Modelling malaria reduction in a highly endemic country: Evidence from household survey, climate, and program data in Zambia

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Abstract

Substantial efforts have seen the reduction in malaria prevalence from 33% in 2006 to 19.4% in 2015 in Zambia. Many studies have used effect measures, such as odds ratios, of malaria interventions without combining this information with coverage levels of the interventions to assess how malaria prevalence would change if these interventions were scaled up. We contribute to filling this gap by combining intervention coverage information with marginal predictions to model the extent to which key interventions can bring down malaria in Zambia. We used logistic regression models and derived marginal effects using repeated cross-sectional survey data from the Malaria Indicator Survey (MIS) datasets for Zambia collected in 2010, 2012 and 2015. Average monthly temperature and rainfall data were obtained from climate explorer a satellite-generated database. We then conducted a counterfactual analysis using the estimated marginal effects and various hypothetical levels of intervention coverage to assess how different levels of coverage would affect malaria prevalence. Increasing IRS and ITNs from the 2015 levels of coverage of 28.9% and 58.9% respectively to at least 80% and rising standard housing to 20% from the 13.4% in 2015 may bring malaria prevalence down to below 15%. If the percentage of modern houses were increased further to 90%, malaria prevalence might decrease to 10%. Other than ITN and IRS, streamlining and increasing of the percentage of standard houses in malaria fight would augment and bring malaria down to the levels needed for focal malaria elimination. The effects of ITNs, IRS and Standard housing were pronounced in high than low epidemiological areas.

Introduction

Malaria is endemic to Zambia, with highest prevalence during the rainy season from December to April.[1] It is among the top causes of disability-adjusted life years (DALYs) lost and it is associated with substantial productivity losses in Zambia.[2] In 2015, the national malaria prevalence was 19.4% in children aged below five years with other parts of the country such as Luapula province in the north, having a prevalence as high as 32%.[3] High malaria prevalence is associated with increased morbidity and mortality among children, chronic anaemia, stunting, and wasting.[4,5]

Substantial efforts have been put in place to bring down malaria, especially after the year 2000, when critical malaria and other interventions were rapidly scaled up following the millennium summit that agreed on the 2015 agenda for global development. This was aided by increases in development assistance for health and improvements in Zambia's economic performance, with economic growth averaging 7% per annum.[6] The malaria program is coordinated by the National Malaria Elimination Program (NMEP) and guided by strategic plans (National Malaria Strategic Plans 2001 – 2005, 2006 – 2010, and 2011 – 2016).[1,7] During this time, malaria prevalence reduced by at least 41.2% of the baseline, from 33% in 2006 to 19.4% in 2015.[3] However, progress towards elimination is slow as the national prevalence of 19.4% in children is still within the high endemic category defined as malaria prevalence above 15% in under-five children.[8] Importantly, there was an upsurge in malaria prevalence between 2010 and 2015 from 16% to 19.4%.[9] This situation is concerning given that the elimination of the disease is now the government's goal in the short to medium term.[7]

There is a lot of literature examining the effects of different interventions, such as Indoor Residual Spraying (IRS) and Insecticide-treated nets (ITNs) on malaria.[10,11] However, most of these studies used effect measures of these interventions without combining these with malaria intervention coverage information. Unlike simply presenting measures of effect such as odds ratios, combining intervention coverage data with effect measures may enable one to directly show the extent to which malaria prevalence would change when these interventions are scaled up. Using several waves of nationally representative survey data in Zambia, we contribute to filling this gap. Apart from providing evidence for policymakers that would better guide efforts to malaria elimination, our study presents a more informative method of assessing program impact that can be replicated in other contexts and countries.

Materials and Methods

Study design

This study used data from repeated cross-sectional survey data from the Malaria Indicator Survey (MIS) for 2010, 2012 and 2015. The study focused on all children aged below five years (from zero to 59 Months) that were captured during the MIS 2010, 2012 and 2015. The MIS uses a two-stage cluster sampling method. The first stage sampling is based on clusters – 25 631 Standard Enumeration Areas (SEAs) — which partitions the whole country, and are based on the 2010 Census of Population and Housing. In 2010, 180 SEAs were sampled, 160 in 2012, and 150 in 2015. In the second stage, 25 households are sampled from each SEA, and all household members were included in the survey.[3,12,13] The MISs are set at 95% confidence level, 80% power, the design effect of 2 and adjusted for a 20% non-response rate and are representative at national, provincial, urban and rural level.

