January 24, 2019

Disease Control Priorities in Developing Countries, 3rd Edition
Working Paper #26

Title: The health and financial benefits for households from averting malaria with RTS,S/AS01 vaccine in Zambia: an extended cost-effectiveness analysis

Author (1): Lingrui Liu
Lingrui.liu@yale.edu

Affiliation: Department of Health Policy and Management Yale School of Public Health
Global Health Leadership Initiative Yale University

Author (2): Allison Portnoy
aportnoy@mail.harvard.edu

Affiliation: Department of Global Health and Population, Harvard T.H. Chan School of Public Health

Author (3): Zoë True
zoe.s.true@gmail.com

Affiliation: Evans School of Public Policy and Governance, University of Washington, Seattle

Author (4): Günther Fink
guenther.fink@swisstph.ch

Affiliation: Department of Epidemiology and Public Health, Swiss Tropical and Public Health Institute, Basel, Switzerland

January 24, 2019

Author (5): Stéphane Verguet
verguet@hsph.harvard.edu

Affiliation: Department of Global Health and Population, Harvard T.H. Chan School of Public Health

Correspondence to: Stéphane Verguet
verguet@hsph.harvard.edu

Keywords: Malaria, vaccination, extended cost-effectiveness analysis, child health, sub-Saharan Africa, Zambia.

Abstract:

Objective: Malaria remains one of the leading causes of mortality for children under five years old in many sub-Saharan African countries. We examined the household health and financial benefits associated with the hypothetical rollout of the malaria vaccine RTS,S/AS01 in Zambia.

Methods: We applied extended cost-effectiveness analysis methods to estimate impact of the RTS,S/AS01 vaccine on the health of children under five, as well as the financial impact on their households. We assumed a three-dose vaccination schedule (over 6-9 months) with initial vaccine efficacy against infection of 91%, waning immunity (half-life of 7.3 months), average vaccination coverage of 68%, and vaccine cost of US$5 per dose. To assess vaccine impact, for each income quintile, we computed: the number of under-five malaria deaths prevented; the household out-of-pocket (OOP) malaria-related treatment expenditure averted; and the number of cases of catastrophic health expenditure averted.

Results: Rolling out the RTS,S/AS01 vaccine in Zambia within one birth cohort would avert an estimated 670 deaths for children under five years of age, and prevent approximately US$1.0 million of OOP expenditure, both largely concentrated among the poorer households. Vaccination would also prevent about 4,400 associated cases of catastrophic expenditure among households in all income quintiles, excluding the highest. The estimated cost of the program would be US$9 million per birth cohort.

Conclusions: A national vaccination program would not only yield important health benefits (malaria deaths averted), but also large reductions in malaria-related OOP expenditure and catastrophic health expenditure among households, with a higher concentration among the poor.

1. Introduction

According to the World Health Organization (WHO), a large majority of malaria-related deaths (approximately 90%) occurred in the African region in 2015, with children under five years of age being most vulnerable to malaria infection and death [1]. The international commitment to fighting malaria has been renewed through the Sustainable Development Goals:SDG3 includes not only universal health coverage and financial risk protection for all, but also explicitly strives to end the malaria epidemic [2].

In sub-Saharan Africa, introduction of a malaria vaccine could potentially be effective in improving population health [3]. The RTS,S/AS01 malaria vaccine directly targets the pre-erythrocytic stage of the *Plasmodium falciparum* parasite to protect children under five years of age in endemic regions [3-5]. The RTS,S vaccine has shown efficacy in phase 3 trials for reducing malaria episodes among young children and infants in sub-Saharan Africa [6-9]. RTS,S can be administered through a series of three doses given at monthly intervals to young children, potentially followed by a booster shot eighteen months later [3] . It was approved by the European Medicines Agency in July 2015 [10].

In 2015, WHO recommended an acceleration of the vaccine pilot implementation in Africa in order to evaluate vaccine efficacy in reducing malaria when integrated into countries' routine immunization programs [11]. In April 2017, WHO officially announced the first phase of a pilot program for RTS,S vaccine (2017-2020) [12]. These policies supporting the introduction of RTS,S into vaccination programs in more African countries have generated a window of opportunity to observe the potential effect of the vaccine. To assist further policy decisions and

recommendations, policymakers must understand the population-level health and economic impact of scaling up RTS,S vaccine.

Previously, a series of studies using the most recent RTS,S trial data provided modeling evidence for the health benefits (i.e., malaria cases and deaths averted) and economic impact (i.e., program costs) from cost-effectiveness analysis (CEA) models, assuming various malaria transmission settings and national contexts [13-17]. These studies focused primarily on cost and epidemiological predictions, and found that adding RTS,S vaccine into existing immunization programs in sub-Saharan African countries could be cost-effective in reducing malaria burden in children, taking into account the feasibility of scaling up existing control programs and operational constraints [13-17].

However, despite these prior efforts, the impact of scaling up RTS,S vaccine on non-health benefits, including the financial consequences for households, remains uncertain. Beyond the direct medical costs incurred by the health system, economic benefits of vaccination may also include savings of out-of-pocket (OOP) expenditures on malaria treatment for patients and their families, and avoiding associated catastrophic health expenditure. In this paper, we studied malaria vaccine in Zambia and applied extended cost-effectiveness analysis (ECEA) methods [18-20] which examine the impact of health policies along four dimensions: the health benefits (premature malaria deaths averted); the financial consequences to households (OOP costs for malaria treatment averted) and associated financial risk protection to them (cases of malaria

related catastrophic expenditure averted); the intervention costs (vaccine program costs); and their distributional consequences across socioeconomic groups (per income quintile).

We chose Zambia as a case study. In many lower middle-income countries like Zambia where, large populations live under the poverty line ($1.90 a day) [21], malaria remains one of the leading causes of mortality for under-five (see Global Burden of Disease study 2016 estimates [22]) and malaria incidence is often unequally distributed among geographical areas and population subgroups [23]. Compared with other malaria-endemic countries, Zambia has achieved relatively high immunization coverage rates (DTP3 coverage, i.e., coverage with three doses of diphtheria-tetanus-pertussis vaccine, was 86% among children aged 12-23 months in 2014 [24]), and the distribution of immunization coverage is relatively flat (e.g., DPT3 coverage was 79% among the lowest vs. 95% among the highest wealth quintile among children aged 12-23 months). Moreover, one recent study [14] projected that among the malaria-endemic countries, Zambia would rank around middle-to-high in terms of the public health impact and averted malaria burden that vaccination would bring. The coverage of key malaria interventions, such as insecticide-treated bednets or indoor residual spraying [24] was rather equally distributed, comparable with other sub-Saharan African countries [25]. Lastly, with respect to income, Zambia was ranked among the most inequal countries in sub-Saharan Africa [21]. While Zambia removed user fees for primary care over 2006-2011, the policy change did not eliminate catastrophic health expenditure[26, 27]. A recent study [27] investigating user fee elimination in Zambia concluded that households would still incur considerable OOP expenditure and associated catastrophic expenditure for health care, even after fee elimination, with significant variation across socioeconomic groups. Given that severe malaria cases can often be admitted as inpatient cases, malaria continues to pose a major threat not only to health, but also to the

financial security of affected households in Zambia. To assess the extent to which these risks could be reduced by the introduction of the RTS,S malaria vaccine, we applied ECEA methods to point to the potential equity benefits of the vaccine.

2. Methods

2.1 Model overview

Using the ECEA approach, we estimated the hypothetical impact of introducing the RTS,S vaccine to one Zambian birth cohort (i.e., all children born in the country in a given year), stratifying children under five and their households by income quintile. RTS,S impact was examined along four dimensions: under-five malaria deaths averted by vaccination; total household expenditure averted, including direct medical costs, transport costs, and lost caretaker wages related to malaria treatment; financial risk protection (FRP) benefits, defined as the number of household cases of catastrophic health expenditure (CHE) averted; and distributional consequences across income quintiles. A CHE case was defined as malaria-related household costs exceeding 10% of monthly household expenditure . We also computed the costs of vaccinating one Zambian birth cohort and expected health care savings on malaria treatment following vaccine introduction from the perspective of the Zambian government. All costs were expressed in 2016 USD.

2.2 Data sources

We largely relied on secondary data from the literature and survey reports. All parameter values used are presented in Table 1. Considering the year of the most recently available disease burden data and health interventions in Zambia, our analysis followed a birth cohort of 622,000

Zambian children in 2016 over their first five years of life [28]. We applied this five-year time horizon to one Zambian birth cohort as focusing on under-five children will show the largest benefit- they are the population group where the large majority of mortality reduction benefits would occur and for whom burden of disease data were readily available.

[TABLE 1 AROUND HERE]

We assumed a three-dose schedule, consistent with previous studies [14, 17]: at ages 6, 7.5, and 9 months, which align with routine visits for children (vitamin A supplementation at 6 months and measles vaccine at 9 months). Acknowledging the potential constraint of lost to follow up, we assumed the vaccine would be administered in three doses, and did not include a fourth (booster) dose. To account for the vaccine waning effect, we used a Weibull decay function for efficacy against infection, with initial efficacy against infection of 91.1% and a half-life of 7.32 months [14, 17, 29].

