

Exploring the use of a general equilibrium method to assess the value of a malaria vaccine: an application to Ghana

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Published in: Medical Decision Making (MDM) Policy & Practice, 2019,
<https://doi.org/10.1177/2381468319894345>

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Financial support for this study was provided by GlaxoSmithKline Biologicals SA (TrackHO number: HO-13-13516). The funding agreement ensured the authors' independence in designing the study, interpreting the data, writing, and publishing the report. The following author is employed by the sponsor: Christophe Sauboin.

Journal: Medical Decision Making Policy & Practice

Abbreviations: CGE, computable generalized equilibrium; GAVI, Global Alliance for Vaccines and Immunization; GDP, gross domestic product; IRS, indoor residual spraying; ITN, insecticide-treated net; LiST, Lives Saved tool; SMC, seasonal malaria

chemoprevention; WHO, World Health Organization

Abstract

Background: Malaria is an important health and economic burden in sub-Saharan Africa. Conventional economic evaluations typically consider only direct costs to the healthcare system and government budgets. This paper quantifies the potential impact of malaria vaccination on the wider economy, using Ghana as an example.

Methods: We used a computable general equilibrium model of the Ghanaian economy to estimate the macroeconomic impact of malaria vaccination in children under the age of five, with a vaccine efficacy of 50% against clinical malaria and 20% against malaria mortality. The model considered changes in demography and labor productivity, and projected gross domestic product (GDP) over a time frame of 30 years. Vaccine coverage ranging from 20% to 100% was compared with a baseline with no vaccination.

Results: Malaria vaccination with 100% coverage was projected to increase the GDP of Ghana over 30 years by US\$6.93 billion (in 2015 prices) above the baseline without vaccination, equivalent to an increase in annual GDP growth of 0.5%. Projected GDP per capita would increase in the first year due to immediate reductions in time lost from work by adults caring for children with malaria, then decrease for several years as reductions in child mortality increase the number of dependent children, then show a sustained increase after Year 11 due to long-term productivity improvements in adults resulting from fewer malaria episodes in childhood.

Conclusion: Investing in improving childhood health by vaccinating against malaria could result in substantial long-term macroeconomic benefits when these children enter the workforce as adults. These macroeconomic benefits are not captured by conventional economic evaluations and constitute an important potential benefit of vaccination.

Word Count: 265

Keywords: malaria vaccine; general equilibrium; human capital; public health; economic growth; Ghana

Introduction

Malaria remains an important public health burden in sub-Saharan Africa, with an estimated 407,000 malaria deaths in 2016.¹ The clinical symptoms of malaria range from non-specific mild febrile illness to life-threatening disease with coma, respiratory distress, severe anemia or shock.² In addition to established preventive malaria interventions, such as insecticide-treated nets (ITNs), indoor residual spraying (IRS) and seasonal malaria chemoprevention (SMC), the RTS,S malaria vaccine candidate is now under evaluation after having been piloted with children (0-5 years of age) in moderate to high transmission settings in sub-Saharan Africa as recommended by the World Health Organization (WHO).²² Decisions on country-level vaccine introduction will need to take into account the potential public health impact of vaccination, together with an evaluation of its potential budgetary and economic impact.

Commonly used forms of economic evaluation such as cost-effectiveness analysis,^{3 4} budget impact analysis^{6 7 8} and budget optimization analysis⁹ are typically limited to considering direct costs to the healthcare system and governmental budgets.¹⁰ Analyses of this type for the RTS,S vaccine are presented elsewhere **[[Citation to the CE-BI paper to be added here when available]]** **[[Citation to BOM paper to be added here when available]]**. However, many of the costs of disease are borne at household level. For example, households may have to pay for treatment and transport to a clinic, and may lose income if a parent has to take time away from work to care for a child with malaria. A study in Ghana, Kenya and Tanzania published in 2013 estimated that 55–70% of the costs of an episode of malaria were borne by households.¹¹ It is possible to include some of these household costs, such as lost income and out-of-pocket expenditure on treatment and transport, in economic evaluations that take a societal perspective. However, even this does not capture the effect of changes in household behavior on the wider economy.