Study settings

Zambia is one of the countries in the southern part of Sub-Saharan Africa (SSA). With a population of about 17 million, of which 40% is urban. It is one of the most urbanized countries in SSA. Although it is classified as a lower-middle-income country, there is high inequality, with more than 60% of the population living below the national poverty line. Access to health facilities is also hard, particularly among rural communities. Improvised housing structures, which allow free entry and exit of malaria vector mosquito, are more prevalent in rural areas than in urban areas. During the 2015 MIS survey, only 8% of households in rural areas had standard housing structures compared to 39% in urban areas while the overall was only at 14%.[3] Standard housing is defined by solid roofs, such as concrete, iron or asbestos, brick walls, and concrete or tiled floors. Sub-standard structures were improvised houses such as grass-thatched roofs and mud or grass walls.[9]

The country has a tropical climate and a high burden of malaria,[9] it is administratively divided into ten provinces. Malaria is highest in the northern parts, where prevalence was as high as 32% in children aged below five years. In the central regions, the disease is moderate, averaging 14%, while it is lowest in the southern parts where prevalence was 0.6% as of 2015.[3] In the east to west direction of the country, there are no significant differences in malaria prevalence. It is probably because rainfall patterns follow latitudes, which change in the north to the southern direction of the

country.[9] The burden of disease is also unequally concentrated on the poor. For example, fever among children less than five years is unfairly concentrated among the poor. There has not been any reduction in inequality between 2007 and 2014.[14]

Spending on Malaria has reduced recently; for example, the recent National Health Accounts show that nominal expenditure on malaria declined by almost 40% between 2015 and 2016, from $172 million to $123 million. However, Malaria accounts for the second-biggest share of health expenditure by disease area after HIV and AIDS.[15]

Data

For this study, datasets from the repository at the National Malaria Elimination Centre of the Ministry of Health in Stata 13 format for 2015 datasets and Microsoft Access 2010 for 2010 and 2012 datasets were obtained. The datasets were exported from the hosting database formats MS Access and Stata 13, respectively into MS Excel 2010. The column names and formats were then standardized in MS Excel 2010.

We then imported the datasets into Stata version 15, appended and saved as .csv files.[16] The data was then cleaned by excluding all persons five years and older before we did the analysis.

Data analysis

We reported basic descriptive statistics such as mean, median, standard deviation and interquartile range for continuous variables. Categorical data were summarized using counts and percentages. We then fitted a multiple logistic regression model, which accounted for complex survey design in Stata version 15. We used *a priori* subject knowledge to establish the coefficients of predictor variables. This model was then used to obtain marginal predictions for malaria prevalence for 2015. The predicted value for 2015 was compared against the observed values in MIS 2015 using a one-sample test of proportions to assess the robustness of the model.

Further, a counterfactual analysis using hypothetical values in the model to predict how malaria prevalence would respond to varying levels of coverage of malaria inter-
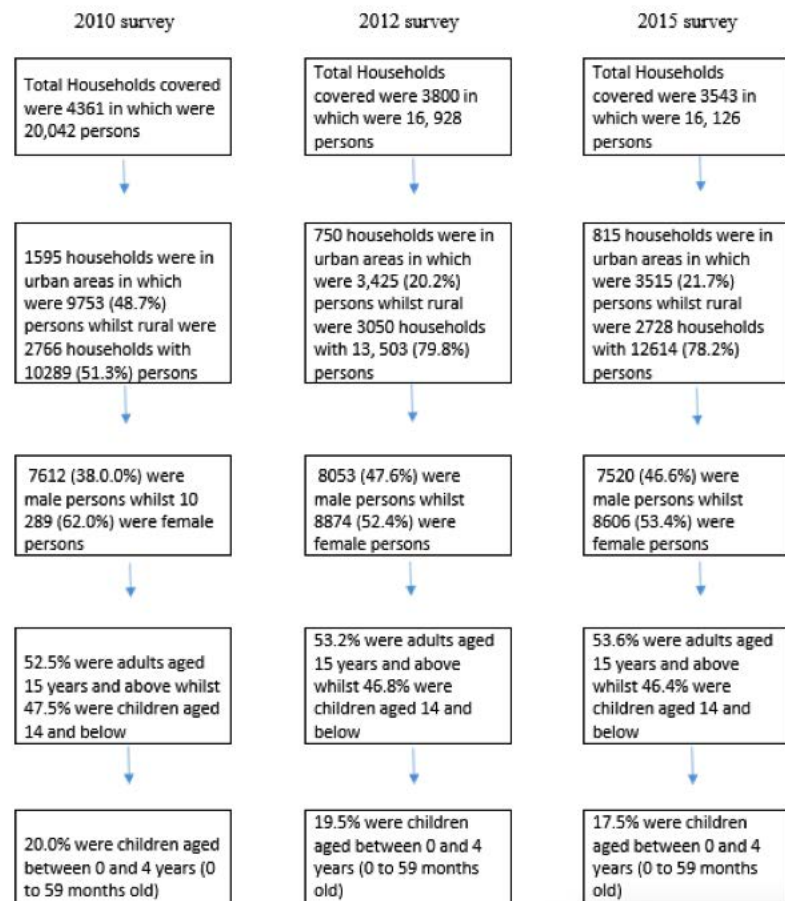

