid with estimates of parasite prevalence in children

aged 2–10 years in 2010 at a resolution of 1 km.[12] We used these estimates to calculate the population-weighted mean parasite prevalence in each first administrative level (ie, province or state). We used UN world population projections to capture substantial population growth for rural and urban populations.[14]

Transmission intensity and vector species

We calibrated the baseline transmission intensity in the model in each first administrative unit with endemic transmission to match the estimated parasite prevalence separately for urban and rural areas (appendix). We made no further adjustments for countries in Africa, except Botswana, Madagascar, Namibia, and South Africa, for which more reliable reported case data were available. For these four countries and countries outside Africa, we scaled the mosquito density (retaining the spatial distribution at the first administrative unit) so that the estimates of uncomplicated malaria in 2010 matched those reported in the WHO 2013 World Malaria Report (WMR).[15]

To capture the global variation in *Anopheles* species, we combined estimates of the spatial distribution of vector species with estimates of their bionomics (appendix).[16–19] We accounted for seasonal variation in transmission in Africa based on rainfall patterns in each location.[20] Since the relation between vector species abundance and rainfall is more complex outside Africa, we assumed a single seasonal profile in south Asia and a non-seasonal profile elsewhere.

Existing intervention coverage

Data about country-specific coverage of interventions from 2000 to 2013 were taken from the WMR 2013,[15] with a few exceptions. For countries in Africa, we used the estimates of use of long-lasting insecticidal nets from 2000 to 2013 from a model combining data from the Demographic Health Survey, Malaria Indicator Survey, and Malaria Indicator Cluster Surveys with manufacturers' delivery data and countries' distribution reports.[21] For countries outside Africa, we used reports of coverage from National Malaria Control Programmes from 2000 to 2012, as reported in the WMR 2013.[15] Our model incorporates insecticide decay in long-lasting insecticidal nets and wear-and-tear over time. For all countries, coverage of indoor residual spraying from 2000 to 2012 was based on data from National Malaria Control Programmes as reported in the WMR 2013[15] and calculated as the number of people protected by indoor residual spraying each year divided by the population at risk.[15] For countries in Africa, antimalarial and artemisinin combination therapy and treatments received in the public or private sectors were based on modelled estimates of coverage from the Demographic Health Survey and the Malaria Indicator Cluster Surveys.[22] For countries outside Africa, we used data from the WMR 2013.[15] These coverage levels show treatment received in the public sector only. We used estimates from the WMR 2013 of the proportion of patients with malaria seeking care in the public and private sectors and mortality rates, and, for cases outside Africa, assumed that the treatment rate given in the private sector was half that given in the public sector.

Future scenarios

We simulated the potential effect of five intervention scenarios (panel). The first (Sustain) assumes that interventions remain at their 2011–13 coverage levels and provides a baseline for comparison with other scenarios. We considered two acceleration scenarios (Accelerate 1 and Accelerate 2) in which coverage of currently recommended interventions (vector control and seasonal malaria chemoprevention) and access to first-line

***Panel:* Summary of intervention scenarios**

Scenario 1: Sustain

Continue long-lasting insecticidal nets, indoor residual spraying, and access to treatment levels as in 2011–13.

Scenario 2: Accelerate 1

Vector control (modelled as long-lasting insecticidal nets) increased from 2013 levels to 80% access from 2015 to 2020 (or retained at present levels if higher), and maintained through continuous redistribution, replacing nets every 3 years.

Access to first-line treatment with artemisinin combination therapy in the public sector rose to 80% between 2015 and 2020 and maintained thereafter.

Access to first-line treatment with artemisinin combination therapy in the communities, as part of integrated community case management and in the private sector, increased to 50% between 2015 and 2025, with scale-up to 75% by 2030.

Seasonal malaria chemoprevention in areas in which it is currently recommended for children aged 6 months to 5 years with sulfadoxine–pyrimethamine plus amodiaquine scaled up to 80% coverage between 2015 and 2020.

Switch from quinine to injectable artesunate for severe disease between 2015 and 2020 for all patients with malaria admitted to hospital.

Scenario 3: Accelerate 2

Accelerate 1 scenario plus:

Access to long-lasting insecticidal nets rose to 90% from 2020 to 2025, with continuous distribution such that individual nets are replaced every 2 years from 2025.

Access to first-line treatment with artemisinin combination therapy in the public sector increased to 90% between 2015 and 2020, and maintained thereafter.