Malaria indirectly effects economic growth because households contribute to the economy by providing labor to firms, by producing goods and services, and by consuming goods and services. When a parent has to take time away from work to care for a child with malaria, not only does the affected household lose income, the employer also loses the value of the lost work time. Furthermore, the household will have less to spend on consumption, thereby reducing the income of individuals and

firms from which the household would otherwise have bought goods or services.

Other examples of indirect effects are reduced investment in education per child, reduced educational attainment resulting from missed schooldays due to illness, lower skills due to impaired cognitive development, lower household savings, and reductions in tourism and foreign direct investment.¹² Cross-country regression analysis using data from 1965–1990 estimated that countries with intensive malaria had an economic growth that was 1.3% lower per person per year than countries without malaria, after taking into account factors such as initial income level, overall health and tropical location.¹³

Conventional economic evaluations (such as partial equilibrium models) do not account for indirect effects of the disease on the wider economy, and therefore provide only a partial view of the economic benefit of interventions to reduce disease.^{10 14 15 16 17} Computable generalized equilibrium (CGE) models offer a promising approach to exploring these wider economic effects.¹⁸ CGE models consider different, but interrelated, elements of the economy including households, government, production sectors (such as manufacturing, agriculture, and transport), capital, labor and foreign trade. The economic relationships between them is calibrated using a social accounting matrix for national income and input–output data by sector.¹⁹ Contrary to other methods, general equilibrium can account for wider changes that result from behavior adjustments (e.g. consumption and production) of all key economic agents. For this reason, this approach is highly suitable to estimate the impact of a positive productivity shock after reducing a widespread disease.

CGE models have been applied to simulate the economic impact of antimicrobial resistance²⁰ and pandemic influenza.^{19 21 22} In our paper, we explore the broader economic impact of malaria vaccination on the Ghanaian economy (An early draft of this paper was catalogued by an ISPOR conference).²³ The impact of malaria vaccination was measured by considering the economic impacts of changes in: (1) malaria-related child mortality, (2) short-term productivity due to caregiving for a child with malaria (which alters the contribution of a malaria-affected household to the economy and the resources available for household consumption). Finally, (3) long-term labor productivity resulting from impaired cognitive development and missed schooling due to malaria in childhood.

Methods

Model structure

We developed a computable general equilibrium (CGE) model that includes the effects of malaria on demography and labor productivity. The core CGE model considers a range of economic agents in Ghana, including the government, households, firms and the rest of the world. The economic behavior and interactions of each agent were modelled using standard preference functional forms, based on established microeconomic theory and computational methods. The model was numerically simulated using the computer program GAMS and its MPSGE solver.²⁴²⁵ GAMS is one of the most commonly used software environment for applied CGE modelling. (See www.gams.com for further information.)

The economy was assumed a small open economy. Firms select the combination of labor, goods and service inputs required to produce their output of goods and/or services and maximize their profits. Households maximize their utility by offering their labor to firms, consuming goods and services and saving from their income. The model finds the equilibrium at which prices of all goods and services are such that the quantity supplied equals the quantity demanded across all sectors. (We provide the full model description in the online supplementary appendix of this paper, including the GAMS/MPSGE code.)

The model's equations are calibrated to the 2007 social accounting matrix (SAM) of Ghana in Breisinger et al.^{26 27} This is a table expressed in terms of incomes and expenditures (i.e., a double entry accounting method) which is now a standard approach to calibrate functional form to real-life data.²⁸ The SAM is subsequently updated to 2015 US\$ by chaining the consumer price index and exchange rate.

The SAM provides measures for three labor skill-types (self-employed, skilled and unskilled), capital, and land, and 90 types of household characterized by administrative district, rural or urban location, and income level. We link the administrative districts to five ecological zones with differences in malaria incidence (further details provided shortly). Furthermore, we assume that the government provided a fixed level of goods and services to the population based on tax revenues.

The model projects 30 years forwards, a period selected because it is long enough to capture effects on the adult labor force of improved health in childhood.