The vaccine was assumed to cost $5 per dose at full market price [14, 17]. Zambia has entered the "preparatory transition" phase of co-financing support from Gavi, the Vaccine Alliance [30], which would bring down the cost per dose to $0.20 in the initial year of RTS,S introduction, the lowest possible subsidized price the government could pay for the vaccine [31]. Therefore, we varied vaccine price from full price to fully-subsidized price in a sensitivity analysis. In addition to vaccine costs, health system costs for the immunization program are comprised of service delivery and supply chain costs. We assumed these costs to be $1.6 per dose, based on a recent study of vaccination program costs [32]; but in one sensitivity analysis, we estimated the consequences of using higher health system costs ($6.2 per dose), based on another study on the costs of routine vaccination programs in Zambia [33]. For simplicity and

due to data availability, we assumed the vaccination program costs based on the program operating at scale and the same coverage rate as coverage of fully-immunized children aged 12-14 months, as reported in Zambia's 2013-14 DHS [24]. Therefore, our study did not account for incremental costs of vaccine introduction (such as worker training and social mobilization). The malaria vaccine was assumed to be delivered in health facilities during routine immunization sessions (i.e., no campaign delivery was modeled).

2.3 Malaria-related deaths and cases

To estimate malaria deaths by income quintile, we obtained the total number of malaria deaths for children under five from the Global Burden of Disease (GBD) study (year 2016 estimates) [22], which we further distributed across income quintiles through an estimated risk index. This risk index was calculated by using three proxy measures: the total fertility rate per quintile [24], the prevalence of fever among under-fives per quintile [23], and the probability of obtaining treatment for fever per quintile [23].. To estimate malaria cases by quintile, we stratified the total number of malaria cases based on total fertility rate and prevalence of fever among children under-five, per quintile.

The hospitalization and outpatient rates among malaria cases for children under five years of age were distributed across income quintiles based on the probability of obtaining treatment for children with fever per quintile (supplementary appendix, section 2).

To determine the number of malaria-related deaths averted by vaccination, we used a static approach and assumed vaccine coverage would match the quintile-specific coverage rate of fully-immunized children aged 12-24 months [24]. The number of malaria deaths averted in each quintile was then estimated, in a simple static way, to be the product of baseline malaria-related

deaths for children under five, vaccine coverage, and vaccine efficacy (including waning over five years) (supplementary appendix, section 3.1).

2.4 Household costs averted by vaccination

Malaria-related costs borne by sick children and their families were estimated with and without vaccination. Household costs were composed of direct medical treatment costs and transportation costs per malaria-related visit (OOP costs), and associated caretaker costs incurred. We computed the lost wages through time losses for caretakers per malaria case. Thus, total household costs averted were computed based on the baseline number of malaria cases for children under five, malaria-related household costs before vaccination, and vaccine coverage and efficacy.

To estimate malaria-related OOP costs, we used data on malaria-related hospitalization and outpatient costs, primarily obtained from WHO's Choosing Interventions that are Cost-Effective (WHO-CHOICE) [34]. Malaria-related inpatient costs per patient at hospitals and health centers included the hospital costs per bed-day (personnel, capital, and food costs), length of hospital stay, and the costs of medications and diagnostics. Further, using Zambia's share of OOP health expenditure out of total health expenditure [21], we derived household OOP costs due to malaria for both inpatient and outpatient care (supplementary appendix, section 3.2). Additionally, drawing from published literature [27, 35], we estimated transportation costs, assuming each outpatient visit or hospitalization admission was associated with a fixed transportation cost. Lastly, lost caretaker wages were estimated by multiplying the number of days lost due to care-seeking and a caretaker's average daily wage. The daily wage was computed based on average household annual income using data from Zambia's Living Conditions Monitoring Survey, adjusted for income quintiles [36]. The length per hospitalization

stay was assumed at 4.6 days [37], and each hospitalized child would be accompanied by one adult caretaker, who would lose 100% of daily wages when accompanying the sick child to inpatient care and 50% of daily wages for outpatient care. Hence, the incurred household OOP expenditure were estimated as a product of: the number of malaria cases per income quintile, the probability of obtaining treatment if sick with malaria, and the OOP cost per treatment (including direct medical costs and transportation costs, and indirect costs due to caretaker wage losses) depending on inpatient/outpatient care. The incurred household costs on malaria treatment averted by vaccination would be estimated by accounting for two additional factors: vaccine coverage and efficacy (supplementary appendix, section 3.2).

Subsequently, the estimated cases of CHE averted by vaccination depended on the number of hospitalized cases that households would encounter before vaccination and, of those hospitalizations, those which resulted in incurred costs exceeding 10% of monthly total household expenditure, as well as on vaccine coverage and efficacy (supplementary appendix, section 3.3).

2.5 Vaccine program costs

From the government's perspective, we estimated the hypothetical costs of the vaccination program, which would depend on vaccine price, coverage, health system costs, and target population. We also estimated the cost savings (malaria-related treatment costs averted) for the government: these were estimated by multiplying the number of malaria cases averted by vaccination by provider treatment costs (inpatient and outpatient), excluding the share of

expenditure that would be borne by households (30%) [21] (supplementary appendix, section 3.4).

All calculations were performed using Microsoft Excel (version 15.21.1) and R version 3.5.1.

2.6 Sensitivity analyses

We ran four univariate sensitivity analyses (supplementary appendix, section 4). First, we tested an alternative vaccine price of $0.20 per dose (under full Gavi subsidization). Second, we set the malaria burden so that it would remain equal across income quintiles, ceteris paribus, so to test the influence of the distribution of malaria burden on our findings. Third, we set vaccine coverage equal across quintiles (68%), ceteris paribus, in order to test the influence of the coverage distribution. Fourth, we tested alternative health system delivery costs ($6.2 per vaccine dose), based on a recent cost analysis of routine immunization programs in Zambia [33].

3. Results

Table 2 shows the distribution of malaria deaths and cases by income quintile before vaccine introduction. Across Zambia, under the model assumptions, a birth cohort of 622,000 children would face about 1.2 million malaria cases over their first five years of life (about 2% of these cases being hospitalized), with an estimated total of 3,500 malaria deaths (Global Burden of Disease study of 2016 estimates [22]).

[TABLE 2 AROUND HERE]

The burden of malaria deaths would be largely concentrated among the poorer households. With the vaccine introduction, about 670 deaths per birth cohort (over the five-year

analytic horizon) would be averted. Over half of these would be among the bottom two income quintiles (Table 3) because these quintiles would be expected to experience a higher burden of malaria in the first place. About $1.0 million in household costs would be averted. Given that malaria incidence is higher among the bottom quintiles, but healthcare utilization increases with income, household costs averted would be more or less evenly distributed across quintiles. Lastly, with the exception of the top quintile who would not likely suffer any CHE case, households in the other four quintiles would avoid about 4,400 cases of CHE.

[TABLE 3 AROUND HERE]

[FIGURE 1 AROUND HERE]

The vaccination program would cost about $9.2 million and save $0.8 million in government spending on malaria treatment. Hence, per each $1 million of net government expenditure on vaccination, estimated by subtracting the government cost-savings on malaria-related treatment from the vaccination program costs, approximately 380 malaria deaths and $0.7 million in household incurred costs would be averted. Per net expenditure, the largest health benefits would accrue to the poorest quintile and the largest household costs averted to the top two quintiles (Figure 2).

[FIGURE 2 AROUND HERE]

When we reduced the price per vaccine dose (with Gavi subsidization), per net $1 million government expenditure, averted household costs and malaria deaths increase substantially as expected, while the differentials across quintiles would remain similar (supplementary appendix, Figures S1). When we set the number of malaria-related cases and deaths equal across quintiles, per net $1 million government spending, an increase would be observed in household costs

averted and health benefits, with both accruing largely to the top two quintiles (Figures S2). When vaccine coverage is set equal across quintiles (68% coverage) and all other conditions remain unchanged, per net $1 million, the deaths averted and household costs averted remained at a similar level as in the base case scenario (Figure S3). Although vaccine coverage was higher among the highest quintile compared to the lowest quintile, there were fewer malaria cases and deaths to avert among the highest quintile. When vaccine coverage is set equal across quintiles, slight increases were observed in the health gains (deaths averted), the household OOP costs averted, the government cost-savings, and the vaccination costs, for the bottom two quintiles which have a lower vaccine coverage in the base case scenario, while decreases were observed in these four domains for the top two quintiles which have a higher vaccine coverage in the base case scenario. Therefore, when accounting for the net government expenditure, the deaths and household costs averted, per $1 million spending, remained at a similar level as in the base-case scenario. When we tested an alternative vaccine delivery cost ($6.2 per dose), per net $1 million spending, a large decrease was observed in averted malaria deaths and household costs, while differentials across quintiles would be maintained (Figures S4).

4. Discussion

The results presented in this paper suggest large household health and financial benefits from rolling out the RTS,S malaria vaccine in Zambia, including impact on OOP costs averted and financial risk protection (FRP), and malaria-related deaths averted.

Our findings provide key insights into the distributional consequences of rolling out malaria vaccine across socioeconomic groups in Zambia. First, the vaccination could provide a large number of deaths averted to the poorest 40% of the population. Second, the household

OOP expenditure averted would be relatively evenly distributed across income quintiles; and per net $1 million government expenditure, higher income groups would benefit more from malaria-related OOP costs averted, notably because wealthier populations have better access to care. Third, the malaria vaccine would bring significant FRP benefits to all income quintiles, except for the top quintile by averting CHE cases.

Our analysis differs from prior studies of RTS,S vaccine in that we have incorporated distributional consequences and FRP benefits into the vaccination evaluation. A limited number of cost-effectiveness studies for endemic sub-Saharan Africa are available to assist policymakers faced with increasingly complex decisions about national immunization and malaria control programs. Such previous studies used traditional cost-effectiveness methods, and focused on understanding country-specific health impacts (deaths or cases to be averted) by adding RTS,S to existing programs [13-17]. To our knowledge, our analysis is the first to provide information about the distributional consequences across socioeconomic groups and FRP benefits.