Rectal artesunate scaled up to 50% coverage by 2025 and to 75% by 2030, and assumed to reduce fatalities by 50% in patients with severe disease but not admitted to hospital.

Increase coverage of seasonal malaria chemoprevention to 95% from 2020 to 2025.

Scenario 4: Innovate (additional near-term methods)

Accelerate 2 scenario plus:

Longer-lasting nets with 4-year half-life from insecticide decay and wear and tear, from 2020 onwards.

Switch seasonal malaria chemoprevention drug to a compound with similar duration of protection that can also be implemented in areas of east Africa that are resistant to sulfadoxine–pyrimethamine.

Increase age range of seasonal malaria chemoprevention up to 10 years from 2020 onwards.

Reverse

Coverage of interventions declines to levels reported in 2006–08.

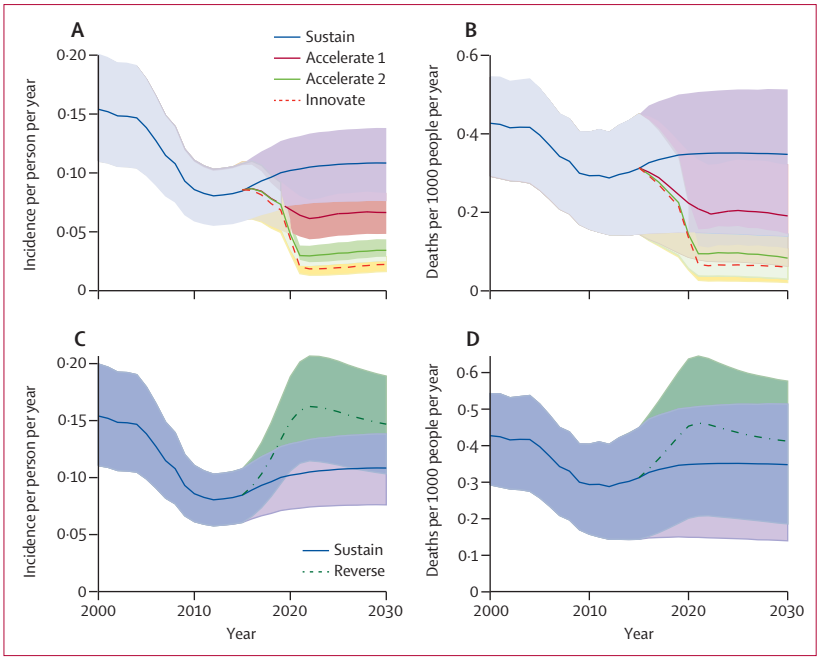


Figure 1: **Predicted trajectories of *Plasmodium falciparum* malaria under a range of scenarios* from 2000 to 2030**
Graphs show (A) the incidence of uncomplicated malaria and (B) mortality rates from malaria under the Sustain, Accelerate, and Innovate scenarios; (C) the incidence of uncomplicated malaria and (D) mortality from malaria under the Reverse scenario compared with the Sustain scenario. Incidence of uncomplicated malaria mortality are for all ages. Shaded bands around the mean projections show 95% credible intervals. *See panel for specifics of the scenarios.

treatment is increased to either 80% (Accelerate 1) or 90% (Accelerate 2) and case management is improved through a switch to injectable artesunate (from quinine) for management of severe disease. For Accelerate 2, we additionally introduced rectal artesunate for the pre-referral treatment of severe malaria at the community level. In the fourth scenario (Innovate), we included near-term innovations, including longer-lasting insecticidal nets and expansion of seasonal malaria chemoprevention with an alternative compound in seasonal areas of Africa (where at least 60% of the annual rainfall occurs in the peak 3 months of the year) with high levels of sulphadoxine–pyrimethamine resistance (where seasonal malaria chemoprevention is not currently recommended) plus expansion in the age range to children aged from 3 months up to 10 years. For all four scenarios we assumed no loss of effect due to drug or insecticide resistance. In a fifth scenario (Reverse) we considered the effect of a scale-back in intervention coverage to levels recorded in 2006–08 (appendix). This scenario could represent a loss of funding, or mimic the potential effect of reduced susceptibility of pyrethroid-based vector control.[23]

For all model runs we assumed that interventions remained at their 2011–13 coverage levels (depending on the data source) up to 2015. We then ran the simulation model at the first administrative unit for each intervention scenario from 2015 to 2030. To calculate the cases and deaths averted we compared the total number of cases or deaths under each scenario between 2015 and 2030 with the predicted number in 2015, accounting for human population growth. We calculated the population at risk at both national and subnational levels (appendix). Local elimination was established on the basis of 50 stochastic realisations and defined as elimination in at least 50% of the realisations. For all scenarios, we did a comprehensive uncertainty analysis in a Bayesian framework with results presented as approximate Bayesian 95% credible intervals (CrI).