Demographic model

Population demographics over the model time horizon were modelled using the existing DemProj demographic model from the Spectrum Policy Modeling System of the Health Policy Project, which projects population size and composition based on fertility, mortality and migration.²⁹ The model was adapted to account for malaria-specific mortality and regional variations in Ghana. It was assumed that any changes in demographic parameters such as migration and fertility rates were not affected by any interventions to prevent malaria.

Impact of malaria

The effect of malaria was taken into account in the model in three ways. First, the demographic model included the specific effect of malaria on child mortality, estimated by combining projected clinical malaria episodes with a case-fatality rate. Second, for each episode of malaria occurring in a child under the age of five, the model estimated the immediate productivity loss resulting from adult caregivers losing time from work. Third, for children exposed to several episodes of malaria during childhood, the model considered long-term reductions in their productivity as adults resulting from missed schooling, greater susceptibility to other health problems and cognitive impairment. Children were assumed to enter the labor force at the age of 15 years.

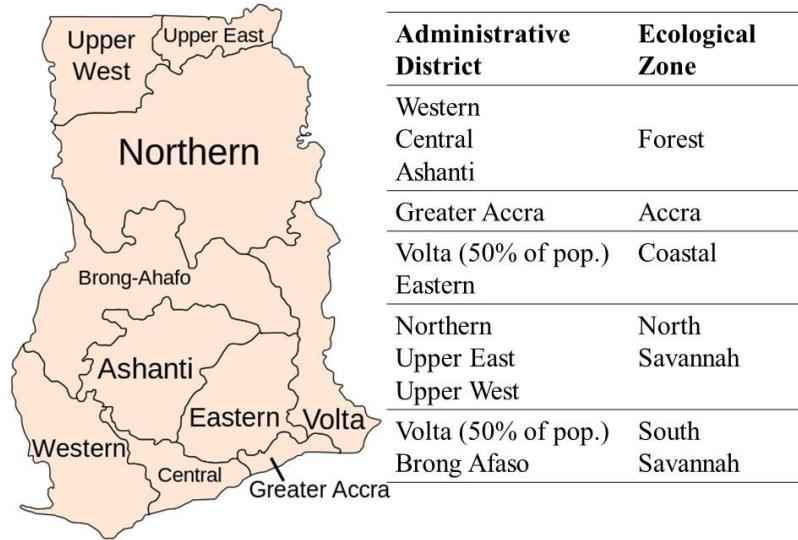
Note that episodes of malaria occurring in adults cause productivity losses due to absence from work or loss in productivity while at work. However, since we assume that the vaccine is provided only to children, its effect cancels out between scenarios.

Malaria episodes were based on regional malaria epidemiology corresponding to five ecological zones with differences in malaria incidence. These are presented in Figure 1. The occurrence of malaria episodes ranged from 0 to a maximum of 9, and was modelled using a Poisson distribution, with a distribution mean equal to the mean baseline number of clinical malaria episodes in each zone (Table 1).

Episodes of malaria occurring in children resulted in productivity losses when an adult had to take time away from work to care for the sick child (Table 1). Furthermore, individuals experiencing multiple episodes of malaria as children were assumed to experience long-term productivity losses throughout their working lives as adults due to lower skills or compromised health. In people with two episodes of childhood malaria, this was modelled as a 10% reduction in productivity, and in those

with three or more episodes as a 25% reduction in productivity, based on published literature (Table 1).

Figure 1: Mapping administrative districts onto malaria ecological zones



Note: the figure shows the link between administrative regions and malaria ecological zones.