Nevertheless, our study has a number of limitations. First, some parameters such as transportation costs for seeking treatment were not specific to Zambia, while most epidemiological and economic estimates used were drawn from Zambian data. Data from neighboring countries were then used for missing parameters. Second, we did not account for incremental costs of vaccine introduction (training for workers on new vaccine usage and operations, social mobilization, costs on cold chain storage expansion). Third, coverage rates of the malaria vaccine were assumed in the calculation to achieve a level similar to the conventional six recommended vaccines for newborns, when in reality, introduction of a new vaccine is an incremental progression towards full implementation over time. Fourth, in quantifying the distribution of malaria deaths and cases, as well as hospitalized and outpatient cases, we used

risk indices proxied by a number of inputs captured from surveys and available by socioeconomic group [23, 24]. Additionally, due to data availability to us, we used the Weibull decay function for vaccine efficacy against infection, but did not project the uncertainty in the efficacy estimate which may depend on transmission intensity. We acknowledge that the malaria vaccine efficacy may vary greatly by level of malaria endemicity, and influence the outcomes of the field implementation trials, which are conducted in different regions. Moreover, our study assumed the three-dose vaccine schedule, at 6, 7.5, and 9 months respectively, which align with routine visits for children (vitamin A supplementation at 6 months and measles vaccine at 9 months). We acknowledge the potential constraint of not following up to include a fourth booster dose. Also, the feasibility of this regimen is unknown in the health systems of different malaria-endemic countries, which may never have provided child vaccines during these time points. Furthermore, we acknowledge a concern that cannot be ignored, of a potential increase in "meningitis-like" cases in children receiving the malaria vaccine, which would need findings from future field implementation trial studies. In addition, although our study focused on understanding the distributional consequences and financial risk protection that the malaria vaccination provided to households, in order to assist policymakers, providing information regarding the relevance of comparing with other malaria interventions, such as insecticide-treated bednets, would be necessary. Lastly, a major limitation is that we did not use a dynamic model of malaria transmission, including epidemiological protection and secondary cases among unvaccinated children [15, 17]. Additionally, the longer-term effects of vaccination, such as the community-wide effect of reduced incidence and death, are not yet known, and are therefore

excluded. In this respect, our approach likely underestimates the malaria deaths and cases averted by vaccination and consequently the averted OOP treatment costs and CHE cases.

We focused our analysis on Zambia, where malaria has remained a leading cause of mortality for children under five years of age, comparable with many other sub-Saharan African countries. Zambia provided an illustrative case for exploring the likely distributional consequences and financial protection benefits of malaria vaccine; and in this respect, our findings can be relevant to many other malaria-endemic sub-Saharan African countries suffering a high malaria burden and similar distributions of key malaria interventions [25]. Our analysis also points to the importance of vaccine pricing and suggests that organizations such as Gavi can play an important role to enhance the benefits of a malaria vaccination program. The vaccination program costs would be much reduced if the government received a fully-subsidized vaccine price ($0.20 per dose). Zambia has been associated with the Gavi co-financing preparatory transition phase, and as such, it would likely face a higher price per dose, leading to the government's incremental contribution to the cost being required. As a result, smaller health and FRP gains per dollar spent would be expected. Furthermore, our ECEA approach goes beyond traditional CEA and provides valuable information for policymakers. ECEA takes into account not only how vaccinating children would decrease the malaria burden and financial risks borne by households resulting from malaria infection, but also how these benefits would be distributed across population subgroups in Zambia. This enables stakeholders to select vaccine packages based on how much health benefits and financial protection could be bought per expenditure on vaccination. Moreover, we find that crucial differences exist in malaria morbidity and mortality; distributional health care utilization among children of different quintiles and government costs of the vaccination policy also vary across population subgroups. The findings provide insight

into the policy trade-offs in the selection of one public health intervention in targeting specific policy goals (i.e., improved health benefits accruing more to the bottom 40% or saved household OOP costs accruing more to the top 40%). This understanding can assist policymakers to better interpret distributional consequences and weigh sometimes competing objectives in the design of intervention in terms of financial burdens to the government vis-à-vis health gains and financial benefits for families from different socioeconomic groups.

5. Acknowledgements

Earlier versions of this paper were presented during several seminars at the Harvard University Global Health Institute, the Harvard T.H. Chan School of Public Health, and University of Washington, the Seattle Global Health Symposium and the Evans School of Public Policy and Governance Research Symposium, the 5th Global Symposium on Health Systems Research, and we received valuable comments from Margaret Kruk, Farzana Muhib, Michael Reich, and Sara Singer.

6. Contributors

SV designed and supervised the study. LL conceived the analysis and collected the data, conducted the research, and wrote the first draft of the manuscript. ZT collected preliminary data, conducted preliminary analyses, and contributed to the writing of the manuscript. All

authors contributed to drafting and critical revision of the manuscript and have approved the final article.

7. Declaration of interests

All authors declare no conflicts of interests.

Table 1. Parameters used for the extended cost-effectiveness analysis of malaria vaccine in Zambia

Parameter	Value	Sources
Epidemiology		
Deaths of under-five children due to malaria	3480	[22]
Total fertility rate (number of children born per woman), from poorest to richest (income quintile 1-5)	7, 7, 6, 4, 3	[24]
Distribution (%) of deaths of under-five children due to malaria, from poorest to richest (income quintile 1-5)	38, 26, 19, 11, 6%	Authors' calculations based on [23, 24]
Total number of malaria cases among children under five	1,248,000	[22]
Prevalence of fever among under-fives, from poorest to richest (income quintile 1-5)	24, 20, 16, 14, 12%	[23]
Number of newborns, from poorest to richest (income quintile 1-5)	177,000, 174,000, 149,000, 105,000, 75,000	Authors' calculations based on [24, 28]
Interventions		
Artemisinin-based combination therapy efficacy on reducing malaria mortality	82%	[38]
Vaccine efficacy, following a Weibull decay after 9 months over 5-year horizon (for 9-12 months, 12-24 months, 24-36 months, 36-48 months, 48-60 months)	85, 63, 37, 22, 13%	Authors' calculations based on [14, 17, 29]
Vaccine coverage, from poorest to richest (income quintile 1-5)	63, 63, 67, 75, 80%	Based on fully immunized coverage of children aged 12-24 months [24]
Costs		
Vaccine base price (3 doses needed)	$5.00 per dose	Authors' assumptions
Gavi-subsidized vaccine price	$0.20 per dose	[31]
Out-of-pocket expenditure on direct medical cost per hospitalized child (including drugs, "hotel" component [a], and investigation and diagnostics)	$27.00	Authors' calculations based on [21, 34, 37]
Transportation cost for seeking inpatient care (per inpatient visit)	$8.60	[35]

Table 1. Parameters used for the extended cost-effectiveness analysis of malaria vaccine in Zambia		
Transportation cost for seeking outpatient care (per outpatient visit)	$1.85	[27]
Out-of-pocket expenditure on direct medical cost for non-hospitalized child (including drugs and diagnostic costs)	$0.68	[27]
Indirect cost of malaria treatment (value of work time lost)		
Hospitalized child	$8.00	Based on [36]
Non-hospitalized child	$0.87	
Health system vaccine delivery cost (per dose)	$1.64	[32]
Health system vaccine delivery cost (per dose, for sensitivity analysis)	$6.23	[33]
Healthcare utilization (%)		
Inpatient hospitalization (percentage hospitalized among under-five malaria cases), from poorest to richest (income quintile 1-5)	1.7, 2.9, 1.8, 2.0, 1.7%	Authors' calculations based on [17, 23]
Outpatient visits, from poorest to richest (income quintile 1-5)	19, 39, 30, 38, 39%	[23]
Out-of-pocket health expenditure (% of total health expenditure on health)	30%	[21]
Average household monthly expenditure (2016 USD)[b]	Income quintile I: $27 Income quintile II: $57 Income quintile III: $99 Income quintile IV: $178 Income quintile V: $568	Authors' calculations based on [36]

[a] "Hotel" component of hospital costs: bed day costs, including costs such as personnel, building, food, and laundry, but excluding drugs and diagnostic tests.
[b] Data was originally reported in 2015 Zambian Kwacha (ZMK), and monetary units were inflated into 2016 USD [21, 39, 40].
All costs are expressed in 2016 USD.

Table 2: Estimated distribution of malaria deaths and cases among children under five in Zambia[†], by income quintile (lowest to highest quintile) (before vaccination introduction)

	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	Total
Malaria cases	349,000	292,000	230,000	206,000	171,000	1,248,000
Malaria deaths	1,324	889	663	379	225	3,480

[†] The estimates presented here represent the cumulative burden over the five-year analytic horizon for the 2016 birth cohort of Zambian children.
Quintile 1, poorest quintile; Quintile 5, richest quintile.
Authors' calculations based on Zambia-DHS 2013-2014 [24], Malaria Indicator Survey 2015 [23], and IHME GBD 2016 [22].