Role of the funding source

Members of the Bill & Melinda Gates Foundation, UK Department for International Development, and US Agency for International Development provided input into the development of the scenarios through their formal roles on the Global Technical Strategy and Global Malaria Action Plan 2 scientific committees. The funders had no role in data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Figure 1 shows the predicted trajectories of the Sustain, Accelerate, and Innovate scenarios. With Sustain, we predicted a rise in case incidence by 28% (95% CrI 23–32) and mortality rates by 11% (1–20) by 2030 from 2015 levels (table). This predicted change was due to population-level loss of immunity induced by increased intervention coverage (appendix).

Under the Accelerate 1 scenario (present interventions scaled up to meet the universal coverage target of 80%) we predicted that case incidence would be reduced from 2015 levels by 21% (19–29) by 2030 (table). Similarly, we predicted that the incidence of mortality would be reduced from 2015 levels by 40% (27–61) by 2030 (table). The faster decline in mortality rates compared with case incidence was due to the additional effect of prompt first-line treatment and improved management of cases of severe disease. Overall, we estimated that this scenario would avert 1·7 billion cases (95% CrI 1·2 billion–2·3 billion) and 6·3 million deaths (3·2 million–8·7 million) deaths over the 15-year period (a mean of 110 million fewer cases [80 million–150 million] and 420 000 fewer deaths [210 000–580 000] per year) compared with the Sustain scenario.

Under the Accelerate 2 scenario, we predicted that case incidence would be reduced from 2015 levels by 59% (95% CrI 56–64) and mortality by 74% (67–82) by 2030 (table), averting a mean of 2·9 billion cases (95% CrI 2·0 billion–3·8 billion) and 10·4 million deaths (4·2 million–14·4 million) over the 15-year period (a mean of 190 million fewer cases [95% CrI 140 million–250 million] and 690 000 fewer deaths [280 000–960 000] per year) compared with Sustain. With

	Percentage change in case incidence (95% approximate credible intervals)			Percentage change in mortality rates (95% approximate credible intervals)		
	2020	2025	2030	2020	2025	2030
Sustain	21% (18 to 23)	27% (23 to 30)	28% (23 to 32)	11% (7 to 16)	12% (5 to 19)	11% (1 to 20)
Accelerate 1	−19% (−22 to −17)	−23% (−28 to −21)	−21% (−29 to −19)	−30% (−43 to −20)	−36% (−51 to −24)	−40% (−61 to −27)
Accelerate 2	−43% (−46 to −42)	−62% (−65 to −59)	−59% (−64 to −56)	−55% (−63 to −48)	−70% (−77 to −62)	−74% (−82 to −67)
Innovate	−48% (−51 to −46)	−77% (−79 to −75)	−74% (−77 to −70)	−57% (−65 to −51)	−79% (−85 to −73)	−81% (−87 to −76)

Positive values show an increase compared with 2015, and negative values show a decrease compared with 2015. Changes in incidence and mortality are per unit population and therefore do not show population growth. *See panel for specifics of the scenarios.

Table: **Effect of four scenarios* on the predicted global incidence of malaria cases and deaths by year, compared with 2015**

Innovate, further progress can be made, with cases reduced by an estimated 74% (95% CrI 70–77) and deaths by 81% (76–87) by 2030, averting an estimated 3·30 billion cases (95% CrI 2·37 billion–4·33 billion) and 11·5 million deaths (4·6 million–16·0 million) over the 15-year period (a mean of 220 million fewer cases [95% CrI 160 million–290 million] and 760 000 fewer deaths [300 000–1 070 000] per year).

With the Reverse scenario, we predicted a rise in case incidence and mortality rates above those estimated for the year 2000, in which coverage for both interventions (ie, longer-lasting insecticidal nets and treatment rates) was low (figure 1). This rise was due to loss of naturally acquired immunity as transmission declines, such that loss of coverage leads to rebound epidemics in many settings. Under this negative scenario we estimated an increase in case incidence of 76% (95% CrI 71–80) and in mortality of 46% (39–51%) from 2015 to 2020 (the peak time of the rebound). This rise translates to an estimated 521 000 additional deaths (95% CrI 216 000–725 000) in 2020 compared with 2015.