Table 1. Key input data used in the model

Parameter	Value	Source
Total number of working days per year	235	Authors' assumption
Range of malaria episodes per person-year	0–9	Authors' assumption
Event distribution	Poisson	Smith et al 2006 ³¹
Baseline mean number of malaria episodes per year		
	Age 0–4 years, age 5–64 years	
National ^a	1.0, 0.5	Asante et al 2011 ³²
Regional ^b		South African Medical Research Council 2002 ³³
Accra	0.53, 0.27	
Coast	0.86, 0.43	
Forest	1.62, 0.81	
North Savannah	1.29, 0.65	
South Savannah	0.69, 0.35	
Adult productivity loss for child's episode of malaria		
Days absent from work to provide care	2	Aikins 1995, ³⁴ Cropper et al 2000, ³⁵ Ettling and Shepard 1991, ³⁶ Ettling et al 1994, ³⁷ Guiguemdé et al 1997, ³⁸ Leighton and Foster 1993, ³⁹ Sauerborn et al 1995, ⁴⁰ Asante et al 2005 ⁴¹
Productivity loss when absent	100%	Authors' assumption
Long-term productivity loss in adulthood resulting from malaria in early childhood		
Days at work but with compromised skills	235	Authors' assumption
Productivity loss with ≤1 episode of childhood malaria	0%	Authors' assumption using Bleakley 2003, ⁴² Cutler et al 2010, ⁴³ Bleakley 2010 ⁴⁴
Productivity loss with 2 episodes of childhood malaria	10%	Authors' assumption using Bleakley 2003, ⁴² Cutler et al 2010, ⁴³ Bleakley 2010 ⁴⁴
Productivity loss with ≥3 episodes of childhood malaria	25%	Authors' assumption using Bleakley 2003, ⁴² Cutler et al 2010, ⁴³ Bleakley 2010 ⁴⁴

^a Asante *et al.* (2011) ³² find 1.3 primary-case-definition episodes per person-years in the first 18 months of life in Ghana. As this study applies episodes for 0 to 4 years of life, and children aged 18 months to 4 years of age have relatively fewer episodes of malaria, we assume 1.0 episode per person-year from 0-4 years. Without academic evidence on adult episodes of malaria across regions of Ghana, authors assume 50% fewer episodes for adults than children.

^b Derived from national mean episodes using Asante *et al.* (2011) ³² and population weighted mean regional malaria prevalence by age group in South African Medical Research Council 2002 ³³

Impact of malaria interventions

The projected impact of a malaria vaccination program was evaluated by running a baseline model simulation with no vaccination program (i.e. with existing malaria interventions only). This was then compared with intervention scenarios introducing a malaria vaccination program that would have a protective effect for children under the age of five, therefore assuming that five birth cohorts have been immunized. We assumed a range of coverage levels, starting at 20% coverage and increasing to 100% coverage in increments of 20 percentage points. The vaccine efficacy in the model was assumed to be 20% against mortality and 50% efficacy against clinical malaria episodes. The model did not account for herd effects, or any impact on the effectiveness of other interventions.

The effect of vaccination on mortality and demographics was estimated using the Lives Saved tool (LiST) from the Spectrum Policy Modeling System of the Health Policy Project.²⁹ This tool estimates the impact of each level of vaccination coverage on childhood mortality rates, and the DemProj tool simultaneously uses this information to generate the resulting demographic population projections. The effect of malaria vaccination would be expected to reduce childhood mortality, thereby increasing the number of surviving children. Fertility rates are projected to decline in the demographic component of the model. We did not assume additional fertility reduction that would be indirectly caused by the reduction of malaria mortality in children with the vaccine.

The effect of vaccination on productivity losses due to malaria episodes was estimated by reducing the number of baseline clinical malaria episodes by 50% (vaccine efficacy) in the proportion of children under the age of five covered in each vaccination scenario. The model assumed no changes in the number of malaria episodes in adults, since the modelled vaccination program targeted only children under the age of five. Therefore, the immediate change in labor productivity due to malaria episodes would reflect only the change in the amount of time lost by adult caregivers.

The effect of vaccination on long-term productivity losses was modelled as a reduction in the proportion of children experiencing two or more malaria episodes, resulting in a lower proportion of young adults entering the workforce with impaired skills due to childhood malaria.

It was assumed that the malaria vaccine costs would be funded by international programs such as the Global Alliance for Vaccines and Immunization (GAVI), which would be consistent with the malaria vaccine pilot implementation.³⁰

The primary model output was gross domestic product (GDP) per capita over time for the different vaccine coverage levels modelled, expressed in 2015 US dollar (US\$). The model can also calculate household revenues across different socio-economic groups and for urban versus rural households.