Table 3:Under-five deaths averted, household out-of-pocket costs averted, and cases of catastrophic expenditure averted by malaria vaccination in Zambia†, as well as vaccine program costs and government cost-savings, by income quintile (from poorest to richest)

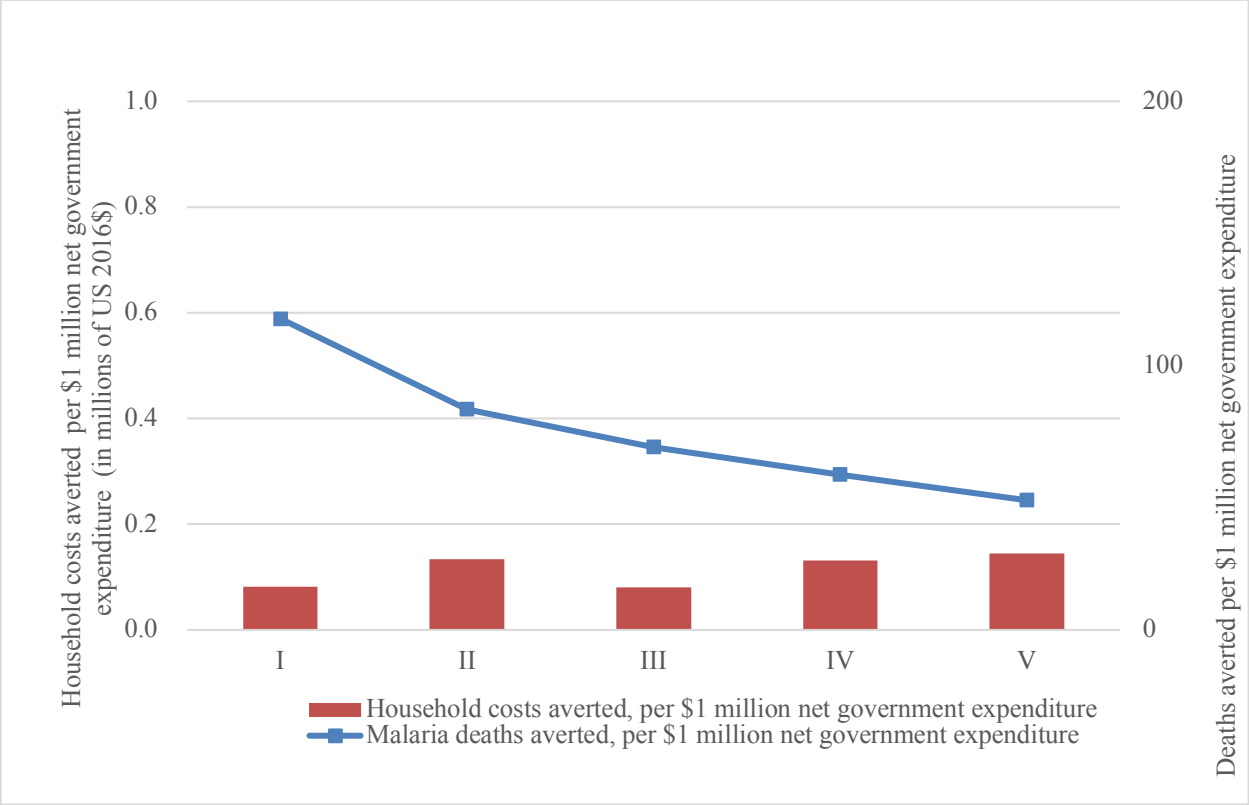
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	Total
Deaths averted for under-five children	240	163	129	83	52	667
Household out-of-pocket costs averted	$167,000	$261,000	$149,000	$186,000	$155,000	$917,000
Cases of catastrophic expenditure averted	1,107	1,581	801	922	0	4,411
Vaccination program costs						
Base-case	$2,200,000	$2,200,000	$1,993,000	$1,570,000	$1,193,000	$9,155,000
With Gavi subsidy	$610,000	$610,000	$552,000	$435,000	$330,000	$2,537,000
Government cost-savings	$165,000	$247,000	$133,000	$159,000	$127,000	$832,000
Government spending on malaria-related treatment *without* vaccination	$480,000	$706,000	$360,000	$384,000	$288,000	$2,219,000
Government spending on malaria-related treatment *with* vaccination	$315,000	$460,000	$227,000	$225,000	$161,000	$1,387,000

† The estimates presented here represent the cumulative burden over the five-year analytic horizon for the 2016 birth cohort of Zambian children.
Quintile 1, poorest quintile; Quintile 5, richest quintile.
Authors' calculations based on Zambia-DHS 2013-2014 [24], Malaria Indicator Survey 2015 [23], and IHME GBD 2016 [22].

Figure 1. Averted household costs, government cost savings, and averted deaths, resulting from RTS,S vaccination against malaria, among one cohort of under-five year-old children, Zambia[†].
I = Poorest; II = Poorer; III = Middle; IV = Richer; V = Richest.

[†] The estimates presented here represent the cumulative burden averted over the five-year analytic horizon for the 2016 birth cohort of Zambian children.

Figure 2. Averted household costs and averted deaths, per $1 million net government expenditure*, resulting from RTS,S vaccination against malaria, among one cohort of under-five year old children, Zambia†.
I = Poorest; II = Poorer; III = Middle; IV = Richer; V = Richest.



*The net government expenditure were estimated with subtracting the government cost-savings on malaria-related treatment from the vaccination program costs.

† The estimates presented here represent the cumulative burden averted over the five-year analytic horizon for the 2016 birth cohort of Zambian children.

8. References

[1] World Health Organization. World Malaria Report 2017. Retrieved from http://www.who.int/malaria/publications/world-malaria-report-2017/en/ (accessed March 15, 2018)
[2] United Nations. Sustainable Development Goals. Retrieved from http://www.un.org/sustainabledevelopment/health/ (accessed January 15, 2017)
[3] World Health Organization. Malaria Vaccine: WHO position Paper-January 2016. Retrieved from http://www.who.int/immunization/policy/position_papers/malaria/en/ (accessed February 22, 2016)
[4] World Health Organization. Malaria Vaccine Development. Retrieved from http://www.who.int/malaria/areas/vaccine/en/ (accessed January 20, 2017)
[5] Program for Appropriate Technology in Health (PATH) Malaria Vaccine Initiative. Development of RTS,S. Retrieved from http://www.malariavaccine.org/malaria-and-vaccines/first-generation-vaccine/rtss (accessed February 20, 2017)
[6] Agnandji ST, Lell B, Soulanoudjingar SS, Fernandes JF, Abossolo BP, Conzelmann C, et al. First results of phase 3 trial of RTS,S/AS01 malaria vaccine in African children. N Engl J Med. 2011;365:1863-75.
[7] Agnandji ST, Lell B, Fernandes JF, Abossolo BP, Methogo BG, Kabwende AL, et al. A phase 3 trial of RTS,S/AS01 malaria vaccine in African infants. N Engl J Med. 2012;367:2284-95.
[8] Rts SCTP, Agnandji ST, Lell B, Fernandes JF, Abossolo BP, Methogo BG, et al. A phase 3 trial of RTS,S/AS01 malaria vaccine in African infants. N Engl J Med. 2012;367:2284-95.
[9] RTS, S Clinical Trials Partnership. Efficacy and safety of RTS, S/AS01 malaria vaccine with or without a booster dose in infants and children in Africa: final results of a phase 3, individually randomised, controlled trial. The Lancet. 2015;386:31-45.
[10] European Medicines Agency. First malaria vaccine receives positive scientific opinion from EMA. Retrieved from http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2015/07/news_detail_002376.jsp&mid=WC0b01ac058004d5c1 (accessed June 24 2018)
[11] World Health Organization. Meeting of the Strategic Advisory Group of Experts on immunization, October 2015-conclusions and recommendations. Retrieved from http://www.who.int/wer/2015/wer9050/en/ (accessed January 15, 2017)
[12] World Health Organization Regional Office for Africa. WHO Malaria Vaccine Pilot Programme. Retrieved from http://www.afro.who.int/ (accessed August 20, 2017)
[13] Penny MA, Galactionova K, Tarantino M, Tanner M, Smith TA. The public health impact of malaria vaccine RTS, S in malaria endemic Africa: country-specific predictions using 18 month follow-up Phase III data and simulation models. BMC Med. 2015;13:170.
[14] Galactionova K, Tediosi F, Camponovo F, Smith TA, Gething PW, Penny MA. Country specific predictions of the cost-effectiveness of malaria vaccine RTS, S/AS01 in endemic Africa. Vaccine. 2017;35:53-60.
[15] Winskill P, Walker PG, Griffin JT, Ghani AC. Modelling the cost-effectiveness of introducing the RTS, S malaria vaccine relative to scaling up other malaria interventions in sub-Saharan Africa. BMJ global health. 2017;2:e000090.