The predicted effect that can be achieved with the scenarios substantially varied between countries. The variation depended on both the intrinsic potential for transmission (which made it more difficult to reduce transmission in high-burden areas) and the extent to which interventions were already at high coverage before 2013. Overall, we predicted that 33 of 80 countries would achieve more than a 90% reduction in incidence—or an incidence of less than one case per 1000 individuals per year—under Accelerate 1; an additional nine countries were predicted to achieve this goal under Accelerate 2 (figure 2).

18 of these countries were predicted to be below the pre-elimination threshold of one case per 1000 individuals per year in 2015. Under Accelerate 1, we estimated that 13 countries would achieve local elimination by 2030, and 20 under Accelerate 2. With the Innovate scenario, we predicted that 22 countries would locally eliminate *P falciparum* by 2030, and that the burden in an additional 18 countries would fall below the pre-elimination threshold (figure 2).

Acceleration of coverage could substantially affect the global map of malaria endemicity. Under Accelerate 2,

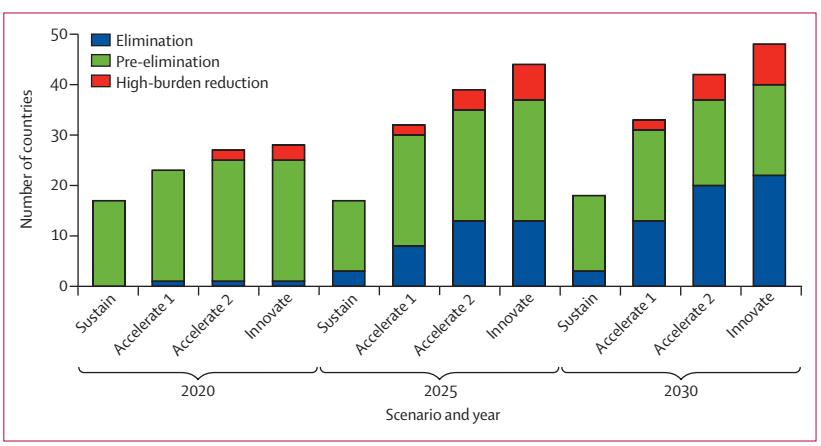


Figure 2: **Estimated number of countries meeting progress milestones under the Sustain, Accelerate, and Innovate scenarios***

Graphs show the number of countries achieving high-burden reduction, pre-elimination levels, and local elimination by the years 2020, 2025, and 2030. Elimination is defined as zero locally acquired cases in that year. Pre-elimination is defined as countries that do not eliminate but reach levels of less than one case per 1000 people per year. High-burden reduction is defined as countries that have not reached pre-elimination but reduce case incidence by at least 90% relative to 2015. *See panel for specifics of the scenarios.

we predicted that large areas of South America, and southeast and south Asia, would become free of endemic transmission by 2030, along with lower transmission achieved in some areas of Africa (figure 3). The videos show the predicted change in global distribution of *P falciparum* malaria from 2015 to 2030 under each scenario.

See **Online** for videos

Figure 4 shows how the global population living in at-risk areas would decrease as a result of the Accelerate 1, Accelerate 2, and Innovate scenarios from 2015 to 2030. Under Accelerate 2, if elimination is defined at the country level, the proportion living in areas that have eliminated *P falciparum* malaria by 2030 would be 6%. However, if elimination is defined at the level of the first administrative unit, then 36% would live in areas that have eliminated the disease. Also under Accelerate 2, we estimated that the population living in areas with persisting transmission (defined at the level of the first administrative unit) would decrease from 1·44 billion in 2015 to 1·23 billion in 2030—a 15% reduction despite a 25% increase in populations of areas that were malaria endemic in 2010.