Sensitivity analysis

In addition to the range of vaccination coverages, the impact of additional input parameters has been tested in a univariate sensitivity analysis. Productivity loss parameters and vaccine efficacy have been varied to assess the resulting variation of outcomes. The two most influential parameters are varied simultaneously in a bivariate analysis to assess larger variations.

Results

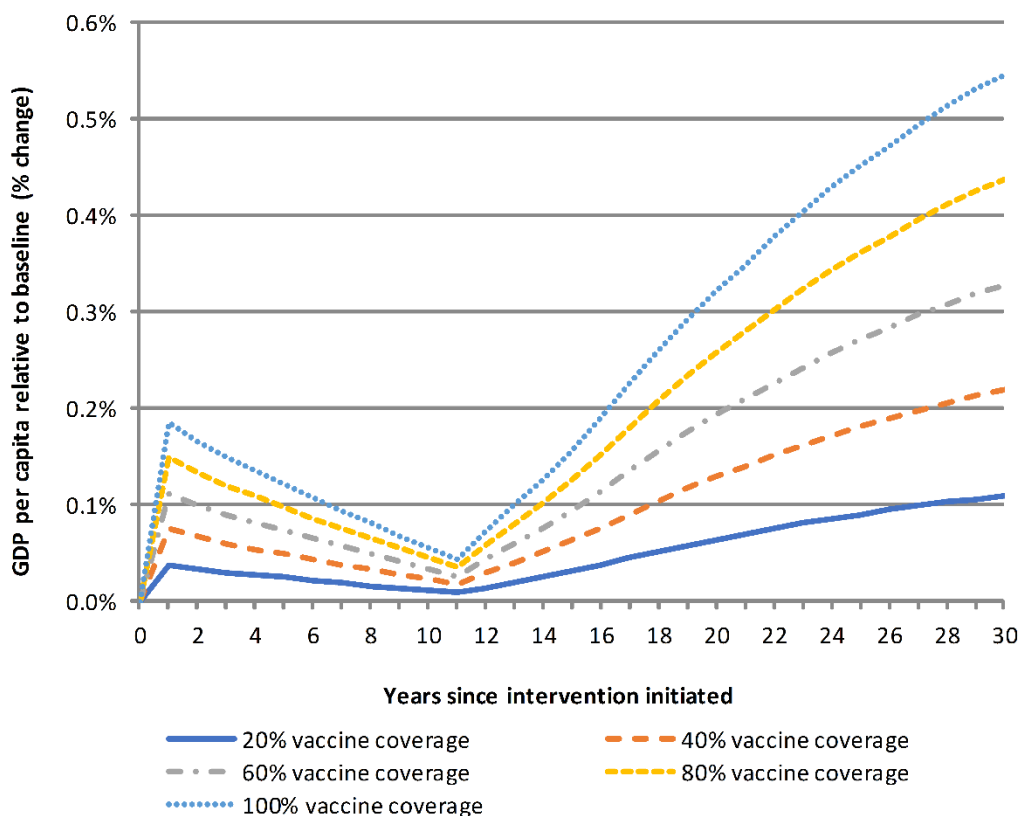
Table 2 shows the projected impact of increasing levels of malaria vaccine coverage on cumulative Ghanaian GDP over 30 years, relative to the baseline of no vaccination.

At 100% malaria vaccine coverage in children under the age of five, the projected economic benefit over 30 years in Ghana would amount to an additional US\$6.93 billion (in 2015 prices) more than the baseline with no vaccine program. Annual mean GDP would increase by US\$46.0 million at 20% vaccine coverage, rising to US\$230.8 million at 100% coverage, equivalent to an increase in annual GDP growth of 0.1% and 0.5%, respectively. Mean annual GDP per capita (i.e. allowing for increases in population size resulting from reduced malaria childhood mortality) would grow by 0.05% at 20% vaccine coverage and by 0.25% at 100% vaccine coverage. This economic gain would occur despite the fact that the vaccinated children are not economically active.

Figure 2 shows the projected evolution in GDP per capita over time. In the first year after beginning the vaccination program, projected GDP per capita would rise immediately compared with the baseline. This reflects the reduction in malaria episodes in children, which allows adults to spend more days at work instead of caring for sick children and thus produces an immediate increase in labor

productivity.