[16] Seo MK, Baker P, Ngo KN-L. Cost-effectiveness analysis of vaccinating children in Malawi with RTS, S vaccines in comparison with long-lasting insecticide-treated nets. Malar J. 2014;13:66.
[17] Penny MA, Verity R, Bever CA, Sauboin C, Galactionova K, Flasche S, et al. Public health impact and cost-effectiveness of the RTS, S/AS01 malaria vaccine: a systematic comparison of predictions from four mathematical models. The Lancet. 2016;387:367-75.
[18] Verguet S, Kim JJ, Jamison DT. Extended Cost-Effectiveness Analysis for Health Policy Assessment: A Tutorial. Pharmacoeconomics. 2016;34:913-23.
[19] Verguet S, Laxminarayan R, Jamison DT. Universal Public Finance of Tuberculosis Treatment in India: An Extended Cost‐Effectiveness Analysis. Health Econ. 2015;24:318-32.
[20] Verguet S, Murphy S, Anderson B, Johansson KA, Glass R, Rheingans R. Public finance of rotavirus vaccination in India and Ethiopia: an extended cost-effectiveness analysis. Vaccine. 2013;31:4902-10.
[21] World Bank. World Bank Data Indicators. Zambia Country Profile. Retrieved from https://data.worldbank.org/country/zambia (accessed March 10, 2018)
[22] Institute for Health Metrics and Evaluation. Global Burden of Disease (GBD) 2016 Data. Retrieved from http://ghdx.healthdata.org/gbd-results-tool (accessed April 24, 2018)
[23] Zambia Ministry of Health. Zambia National Malaria Indicator Survey 2015. Retrieved from http://www.makingmalariahistory.org/wp-content/uploads/2017/06/Zambia-MIS2015_Jan20-nosigs.pdf (accessed April 24, 2018)
[24] Central Statistical Office (CSO) [Zambia], Ministry of Health (MOH) [Zambia], and ICF International. Zambia Demographic and Health Survey 2013-14. Rockville, Maryland, USA: Central Statistical Office, Ministry of Health, and ICF International; 2014.
[25] Galactionova K, Smith TA, de Savigny D, Penny MA. State of inequality in malaria intervention coverage in sub-Saharan African countries. BMC Med. 2017;15:185.
[26] Masiye F, Chitah BM, McIntyre D. From targeted exemptions to user fee abolition in health care: experience from rural Zambia. Soc Sci Med. 2010;71:743-50.
[27] Masiye F, Kaonga O, Kirigia JM. Does User Fee Removal Policy Provide Financial Protection from Catastrophic Health Care Payments? Evidence from Zambia. PLoS One. 2016;11:e0146508.
[28] United Nations. Population Division World Population Prospects 2017. Retrieved from https://esa.un.org/unpd/wpp/dataquery/ (accessed April 24, 2018)
[29] Penny MA, Pemberton-Ross P, Smith TA. The time-course of protection of the RTS, S vaccine against malaria infections and clinical disease. Malar J. 2015;14:437.
[30] Gavi, the Vaccine Alliance. GAVI Country Profile-Zambia. Retrieved from http://www.gavi.org/country/zambia/ (accessed August 10, 2017)
[31] Gavi, the Vaccine Alliance. GAVI Co-financing Policy. Retrieved from http://www.gavi.org/about/governance/programme-policies/co-financing/ (accessed August 12, 2017)
[32] Portnoy A, Ozawa S, Grewal S, Norman BA, Rajgopal J, Gorham KM, et al. Costs of vaccine programs across 94 low-and middle-income countries. Vaccine. 2015;33:A99-A108.
[33] Schütte C, Chansa C, Marinda E, Guthrie TA, Banda S, Nombewu Z, et al. Cost analysis of routine immunisation in Zambia. Vaccine. 2015;33:A47-A52.
[34] Cost effectiveness and strategic planning (WHO-CHOICE). WHO-CHOICE Country-specific Unit Cost. Retrieved from http://www.who.int/choice/country/country_specific/en/ (accessed March 10, 2017)

[35] Kim S-Y, Sweet S, Slichter D, Goldie SJ. Health and economic impact of rotavirus vaccination in GAVI-eligible countries. BMC Public Health. 2010;10:253.
[36] Zambia Central Statistical Office. Living Conditions Monitoring Survey Report 2015. Living Conditions Monitoring Branch, Central Statistical Office, Lusaka, Zambia; 2016.
[37] Ayieko P, Akumu AO, Griffiths UK, English M. The economic burden of inpatient paediatric care in Kenya: household and provider costs for treatment of pneumonia, malaria and meningitis. Cost effectiveness and resource allocation. 2009;7:1.
[38] Thwing J, Eisele TP, Steketee RW. Protective efficacy of malaria case management for preventing malaria mortality in children: a systematic review for the Lives Saved Tool. BMC Public Health. 2011;11:S14.
[39] World Bank. World Development Indicators Retrieved from http://databank.worldbank.org/data/reports.aspx?source=2&series=FP.CPI.TOTL (accessed June 29 2018)
[40] Organisation for Economic Co-operation and Development (OECD) Database. Retrieved from https://data.oecd.org/conversion/purchasing-power-parities-ppp.htm#indicator-chart (accessed June 29 2018)

9. Supplementary Appendix

9.1. Estimating the distribution of malaria deaths

The number of deaths due to malaria in income quintile *i*, denoted D_i, depends on the birth cohort of under-five children, denoted N_i, the probability of being infected with malaria, Pm_i, and the probability of dying from malaria conditional on being infected with malaria, Pd_i :

$$D_i = N_i * Pm_i * Pd_i \ . \quad (1)$$

where *i* is the income quintile ($1 \leq i \leq 5$).

The probability of dying from malaria in quintile *i*, conditional on being infected with the disease, Pd_i, is assumed to depend on the probability of obtaining treatment Pt_i, treatment efficacy S, and untreated disease case fatality ratio D_0:

$$Pd_i = Pt_i * (1 - S) * D_0 + (1 - Pt_i) * D_0 \ . \quad (2)$$

The distribution across quintiles of the probability of being infected with malaria Pm_i is estimated based on the distribution of fever prevalence among under-five children [1]; the distribution across quintiles of Pt_i is estimated based on the distribution of the percentage of under-five children with fever for whom treatment was sought [1]; and the number of births across

quintiles N_i is estimated from the distribution of the total fertility rate (number of children per woman of reproductive age) across income quintiles [2].

9.2. Estimating the distribution of malaria cases

The total number of under-five malaria cases, denoted *C*, was initially obtained from the Global Burden of Disease study 2016 estimates [3], and was further distributed across income quintiles based on N_i and the distribution of Pm_i (see Table 2 in the main text).

Using an average hospitalization rate among under-five malaria cases of about 2% (see Table 1 in the main text), we distributed across income quintiles the number of hospitalized/inpatient cases, denoted $C_{inpt,i}$, among malaria cases using the distribution of Pt_i across income quintiles. Likewise, for those malaria cases that were not hospitalized, a fraction of them would seek outpatient care, denoted $C_{out,i}$, following the distribution of Pt_i across income quintiles.

9.3 Estimating malaria vaccine impact

9.3.1. Deaths averted

Deaths averted by malaria vaccination, denoted $D_{av,i}$, depend on the number of under-five malaria deaths before the vaccination program, denoted D_i above, vaccine coverage per income quintile, denoted Cov_i, and vaccine efficacy, denoted VE (in a simple static formulation):

$$D_{av,i} = D_i * Cov_i * VE. \quad (3)$$

9.3.2. Household costs averted

The overall number of malaria cases C was stratified into hospitalized cases $C_{inpt,i}$ and outpatient cases $C_{out,i}$, respectively.

Household costs on malaria-related treatment (in the base-case scenario without vaccination), denoted $OOP_{base,i}$ (per quintile i), would depend on: hospitalized/outpatient cases per quintile, denoted $C_{inpt,i}$ and $C_{out,i}$; the direct out-of-pocket (OOP) costs to households due to malaria (including direct medical costs and transportation costs), denoted $OOP_{direct,inpt,i}$ and $OOP_{direct,out,i}$; and the indirect costs (caretaker wage losses) due to malaria, denoted $OOP_{indirect,inpt,i}$ and $OOP_{indirect,inpt,i}$. Therefore:

$$OOP_{base,i} = C_{inpt,i} * \left(OOP_{direct,inpt,i} + OOP_{indirect,inpt,i} \right) + C_{out,i} * \left(OOP_{direct,out,i} + OOP_{indirect,inpt,i} \right) \quad . \tag{4}$$

Household costs averted by malaria vaccination, denoted $OOP_{av,i}$, further depend on vaccine coverage Cov_i and vaccine efficacy VE. Hence:

$$OOP_{av,i} = VE * Cov_i * (OOP_{base,i}) \quad . \tag{5}$$

9.3.3. Cases of catastrophic health expenditure averted

Let y_i be the average household monthly expenditure (per income quintile), and $OOP_{base,inpt,i}$ be the unit household OOP expenditure on inpatient malaria treatment in quintile i. Then, if $OOP_{base,inpt,i}$ exceeds 10% of y_i, those inpatient malaria cases, $C_{inpt,i}$, would lead to

catastrophic health expenditure (CHE), and we would count those numbers of inpatient cases as $CHE_{base,i}$. Then, in the vaccination scenario, the number of cases of CHE averted per income quintile would be estimated as:

$$CHE_{vacc,i} = Cov_i * VE * CHE_{base,i} \quad . \tag{6}$$

9.3.4. Government cost savings

Cost savings to the Zambian government Ts are defined as public expenditure averted by malaria vaccination. Ts would depend on household direct medical costs averted by malaria vaccination, denoted $OOP_{dir\ med,i}$, and the share q of total health expenditure that are borne by households (i.e. share of out-of-pocket expenditure out of total health expenditure [4]):

$$Ts = OOP_{dir\ med,i} * \frac{1-q}{q} . \tag{7}$$

Table S1. List of key parameters and symbols used in the calculations.