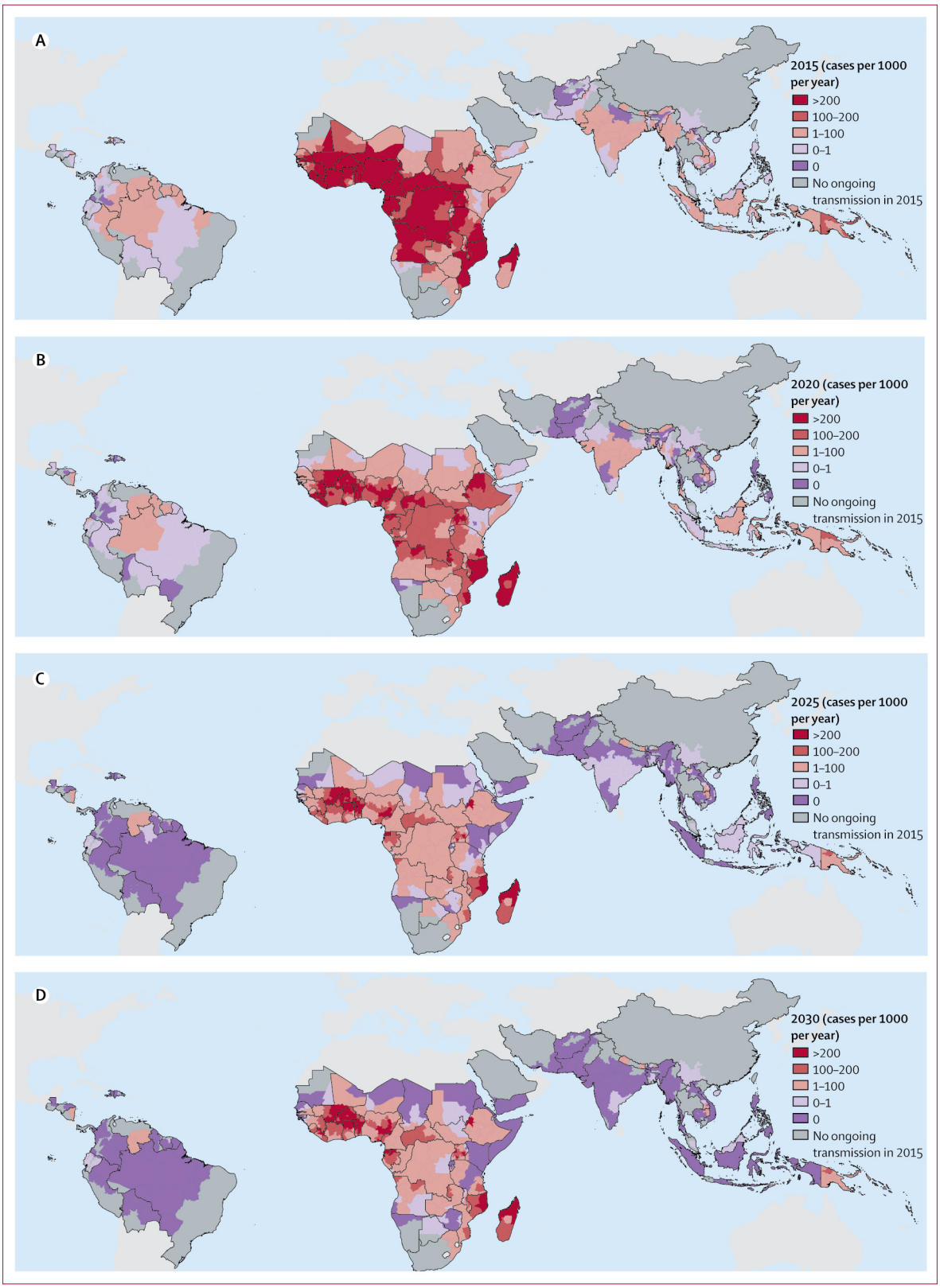


Figure 3: **Projected geographical distribution of *Plasmodium falciparum* malaria under the Accelerate 2 scenario between 2015 and 2030**
Graphs show projected distribution for the years 2015 (A), 2020 (B), 2025 (C), and 2030 (D). Red changing to pink shows a gradient of reducing case incidence. Purple areas are those in which local elimination is predicted. See videos for projections by year with all scenarios. See panel for specifics of the scenarios.

Discussion

Despite the gains made in reducing malaria transmission during the past 15 years, the burden of malaria remains high. Our results show that over the next 15 years additional substantial reductions could be achieved, provided malaria control interventions are scaled up towards the universal coverage targets set out in the original global malaria action plan.[4] In particular, if scale-up is accelerated so that 90% of the population in at-risk areas has access to vector control, chemoprevention, and appropriate treatment, we predict a marked global decline in malaria transmission that will result in a substantial decrease in case incidence and mortality rates, with a particularly large effect in the high-burden countries.

