Estimating the most efficient allocation of interventions to achieve reductions in *Plasmodium falciparum* malaria burden and transmission in Africa: a modelling study

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Summary

Background Reducing the burden of malaria is a global priority, but financial constraints mean that available resources must be allocated rationally to maximise their effect. We aimed to develop a model to estimate the most efficient (ie, minimum cost) ordering of interventions to reduce malaria burden and transmission. We also aimed to estimate the efficiency of different spatial scales of implementation.

Methods We combined a dynamic model capturing heterogeneity in malaria transmission across Africa with financial unit cost data for key malaria interventions. We combined estimates of patterns of malaria endemicity, seasonality in rainfall, and mosquito composition to map optimum packages of these interventions across Africa. Using non-linear optimisation methods, we examined how these optimum packages vary when control measures are deployed and assessed at national, subnational first administrative (provincial), or fine-scale (5 km² pixel) spatial scales.

Findings The most efficient package in a given setting varies depending on whether disease reduction or elimination is the target. Long-lasting insecticide-treated nets are generally the most cost-effective first intervention to achieve either goal, with seasonal malaria chemoprevention or indoor residual spraying added second depending on seasonality and vector species. These interventions are estimated to reduce malaria transmission to less than one case per 1000 people per year in 43·4% (95% CI 40·0–49·0) of the population at risk in Africa. Adding three rounds of mass drug administration per year is estimated to increase this proportion to 90·9% (95% CI 86·9–94·6). Further optimisation can be achieved by targeting policies at the provincial level, achieving an estimated 32·1% (95% CI 29·6–34·5) cost saving relative to adopting country-wide policies. Nevertheless, we predict that only 26 (95% CI 22–29) of 41 countries could reduce transmission to these levels with these approaches.

Interpretation These results highlight the cost–benefits of carefully tailoring malaria interventions to the ecological landscape of different areas. However, novel interventions are necessary if malaria eradication is to be achieved.

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Introduction

The 21st century has seen an unprecedented financial commitment towards reducing the burden of *Plasmodium falciparum* malaria.[1] Over the past decade, the proportion of the population of sub-Saharan Africa (the region with most global cases of malaria and deaths from the disease) with access to an insecticide-treated net has increased from 4% to 67% (95% CI 61–71) between 2004 and 2015, with an estimated 189 million long-lasting insecticide-treated nets delivered in 2014 alone.[2] This rapid scale-up in vector control has coincided with substantial improvements in access to prompt diagnosis and treatment using highly effective artemisinin combination therapies and chemoprevention within core risk groups, including young children and pregnant women.[3] These efforts have contributed to an estimated 26% reduction in the global incidence of clinical malaria and roughly 4·3 million deaths averted between 2000 and 2013.[3]

To date, with one exception (the recommendation of seasonal malaria chemoprevention),[4] universal coverage has been promoted—namely, all interventions are recommended in all settings. However, malaria transmission shows considerable variation at all spatial scales, ranging from hotspots within villages to differences between countries and continents.[5,6] Previous analyses have looked at how the cost-effectiveness of different combinations of interventions to reduce clinical disease and the morbidity associated with malaria vary according to different factors affecting transmission.[7–10] However, to date, no one has attempted to assess comprehensively how the optimum combinations of interventions to achieve malaria control targets vary across Africa as a result of such heterogeneity. In view of the current plateau in available funding for further malaria control and the subsequent shortfall in resources to achieve global goals,[1,3,11,12] there is a need to develop a rational basis to allocate the finite resources to achieve the greatest and most equitable effect.

To address this problem, we combined an existing malaria transmission model with estimates of the financial

Research in context

Evidence before this study

We searched PubMed with no date restriction for publications in English that combined models of malaria transmission with estimates of the resources needed to implement interventions, with the terms ("resource allocation" OR "optimal intervention" OR "cost minimisation" OR "cost effectiveness" OR "cost-effectiveness" OR "economic evaluation") AND ("model" OR "modelling") AND ("malaria" OR "falciparum" OR "plasmodium"). Our search yielded 147 results, 17 of which were judged relevant. Publications included various analyses of the cost-effectiveness of one or more malaria control interventions, sometimes taking into account ecological factors such as transmission intensity and vector behaviour and assessing how these affect the most cost-effective combination of interventions.