Figure 2. Projected mean annual percentage change in GDP per capita in Ghana over 30 years with increasing levels of malaria vaccination coverage, relative to baseline with no vaccination



Over the subsequent years, up to Year 11, projected GDP per capita falls, as more children survive but they are not yet old enough to enter the labor force; so the dependency ratio increases. At Year 11, the first cohort of vaccinated children (those vaccinated at the age of four (i.e. just under the age of five) in the first year of the vaccination program) move into the labor force. These vaccinated children would have experienced fewer malaria episodes in childhood, and consequently have improved labor productivity resulting from fewer missed schooldays and less malaria-related cognitive impairment. The projected GDP per capita thus begins to increase after Year 11, and progressively increases over the remaining timeframe of the model. The improved GDP per capita in this later phase of the model, after the children who benefited from vaccination enter the workforce, outweighs the temporary decrease in GDP per capita in the earlier phase when these children were

still dependent. Therefore, the cumulative effect over the 30-year time horizon would be a net gain in GDP per capita (Table 2). The overall effect of malaria vaccination of children under the age of five behaves as an initial investment providing long-term economic benefits.

Table 2. Projected impact of increasing malaria vaccine coverage on GDP in Ghana over 30 years, relative to baseline with no vaccination

	Vaccine coverage in children under the age of five				
	20%	40%	60%	80%	100%
Cumulative GDP (2015 US\$, billions)	1.38	2.77	4.15	5.54	6.93
% of total cumulative GDP	0.13%	0.26%	0.39%	0.52%	0.65%
Annual mean GDP (2015 US\$, millions)	46.0	92.2	138.4	184.6	230.8
Mean annual GDP growth (%)	0.1%	0.2%	0.3%	0.4%	0.5%
Mean annual GDP per capita growth (%)	0.05%	0.10%	0.15%	0.20%	0.25%
Mean annual household disposable income (2015 US\$, millions)	45.8	91.7	137.5	183.5	229.5

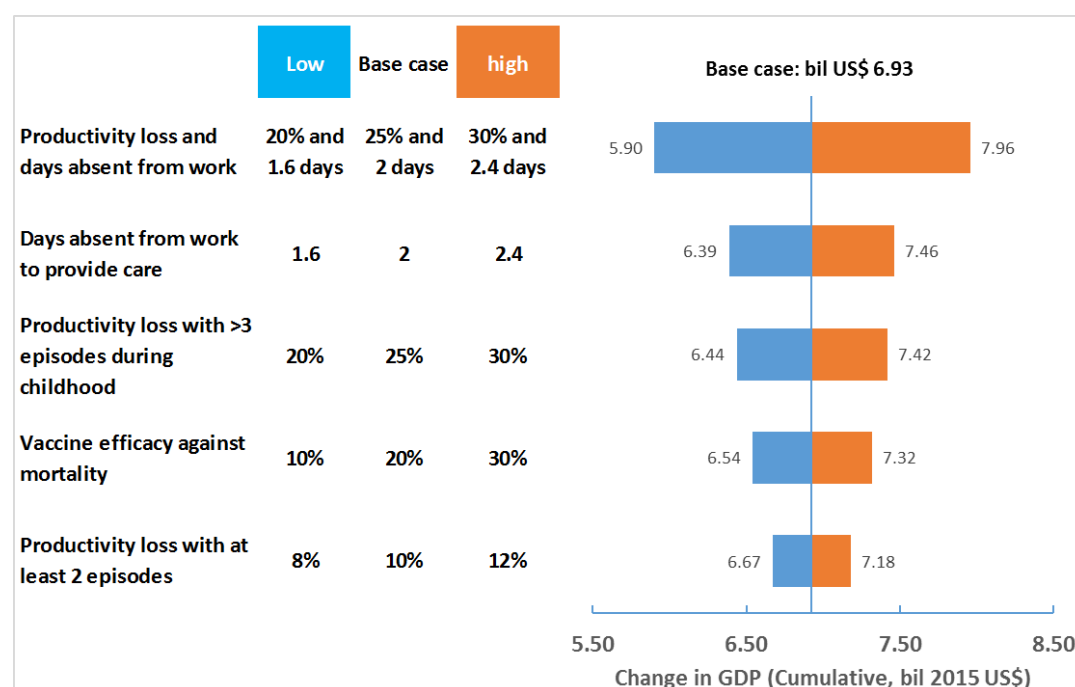
We furthermore test the model by varying key parameters, for the 100% coverage scenario. Results are summarized in Figure 3. As expected, the model is stable around the mid-point estimates, and varying parameter values raise (lower) the vaccine's economic benefit.