Figure 1. Baseline characteristics of respondents.

ventions was done. Finally, the country was stratified into three malaria epidemiological zones based on the WHO Global Technical Strategy (GTS).[8] We then applied the counterfactual analysis in each of the epidemiological zones to address the effect modification in low, medium and high burden zones.

Ethical considerations

ERES Converge Institutional Review Board approved this study (IRB) Ref No. 2017-Aug-005 and by the National Health Research Authority (NHRA). The Ministry of Health (MoH) also granted permission to access the datasets for this study. This study did not deal with individual respondents but anonymised datasets, so there was no need for individual respondents' consent. The data was anonymised by the NMEP who removed all personal identifiers and household GPS, so we only handled data with coded IDs without the code keys.

Results

Basic demographic characteristics of respondents

The response rates for all the three[3] surveys were more than 95%. The demographics were comparable across the studies. Figure 1 summarises the demographic characteristics of the participants.

Model estimation of 2015 malaria prevalence observed by malaria indicator survey

Table 1 summarises the coefficients, confidence intervals and the respective P values of the logistic regression model, which was the basis for the obtained marginal effects used in estimating malaria prevalence. Using these post-estimation margins, we were able to predict the 2015 Malaria Prevalence at national and provincial levels, which were very close to the

observed values of malaria prevalence in 2015. The only exceptions were provinces with values of malaria prevalence of less than 10%. Table 2 shows observed values in 2015 Malaria Indicator Survey, the predicted values using the post-estimation margins of the model and respective P-values for comparisons of the observed 2015 MIS prevalence and predicted values.

Counterfactual analysis of malaria prevalence by varying levels of interventions

Figure 2 shows how malaria prevalence varied with different levels of coverage of IRS, ITN and Standard housing while keeping all other variables constant at 2015 levels for the whole country. Malaria prevalence would reduce from 20.5% (95% CI 10.4 – 30.6%) when IRS coverage is at 10%

to 16.0% (6.8 – 25.3%) when IRS is at 90%. When ITN utilisation the previous night among children aged below five years is varied from 10% to 90%, malaria prevalence may reduce from 20.8% (95%CI 10.1 – 31.6%) to 18.4% (95%CI 9.1 – 27.7%) respectively. Further, malaria prevalence would reduce from 19.6% (95% CI 9.8 – 29.7%) when standard housing is at 10% to 12.4 (95% CI 4.6 – 20.2) when standard house is at 90%. Finally, we also presented the best-case scenario where IRS and ITNs were fixed at 80% coverage, and standard housing was varied while keeping all other variables constant at 2015 levels. Prevalence reduced from 16.3% (95%CI 7.2 – 25.4%) when standard accommodation was at 10%, to 10.1% (96%CI 3.3 – 16.9%) when standard accomodation was at 90%. With the latter scenario, prevalence
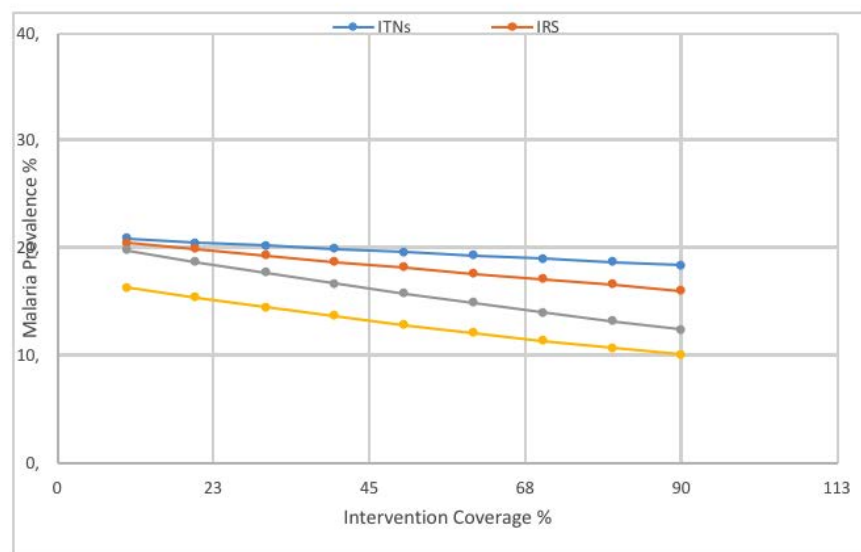
Figure 2. Varying ITNs, IRS and Standard house while keeping all other variables constant at 2015 for the whole country.