Our results also show the contribution that scaling up of coverage of currently recommended interventions could make to malaria elimination. Although timescales for elimination are difficult to predict, our results suggest that several areas in South America and Asia could eliminate malaria by 2030. Our modelled scenarios assumed that a high proportion of cases are identified and promptly treated, which is essential to prevent resurgent epidemics. Thus investment in information systems and surveillance will be essential.

Our results further show the fragility of malaria control. If intervention coverage remains at the levels achieved from 2011 to 2013, we predict a moderate rise in malaria incidence and mortality. This rise is due to the changing immunity profile in the population, with people born after interventions have been scaled up being exposed more slowly and hence acquiring their first and subsequent cases at an older age. If intervention coverage falls, or if interventions become less effective (which could occur, for example, if levels of resistance to the pyrethroids used in insecticide-treated nets continue to increase[23]), our simulations show the potential for resurgent epidemics, as noted in settings in which malaria prevention was removed before elimination had been achieved.[24] Thus, adequate intervention coverage must be maintained while transmission continues.

Although substantial progress can be made with current interventions, innovation to develop new products and strategies is urgently needed to accelerate further towards malaria elimination. Such innovation is particularly necessary in areas with intense transmission, in which high levels of intervention coverage are insufficient to lead to elimination or where substantial residual transmission happens because of a combination of human and vector behaviour.[25] Such innovation is also needed to effectively manage or contain resistance to insecticides and drugs.[23,26]

One limitation of our study is that the same scenario is applied ubiquitously across all countries with persisting stable malaria transmission. Although this method enables the magnitude of achievable gains to be estimated, tailored strategies are needed for different local contexts and to make best use of the finite resources available. These strategies will need strengthening of information systems so that appropriate intervention programmes can be designed, monitored, and adapted as malaria transmission declines. Some countries might be able to proceed more rapidly than assumed here, although in others with hard-to-access populations or instability due to behavioural or civil unrest, progress might be slower. Additionally, new methods and strategies are likely to become available (including focally targeted strategies for low transmission settings) and hence could accelerate the trends modelled here. Our results suggest that to achieve malaria eradication, investment in such methods is essential.

A second limitation is that our model was developed for *P falciparum* only. Although trends in *Plasmodium vivax* cases tend to track those for *P falciparum* in many countries, the former has proven more difficult to eliminate because of the hidden reservoir of parasites (hypnozoites) that can remain in the liver for months to years.[27] Several models for *P vivax* are now being developed to fill this gap.[28–30] Third, the strategies were applied at the first administrative unit with no connectivity. Finer spatial granularity and movement between locations is needed to guide individual country decisions and regional prioritisation, particularly as transmission declines and the spatial distribution of malaria becomes more heterogeneous. Finally, many factors not captured here might affect malaria transmission, including changing health systems, housing, education, climate, and land use.

In summary, reductions in malaria transmission and burden can be accelerated over the next 15 years if the level of coverage of current interventions is increased. However, to further accelerate efforts towards elimination, new transformative methods will need to be developed. Essentially, the momentum achieved up to

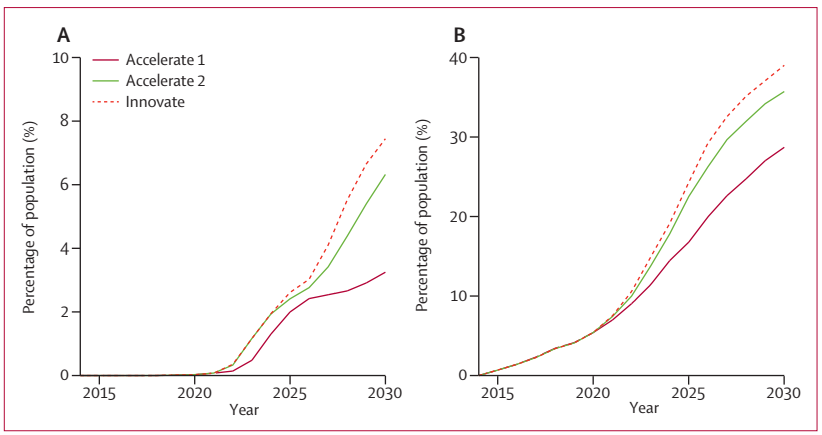


Figure 4: **Changing global population at risk of *Plasmodium falciparum* malaria under a range of scenarios between 2015 and 2030**

Graphs show the percentage of the population residing in areas that are malaria endemic before 2015 who are predicted to live in areas in which malaria has been locally eliminated in subsequent years. (A) Elimination is defined at the country level. (B) Elimination is defined at the first administrative level.

now should be continued, to reduce malaria burden and move rapidly towards the elimination, and ultimately eradication, of malaria.