The two parameters that have the largest impact on our results are (1) days absent from work to provide care for children, and (2) productivity loss with >3 episodes of childhood malaria (from Table 1). To provide the highest (lowest) boundary for the benefit of the malaria vaccine's, we run the model with these parameters. The cumulative GDP for a 30-year time-horizon is between US\$5.90 to 7.96 billion with the mid-point value US\$6.93 (see results in Figure 3 and Table 2).

Our result and the sensitivity analysis show the importance of the labor efficiency to the health intervention. We are more comprehensive with how malaria episodes affect labor efficiency by including impacts on childhood human capital development,

children’s health on adults’ work absenteeism, and adult absenteeism due to malaria illnesses. Demographic projections are based on fertility, mortality, and migration; however, only the direct effect of malaria reduction on mortality is included in our model because we do not have good evidence on the fertility and migration responses to malaria, which could have reversed these trends. Future avenues of research could introduce these elements as well.

Figure 3. Tornado diagram: change in cumulative GDP (bil. 2015 US\$) with full coverage



Discussion

To our knowledge, this modeling study represents the first attempt to explore the potential macroeconomic impact of malaria vaccination in children in sub-Saharan Africa. Our approach uses the established economic technique of CGE modeling, combined with an explicit component to model the impact of malaria on the economy via the mechanisms of effects on childhood mortality and labor productivity.

Taking Ghana as an example, our results indicate that a vaccination program in children under the age of five using a vaccine with 50% efficacy against malaria episodes and 20% efficacy against malaria mortality would raise projected annual GDP growth by 0.1% to 0.5%, depending on the level of vaccine coverage. This projected economic benefit is remarkable given that our model only considered the

impact of vaccination on malaria in children. It reflects the value of investing in improved childhood health to obtain long-term economic benefits resulting from higher productivity when these healthier children enter the workforce as adults.

Our results are likely to be conservative, because the model focuses on improved labor productivity resulting from improved childhood health, and does not include several other factors that could be affected by malaria vaccination. First, a reduction in childhood mortality could lead to a reduction in total fertility in the long-term (sometimes referred to as a 'demographic dividend' or 'demographic transition'), and our model does not take this into account as a specific effect of malaria vaccination. Second, the model does not include any potential increases in trade, tourism or foreign investment that could result from a reduction in malaria. Third, fewer childhood malaria episodes would mean that households have to spend less on out-of-pocket expenses such as treatment and transport to a clinic. They would then be free to divert more of their income to consumption of other goods and services, which would tend to increase demand in the economy and further increase GDP. This is not considered in the model, which will therefore tend to underestimate vaccine benefit.

A previous study estimated the direct economic cost of malaria in children under the age of five in Ghana, Tanzania and Kenya using a probabilistic accounting model.¹¹ This study estimated a net income benefit of only US\$27.8 million (in 2015 prices) per year for Ghana, which is much lower than our estimate of a net benefit of US\$ 229.5 million per year in household disposable income with 100% vaccine coverage. This difference illustrates the potential importance of CGE modelling that combines both direct and indirect effects, which were absent from the previous study that only considered direct costs.

The results show the variation in the timing of different effects (see Figure 2). The vaccine intervention provides an immediate increase in GDP per capita resulting from fewer days lost to care for sick children, which thereafter declines in the medium-run as the number of dependent children in the population increases because of reduced childhood mortality. Finally, in the long-term, there is a sustained increase in GDP per capita as cohorts of vaccinated children enter the workforce with improved labor productivity resulting from better health in childhood.