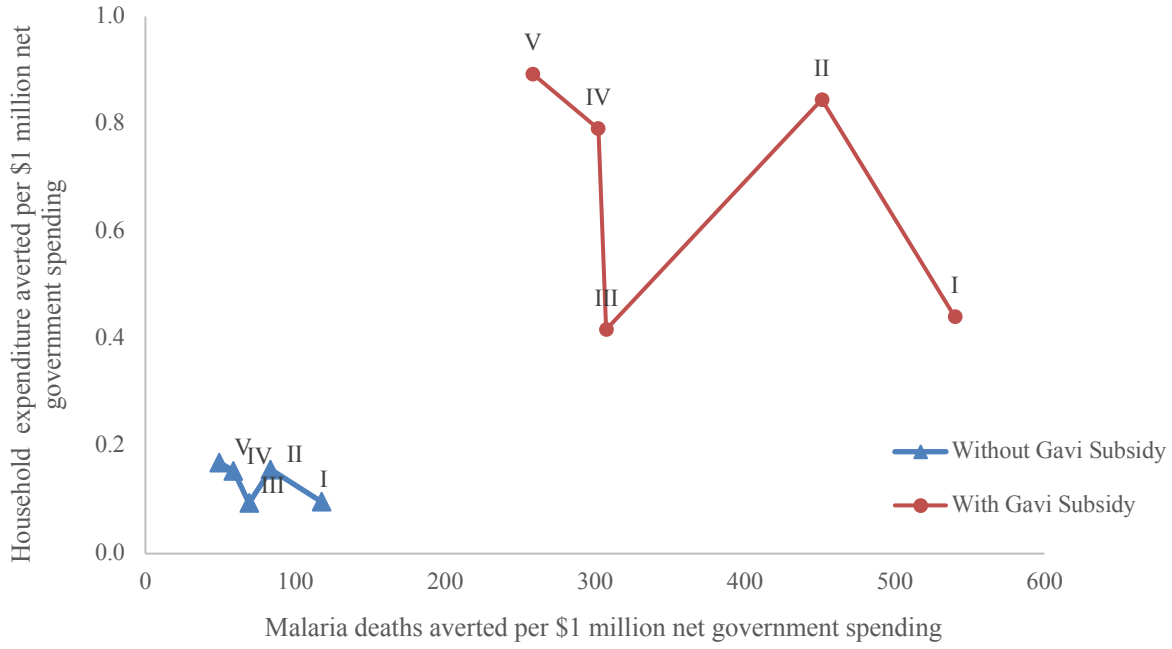
Parameter	Symbol
Deaths due to malaria	D_i[†]
Deaths averted by malaria vaccine	$D_{av,i}$
Birth cohort	N_i
Probability of being infected with malaria	$P_{m,i}$
Probability of dying from malaria conditional on being infected with malaria	$P_{d,i}$
Probability of utilizing treatment	$P_{t,i}$
Malaria treatment efficacy rate	S
Malaria untreated disease case fatality ratio	D_0
Vaccine coverage	Cov_i
Vaccine efficacy	VE
Number of malaria cases	C_i
Inpatient malaria cases	$C_{inpt,i}$
Outpatient malaria cases	$C_{out,i}$
OOP costs on malaria-related treatment without vaccination	$OOP_{base,i}$
OOP costs on malaria-related treatment averted by malaria vaccine	$OOP_{av,i}$
Direct OOP costs due to malaria (including medical costs and transportation costs)	$OOP_{direct,i}$
Indirect OOP costs due to malaria (caretaker wage losses)	$OOP_{indirect,i}$
Average household monthly income	y_i
Unit OOP costs on inpatient malaria treatment	$OOP_{base,inpt,i}$
Unit OOP costs on inpatient malaria treatment	$CHE_{base,i}$
Cases of catastrophic health expenditure without vaccination	$CHE_{vacc,i}$
Out-of-pocket health expenditure (% of total expenditure on health)	q
Government cost savings	Ts

[†] i is the income quintile, i = 1-5 (1= poorest, 5= richest). OOP = out-of-pocket.

9.4. Sensitivity analyses

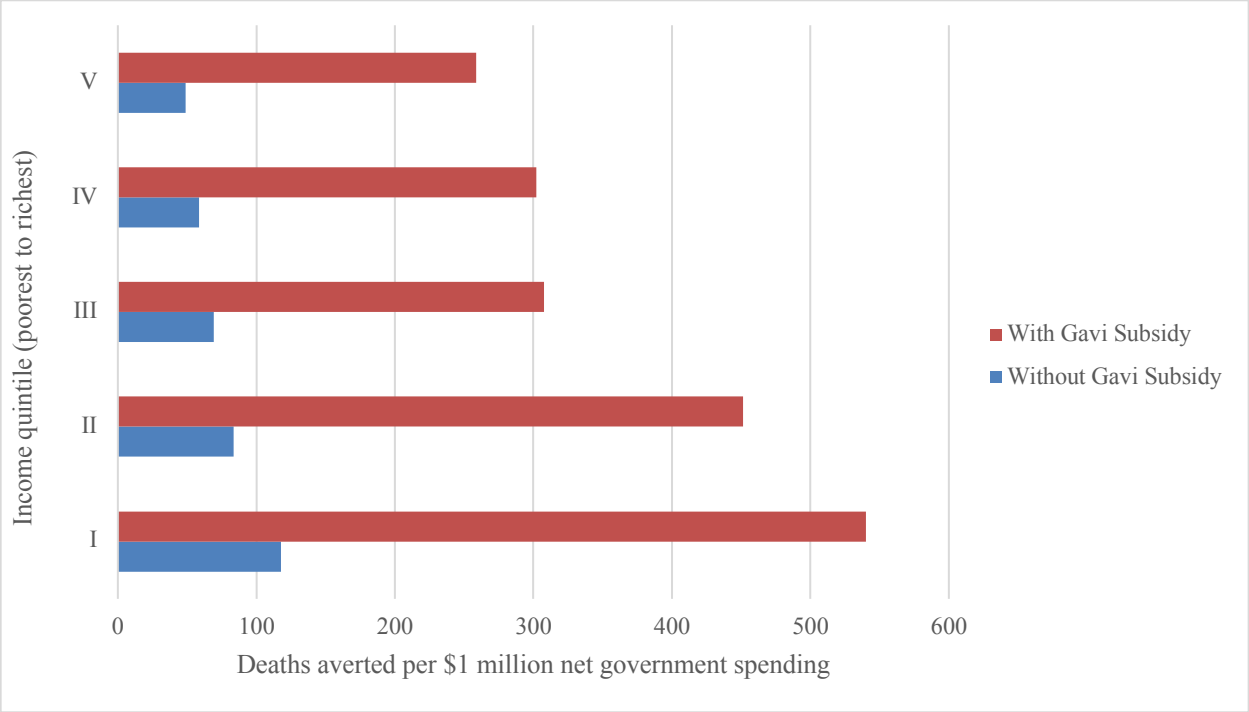
We report below on the results for the four sensitivity analyses conducted.

Figure S1.1. Household costs averted (in $ million) and malaria deaths averted by malaria vaccination in Zambia, per income quintile and $1 million net government expenditure*, with base-case and reduced vaccine price per dose† (in 2016 USD).
I = Poorest; II = Poorer; III = Middle; IV = Richer; V = Richest.



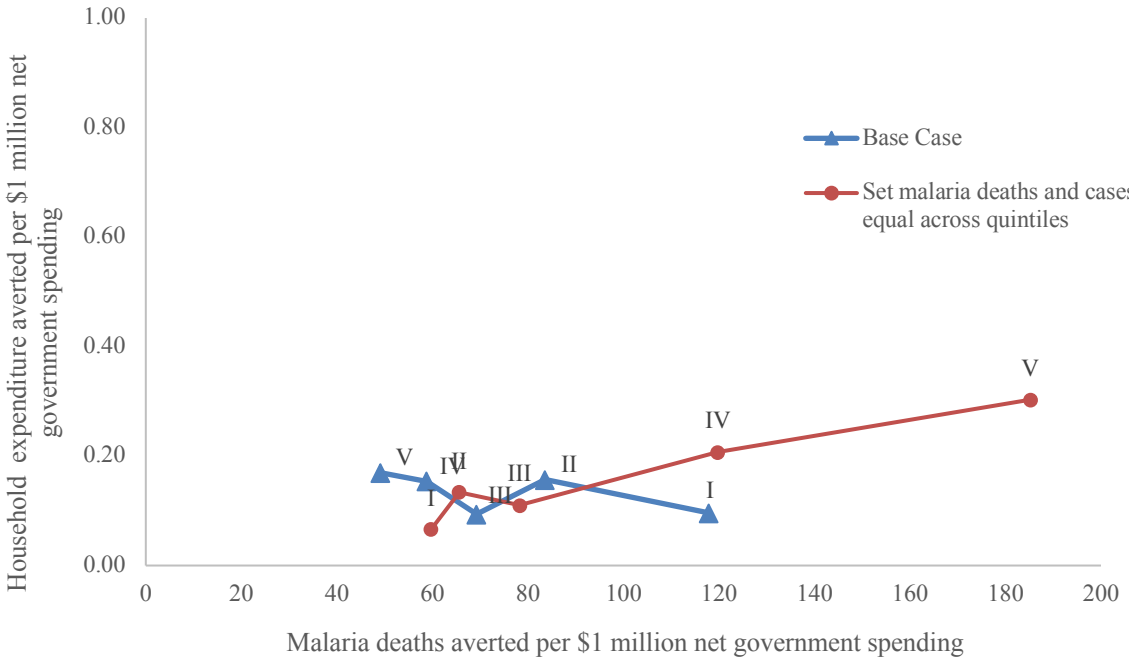
Note: Gavi subsidy: $0.20 per vaccine dose; no Gavi subsidy: $5.00 per vaccine dose.
*The net government expenditure were estimated with subtracting the government cost-savings on malaria-related treatment from the vaccination program costs.
†The estimates presented are cumulative over the five-year analytic horizon following the 2016 birth cohort.

Figure S1.2. Malaria deaths averted by malaria vaccination in Zambia, per income quintile and $1 million net government expenditure*, with base-case and reduced vaccine price per dose† (in 2016 USD).