Contributors

JTG, REC, and ACG designed the study with additional input from EP, ES, RDN, and PA. JTG did the model simulations. SB, MES, PWG, and ML provided input data and support for setting the parameters for the model. ACG drafted the manuscript. All authors contributed to writing of the report.

Declaration of interests

JTG reports grants from the UK Medical Research Council (MRC) during the study. ACG reports grants from the Bill & Melinda Gates Foundation and the MRC during the study; and grants from the Malaria Vaccine Initiative, Medicines for Malaria Venture, the Integrated Vector Control Consortium, the Wellcome Trust, National Institutes of Health, and WHO, and other financial support from Oxford Policy Management, the UK Department for International Development, The Global Fund for AIDs, Tuberculosis, and Malaria, and non-financial support from GlaxoSmithKline, outside the submitted work. All other authors declare no competing interests.

Acknowledgments

JTG is an MRC Methodology Fellow (G1002284) funded by the UK Medical Research Council (MRC) and the UK Department for International Development (DFID) under the MRC/DFID Concordat agreement. ACG acknowledges research grant support from the Bill & Melinda Gates Foundation (OPP1068440) and Centre support from the MRC and DFID under the MRC/DFID Concordat agreement. EP is supported by funding from the Swiss Development Agency. ML, ES, RDN, PA, and REC acknowledge support from DFID, the Bill & Melinda Gates Foundation, and the US Agency for International Development. PWG is a Career Development Fellow (K00669X) jointly funded by the MRC and DFID under the MRC/DFID Concordat agreement and receives support from the Bill & Melinda Gates Foundation (OPP1068048 and OPP1106023). These grants also support SB. MES is funded by the Bill & Melinda Gates Foundation through the Vector-Borne Disease Network. We thank Andrea Bosman, Abraham Mnzava, Tessa Knox, Hoda Atta, Charlotte Rasmussen, Pascal Ringwald, Graham Brown, Tom McLean, George Jagoe, Farzana Muhib, and Steve Kern for their input into the modelled scenarios; and members of the Global Technical Strategy (GTS) Steering Committee, the Technical Expert Group on Surveillance Monitoring and Evaluation, the Malaria Policy Advisory Committee, and participants in the GTS Regional Workshops for helpful comments on earlier drafts of this report.