Added value of this study

To our knowledge, our study is the first that has attempted to estimate the optimum combination of interventions to achieve milestones for malaria burden and transmission reduction and to quantify how these packages are likely to vary across Africa. It is also the first study, to our knowledge, that looks at the extent to which the resources needed to achieve these targets can be reduced using control policies tailored to local ecology at the subnational first administrative (provincial) level.

Implications of all the available evidence

After universal coverage of long-lasting insecticide-treated nets, the optimum subsequent package of interventions differs depending on whether the target is a rapid reduction in malaria burden or sustained reductions in transmission. Nevertheless, currently recommended interventions are unlikely to achieve elimination in most malaria-endemic countries in Africa. New transmission-reducing interventions—eg, mass drug administration—could increase the number of countries in which elimination is feasible. For all policies, in countries with a high degree of heterogeneity in transmission, we find that interventions tailored to the provincial level are substantially more cost-efficient than are national policies. Moreover, these provincial-level policies typically capture most of the cost savings that could be obtained when attempting to achieve pre-elimination levels of transmission with finer spatial (5 km² pixel) stratification.

Panel: Summary of the model

We used an individual-based simulation model of the transmission dynamics and clinical burden of *Plasmodium falciparum* malaria, incorporating:

- Acquired immunity, which alters the likelihood that infection results in clinical disease, modifies onward infectivity to mosquitoes, affects the detectability of infection, and modifies the duration of parasitaemia
- Mosquito dynamics and behaviour relevant to control, including lifespan, density-dependent larval development, and feeding and resting behaviour
- Seasonality in larval carrying capacity informed by seasonal patterns in rainfall
- Characteristics of various first-line treatments for malaria, with profiles based on pharmacokinetic/pharmacodynamic (PK/PD) model fits to trial data
- A process-based model of the effect of vector control (long-lasting insecticide-treated nets [LLINs] and indoor residual spraying [IRS]), with parameters taken from detailed hut studies and fitted to intervention trial data
- Population-based, drug-based, intervention strategies, including seasonal malaria chemoprevention and mass drug administration, informed by PK/PD model fits to the individual drug properties and calibrated against trial data
- Realistic intervention variables, including attrition of LLINs due to wear and tear, waning of insecticides used within IRS or LLINs, and prespecified correlation between interventions and rounds of the same intervention

cost of different interventions to capture the non-linear dynamics of intervention effect and expenditure. We used this model to estimate the most cost-efficient strategies to achieve goals for reducing burden and transmission across a wide range of environments representative of areas in which the disease is currently prevalent in Africa.

Methods

Modelling specification and sampling framework

See Online for appendix

Using an individual-based mathematical model of *P falciparum* malaria transmission (panel),[13,14] we attempted to reflect the range of transmission settings across Africa, while maintaining a sampling framework that was computationally feasible. We simulated 288 baseline transmission settings comprising 18 transmission intensity strata (1% prevalence, then 5–85% prevalence in increments of 5%), four seasonality profiles, and four vector behaviours, ranging from mainly endophilic (indoor resting) and endophagic (indoor feeding) vectors, such as *Anopheles gambiae* sensu stricto or *Anopheles funestus*, to a vector with a lower human-biting index and higher propensity to feed and rest outdoors, such as *Anopheles arabiensis* (figure 1; appendix pp 2–8). For every setting, we simulated the effect of intervention packages over a 20-year time horizon, with all possible combinations of long-lasting insecticide-treated nets, indoor residual spraying, and seasonal malaria chemoprevention, ranging from 0% to 90% coverage in 15% increments. This simulation generated 98 784 scenarios.

We achieved scale-up of long-lasting insecticide-treated nets by providing a quarter of the total required nets for