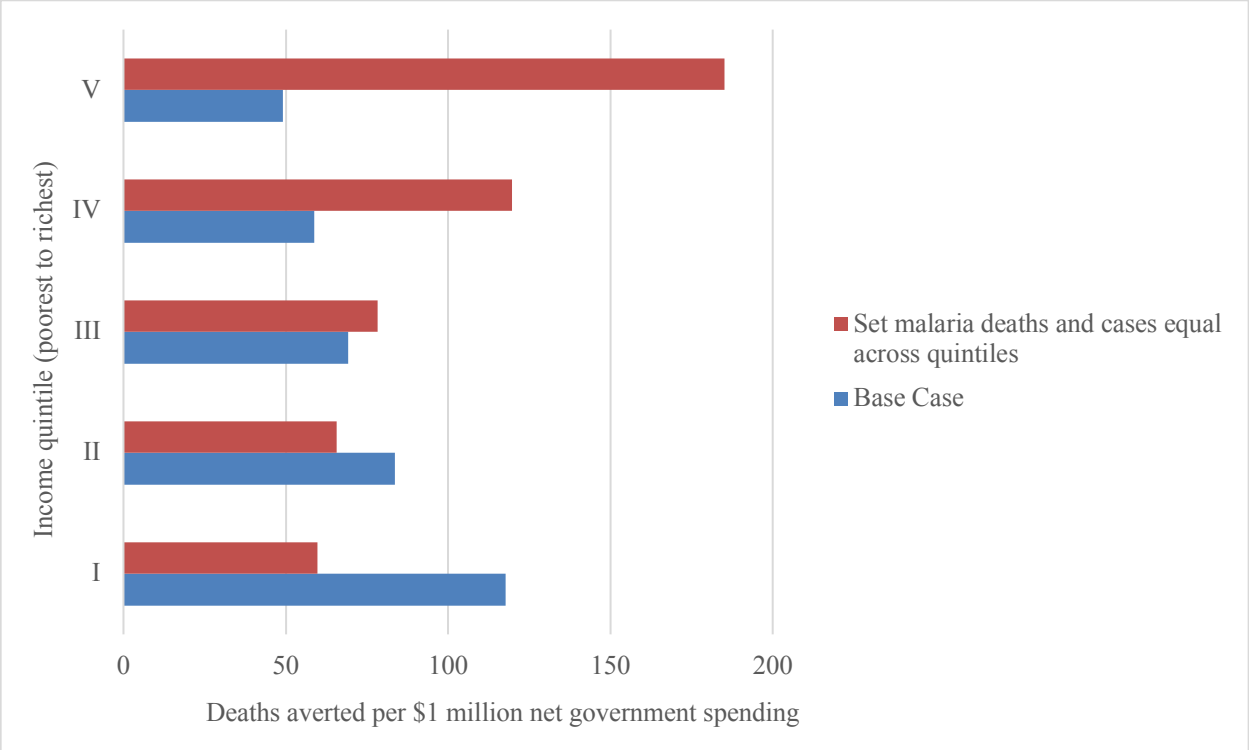
Note: Gavi subsidy: $0.20 per vaccine dose; no Gavi subsidy: $5.00 per vaccine dose.
*The net government expenditure were estimated with subtracting the government cost-savings on malaria-related treatment from the vaccination program costs.
†The estimates presented are cumulative over the five-year analytic horizon following the 2016 birth cohort.

Figure S2.1. Household costs averted (in $ million) and malaria deaths averted by malaria vaccination in Zambia, per income quintile and $1 million net government expenditure*, with base-case and with malaria deaths/cases equal across income quintiles† (in 2016 USD).
I = Poorest; II = Poorer; III = Middle; IV = Richer; V = Richest.



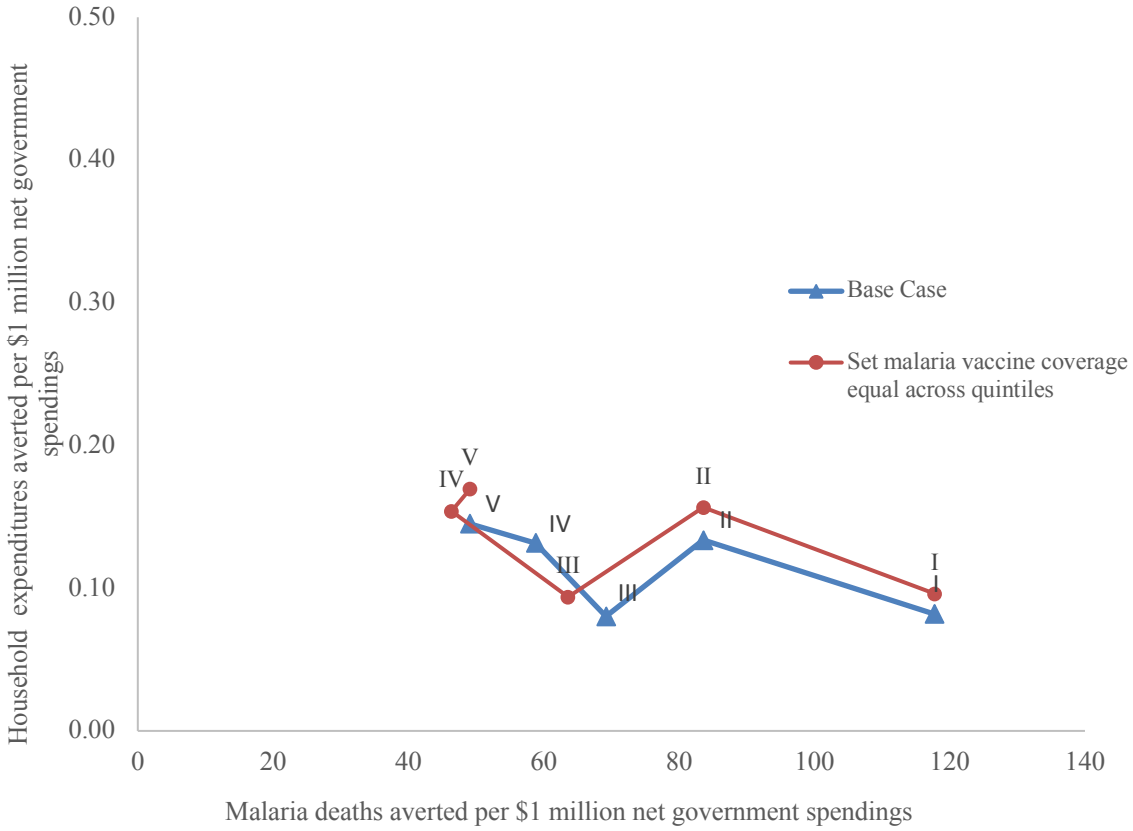
*The net government expenditure were estimated with subtracting the government cost-savings on malaria-related treatment from the vaccination program costs.
†The estimates presented are cumulative over the five-year analytic horizon following the 2016 birth cohort.

Figure S2.2. Malaria deaths averted by malaria vaccination in Zambia, per income quintile and $1 million net government expenditure*, with base-case and with malaria deaths/cases equal across income quintiles† (in 2016 USD).



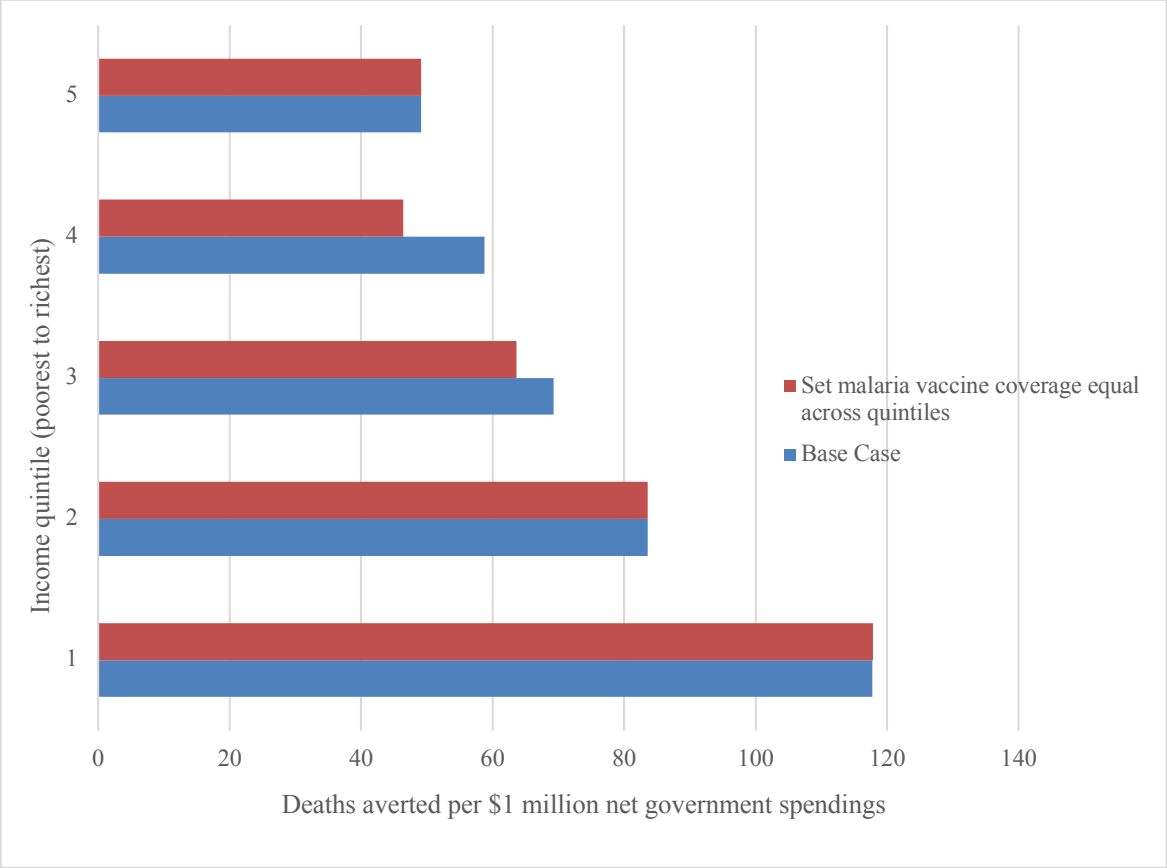
*The net government expenditure were estimated with subtracting the government cost-savings on malaria-related treatment from the vaccination program costs.
†The estimates presented are cumulative over the five-year analytic horizon following the 2016 birth cohort.