References

1 WHO. World malaria report, 2015. http://www.who.int/malaria/publications/world_malaria_report_2015/en/ (accessed Jan 6, 2016).
2 WHO and UNICEF. Achieving the MDG target: reversing the incidence of malaria 2000–2015. Geneva: World Health Organization, 2015.
3 WHO. Global Technical Strategy for Malaria 2016–2030. Geneva: World Health Organization, 2015.
4 Roll Back Malaria Partnership. The global malaria action plan, 2008. http://www.rollbackmalaria.org/microsites/gmap/0-5.pdf (accessed Jan 5, 2016).
5 Roll Back Malaria Partnership. Action and investment to defeat malaria 2016–2030. Geneva: World Health Organization, 2015.
6 Griffin JT, Ferguson NM, Ghani AC. Estimates of the changing age-burden of *Plasmodium falciparum* malaria disease in sub-Saharan Africa. *Nat Commun* 2014; **5:** 3136.
7 Griffin JT, Hollingsworth TD, Okell LC, et al. Reducing *Plasmodium falciparum* malaria transmission in Africa: a model-based evaluation of intervention strategies. *PLoS Med* 2010; **7:** e1000324.
8 Griffin JT, Hollingsworth TD, Reyburn H, Drakeley CJ, Riley EM, Ghani AC. Gradual acquisition of immunity to severe malaria with increasing exposure. *Proc Biol Sci* 2015; **282:** 20142657.
9 White MT, Griffin JT, Churcher TS, Ferguson NM, Basanez MG, Ghani AC. Modelling the impact of vector control interventions on *Anopheles gambiae* population dynamics. *Parasit Vectors* 2011; **4:** 153.
10 Okell LC, Cairns M, Griffin JT, et al. Contrasting benefits of different artemisinin combination therapies as first-line malaria treatments using model-based cost-effectiveness analysis. *Nat Commun* 2014; **5:** 5606.
11 Walker PG, White MT, Griffin JT, Reynolds A, Ferguson NM, Ghani AC. Malaria morbidity and mortality in Ebola-affected countries caused by decreased health-care capacity, and the potential effect of mitigation strategies: a modelling analysis. *Lancet Infect Dis* 2015; **15:** 825–32.
12 Gething PW, Patil AP, Smith DL, et al. A new world malaria map: *Plasmodium falciparum* endemicity in 2010. *Malar J* 2011; **10:** 378.
13 Center for International Earth Science Information Network (CIESIN), Columbia University, International Food Policy Research Institute (IFPRI), The World Bank, Centro Internacional de Agricultura Tropical (CIAT). Global rural-urban mapping project version 2 (GPW-UR): gridded population of the world. Palisades: NASA Socioeconomic Data and Applications Center (SEDAC), 2011.
14 UN Department for Economic and Social Affairs. World population prospects: the 2012 revision. New York: Department for Economic and Social Affairs, 2013.
15 WHO. World Malaria Report, 2013. http://www.who.int/malaria/publications/world_malaria_report_2013/en/ (accessed Jan 5, 2016).
16 Sinka ME, Bangs MJ, Manguin S, et al. The dominant Anopheles vectors of human malaria in the Asia–Pacific region: occurrence data, distribution maps and bionomic precis. *Parasit Vectors* 2011; **4:** 89.
17 Sinka ME, Bangs MJ, Manguin S, et al. The dominant *Anopheles* vectors of human malaria in Africa, Europe and the Middle East: occurrence data, distribution maps and bionomic precis. *Parasit Vectors* 2010; **3:** 117.
18 Sinka ME, Bangs MJ, Manguin S, et al. A global map of dominant malaria vectors. *Parasit Vectors* 2012; **5:** 69.
19 Sinka ME, Rubio-Palis Y, Manguin S, et al. The dominant *Anopheles* vectors of human malaria in the Americas: occurrence data, distribution maps and bionomic precis. *Parasit Vectors* 2010; **3:** 72.
20 National Weather Service Climate Prediction Center. Africa rainfall estimates, 2010. http://www.cpc.ncep.noaa.gov/products/fews/rfe.shtml (accessed Jan 7, 2016).
21 Bhatt S, Weiss DJ, Mappin B, et al. Coverage and system efficiencies of insecticide-treated nets in Africa from 2000 to 2017. *eLife* 2015; published Dec 29. DOI: http://dx.doi.org/10.7554/eLife.09672.
22 Cohen JM, Woolsey AM, Sabot OJ, Gething PW, Tatem AJ, Moonen B. Public health. Optimizing investments in malaria treatment and diagnosis. *Science* 2012; **338:** 612–14.
23 Ranson H, N'Guessan R, Lines J, Moiroux N, Nkuni Z, Corbel V. Pyrethroid resistance in African anopheline mosquitoes: what are the implications for malaria control? *Trends Parasitol* 2011; **27:** 91–98.
24 Cohen JM, Smith DL, Cotter C, et al. Malaria resurgence: a systematic review and assessment of its causes. *Malar J* 2012; **11:** 122.
25 WHO. Control of residual malaria parasite transmission—guidance note. Geneva: World Health Organization, 2014.
26 Ashley EA, Dhorda M, Fairhurst RM, et al. Spread of artemisinin resistance in *Plasmodium falciparum* malaria. *N Engl J Med* 2014; **371:** 411–23.
27 Wells TN, Burrows JN, Baird JK. Targeting the hypnozoite reservoir of *Plasmodium vivax*: the hidden obstacle to malaria elimination. *Trends Parasitol* 2010; **26:** 145–51.
28 Chamchod F, Beier JC. Modeling *Plasmodium vivax*: relapses, treatment, seasonality, and G6PD deficiency. *J Theor Biol* 2013; **316:** 25–34.
29 Roy M, Bouma MJ, Ionides EL, Dhiman RC, Pascual M. The potential elimination of *Plasmodium vivax* malaria by relapse treatment: insights from a transmission model and surveillance data from NW India. *PLoS Negl Trop Dis* 2013; **7:** e1979.
30 White MT, Karl S, Battle KE, Hay SI, Mueller I, Ghani AC. Modelling the contribution of the hypnozoite reservoir to *Plasmodium vivax* transmission. *eLife* 2014; **3:** e04692.