Only RTS,S was assessed in the current model to reduce malaria in order to capture its specific effect. However, several other preventive malaria interventions, mainly bednet distribution have been implemented in Ghana and these were assumed to be

maintained at their current coverage for all baseline and counterfactual scenarios. The overall impact of intensifying preventative interventions could bring an extra economic growth when reducing malaria further. However if RTS,S is introduced when malaria has already been reduced, the potential extra gain with RTS,S will also be reduced.

The model currently assumes that malaria vaccination would be costless to the Ghanaian economy, with the costs of the vaccine funded by programs such as GAVI. This is a simplified assumption, and is consistent with the funding of the pilot vaccination program. However, in the longer-term, Ghana may be self-financing for vaccines. Future research could extend the model to introduce vaccine costs and sources of funding, which could explore issues such as the long-term financial sustainability and the return on investment of potential vaccine programs. In addition, future research could further explore the impact of malaria vaccination on households at different socioeconomic levels, which could provide valuable information on the equity of malaria prevention programs.

Conclusion

We have adapted a CGE model by adding a health component to simulate the impact of malaria and malaria vaccination on economic growth via effects on demography and labor productivity. Using Ghana as an example, our results indicate that vaccination of children under the age of five against malaria with 100% coverage could increase GDP by an average of 0.5% per year over a 30-year period. Investing in improving childhood health by vaccinating against malaria could result in substantial long-term macroeconomic benefits when these children enter the workforce as adults. These macroeconomic benefits are not captured by conventional cost-effectiveness analyses, which may therefore underestimate the economic benefits of vaccination.

Acknowledgements

The authors are grateful to James Thurlow, Xinshen Diao and their co-authors from the International Food Policy Research Institute (IFPRI) for providing access to the Ghana Social Accounting Matrix. The authors also thank Christopher Adam, Patricia Akweongo, Jonathan Cave, Simo Goshev, Clara Helene Rübner Jørgensen, Carlo Perroni, Jeffrey Round, Lei Zhang, Sani Ziv, and RAND Health researchers for helpful discussions, advice and suggestions that improved earlier versions of this

study. The authors thank Benoit Guerin, Eanna Kelly, Jirka Taylor and Shelly Culbertson (RAND Europe) for research assistance and editorial support. The authors would also like to thank Carole Nadin (Fleetwith Ltd, on behalf of GSK) for medical writing assistance and Business & Decision Life Sciences platform for editorial assistance and manuscript coordination, on behalf of GSK. Fabien Debailleul coordinated manuscript development and editorial support.

This study benefited from comments and suggestions from discussants and participants in the Sustainable Development, Energy & the Environment meeting on Malaria at Wilton Park 2012, Poverty Reduction, Education & Growth (PEGNet) Conference in Senegal 2012, International Society For Pharmacoeconomics and Outcomes Research (ISPOR) Annual European Congress in Berlin 2012, the Centre for the Study of African Economies Conference (CSAE) in Oxford 2013, and the University of Warwick economic seminar series.

Disclosure

Erez Yerushalmi, Priscilla Hunt and Stijn Hoorens report that this work was supported by an unrestricted research grant from the GSK group of companies. Christophe Sauboin is an employee of the GSK group of companies and reports ownership of stock options/restricted shares from the GSK group of companies. Richard Smith reports no conflict of interest.

Author contributions

All authors comply with the ICMJE criteria for authorship. S. Hoorens, P. Hunt, C. Sauboin, R. Smith, E. Yerushalmi were involved in the conception and/or the design of the study. S. Hoorens, P. Hunt, C. Sauboin, R. Smith, E. Yerushalmi participated in the collection or generation of the study data. S. Hoorens, P. Hunt, R. Smith, E. Yerushalmi performed the study. P. Hunt, C. Sauboin, E. Yerushalmi contributed to the analysis tools. S. Hoorens, P. Hunt, C. Sauboin, R. Smith, E. Yerushalmi were involved in the analyses and/or the interpretation of the data. All authors read and approved the present manuscript.

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