Figure S3.1. Household costs averted (in US$ million) and malaria deaths averted by malaria vaccination in Zambia, per income quintile and $1 million net government expenditure*, with base-case and with malaria vaccination coverage equal across income quintiles † (in 2016 USD).
I = Poorest; II = Poorer; III = Middle; IV = Richer; V = Richest.



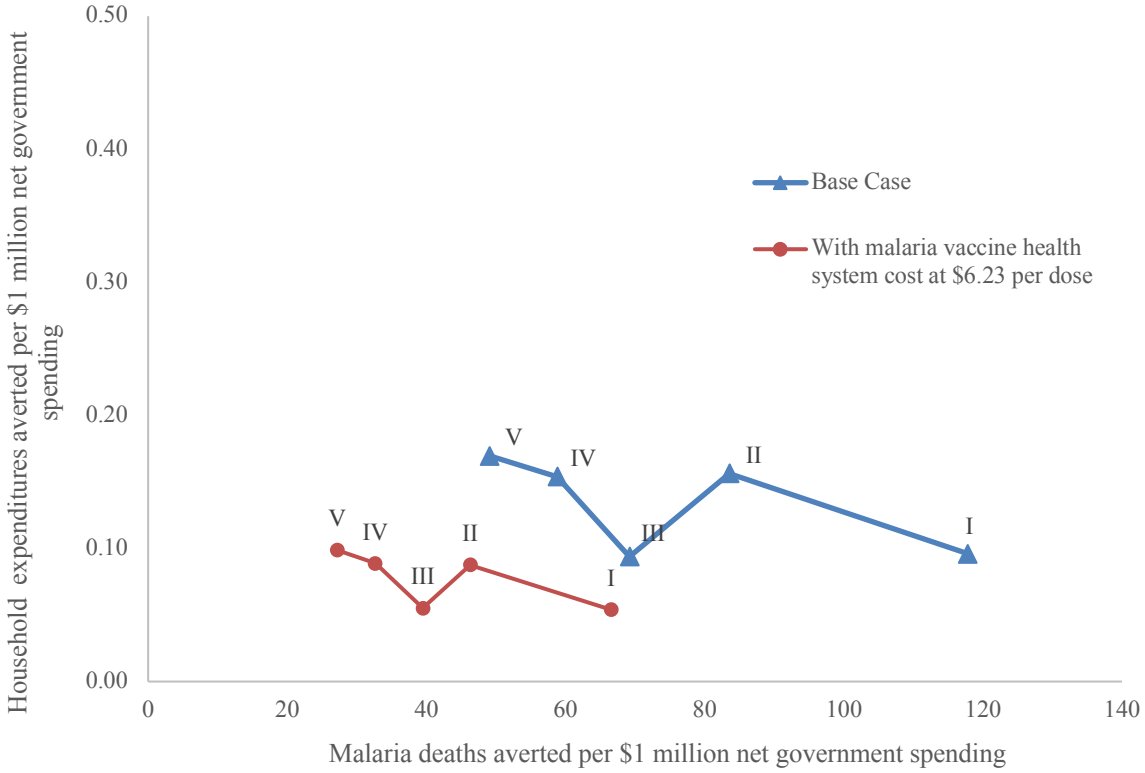
*The net government expenditure were estimated with subtracting the government cost-savings on malaria-related treatment from the vaccination program costs.
† The estimates presented are cumulative over the five-year analytic horizon following the 2016 birth cohort.

Figure S3.2. Malaria deaths averted by malaria vaccination in Zambia, per income quintile and $1 million net government expenditure*, with base-case and with malaria vaccination coverage equal across income quintiles† (in 2016 USD).



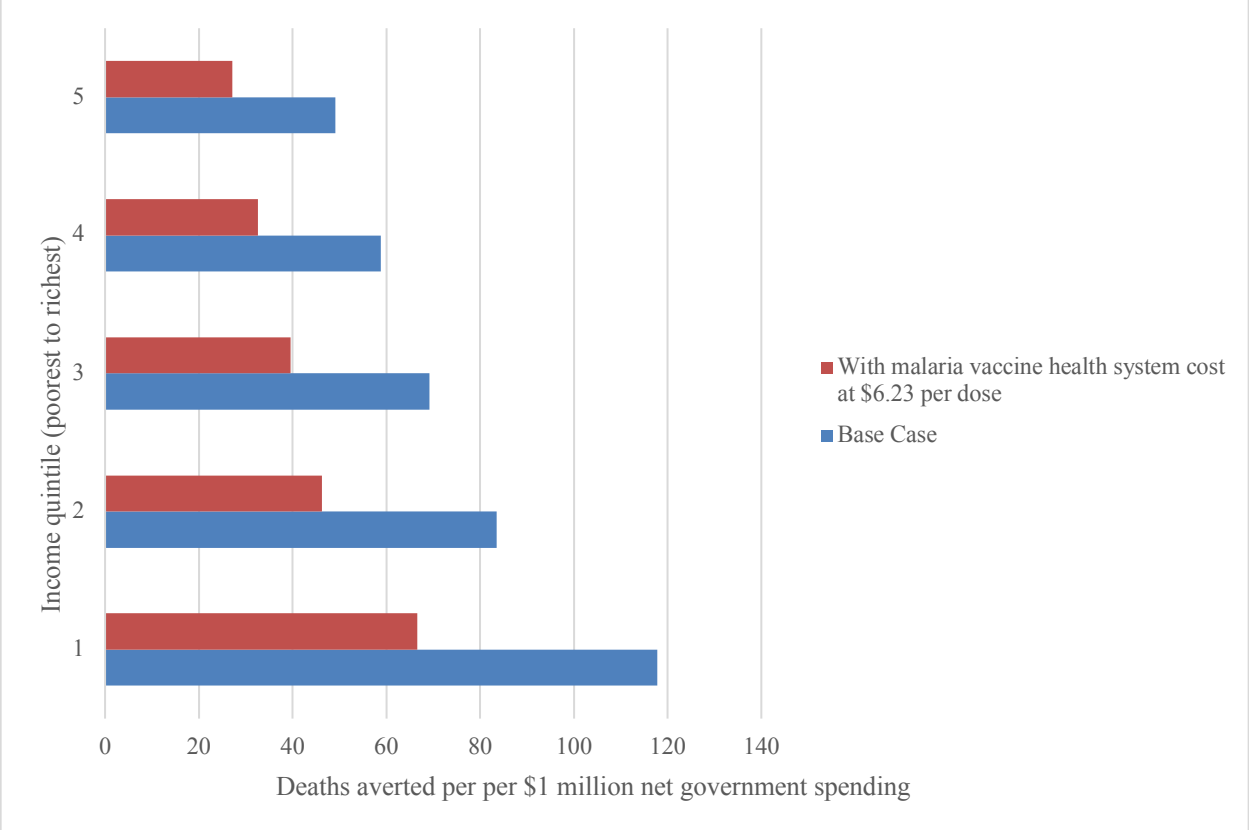
*The net government expenditure were estimated with subtracting the government cost-savings on malaria-related treatment from the vaccination program costs.
†The estimates presented are cumulative over the five-year analytic horizon following the 2016 birth cohort.

Figure S4.1. Household costs averted (in US$ million) and malaria deaths averted by malaria vaccination in Zambia, per income quintile and $1 million net government expenditure*, with base-case and with malaria vaccine health system cost of $6.23 per dose† (in 2016 USD).
I = Poorest; II = Poorer; III = Middle; IV = Richer; V = Richest.



*The net government expenditure were estimated with subtracting the government cost-savings on malaria-related treatment from the vaccination program costs.
†The estimates presented are cumulative over the five-year analytic horizon following the 2016 birth cohort.

Figure S4.2. Malaria deaths averted by malaria vaccination in Zambia, per income quintile and $1 million net government expenditure*, by malaria vaccine in Zambia, with base-case and with malaria vaccine delivery cost $6.23 per dose†.



*The net government expenditure were estimated with subtracting the government cost-savings on malaria-related treatment from the vaccination program costs.
†The estimates presented are cumulative over the five-year analytic horizon followin

9.5. References

[1] Zambia Ministry of Health. Zambia National Malaria Indicator Survey 2015. Retrieved from http://www.makingmalariahistory.org/wp-content/uploads/2017/06/Zambia-MIS2015_Jan20-nosigs.pdf (accessed April 24, 2018)
[2] Central Statistical Office (CSO) [Zambia], Ministry of Health (MOH) [Zambia], and ICF International. Zambia Demographic and Health Survey 2013-14. Rockville, Maryland, USA: Central Statistical Office, Ministry of Health, and ICF International; 2014.
[3] Institute for Health Metrics and Evaluation. Global Burden of Disease (GBD) 2016 Data. Retrieved from http://ghdx.healthdata.org/gbd-results-tool (accessed April 24, 2018)
[4] World Bank. World Bank Data Indicators. Zambia Country Profile. Retrieved from https://data.worldbank.org/country/zambia (accessed March 10, 2018)