Table 1. Coefficients from a logistic regression model.

Variable (X_i)	Coefficient	95% Conf. Interval		P-Value
Age category (12-59 months)	1.563	1.184	1.942	< 0.001
Sex (females)	-0.100	-0.278	0.078	0.270
Residence location (urban)	-1.496	-1.950	-1.042	<0.001
Altitude (meters)	-0.001	-0.001	0.000	0.065
Standard house (yes)	-0.693	-1.031	-0.354	<0.001
Wealth status (not poorest quartile)	-0.411	-0.640	-0.182	<0.001
Indoor residual sprayed (yes)	-0.376	-0.673	-0.079	0.013
Slept under a net (yes)	-0.196	-0.352	-0.039	0.015
Rainfall (mm)	0.001	-0.001	0.003	0.302
Temperature (°C)	-0.323	-0.456	-0.190	<0.001
_cons	5.239	1.242	9.236	0.010

reduced to the moderate level of less than 15% when standard accommodation was at 25% where it is permissible to commence elimination activities. Finally, the worst-case scenario was assumed where interventions like ITNs and IRS were reduced to 10%. All other variables remained constant at 2015 levels, and prevalence would increase from 2015's 19.4 to 22.0 (95%CI 11.0 – 33.1%).

The situation presented in Figure 2 used the dataset for the whole country. However, Zambia shows heterogeneity in prevalence, with some provinces showing low prevalence below five per cent in children below the age of five years, namely Southern and Lusaka provinces. Four other areas, namely Eastern, Central, Copper-belt and Western provinces, showed a moderate prevalence of between five and fifteen per cent. Four more regions, namely Luapula, Muchinga, Northern and North-western, had a higher prevalence of more than 15% in children aged below five years. The framework used to categorise the provinces into low, moderate and high endemic areas is the WHO Global Technical Strategy for malaria elimination (GTS).[8] We then did simulations of the effects of three interventions in these three malaria epidemiological zones.

Effects in the low malaria epidemiological zone

The estimated mean prevalence for Lusaka and Southern provinces was 1.3% (95% CI, 0.6% – 3.1%) while the individual provincial prevalence in 2015 was 2.4% and 0.6% respectively. The marginal effect of ITNs in this zone was -0.008 (95% CI, -0.0198, 0.0038; P-value = 0.180), whilst that of IRS was - 0.052 (95%CI, -0.037, 0.007; P-value = 0.178) and that of standard housing was -0.010 (95%CI, -0.030, 0.009; P-value = 0.300). All three interventions did not have statistically significant effects on malaria prevalence in this epidemiological

zone. Figure 3 shows the effects of varying ITN, IRS and standard housing in the low malaria epidemiological zone.

Effects in the moderate malaria epidemiological zone

The estimated mean prevalence in the moderate malaria epidemiological zone was 14.1% (95% CI, 10.3% – 18.0%). The marginal effect of ITNs in this zone was -0.019 (95% CI, -0.054, 0.016; P-value = 0.301), whilst that of IRS was - 0.030 (95%CI, -0.060, 0.009; P-value = 0.133) and that of standard housing was -0.029 (95%CI, -0.078, 0.020; P-value = 0.248). All three interventions did not have statistically significant effects on malaria prevalence in this epidemiological zone. Figure 4 shows the effects of varying ITN, IRS and standard housing in the moderate malaria epidemiological zone.

Effects in the high malaria epidemiological zone

The estimated mean prevalence in the high malaria epidemiological zone was

28.7% (95% CI, 23.3% – 34.1%). The marginal effect of ITNs in this zone was -0.041 (95% CI, -0.074, -0.009; P-value = 0.012), whilst that of IRS was - 0.094 (95%CI, -0.179, -0.008; P-value = 0.031) and that of standard housing was -0.156 (95%CI, -0.246, -0.066; P-value = 0.001). All three interventions had statistically significant effects on malaria prevalence in the high malaria epidemiological zone. Figure 5 shows the effects of varying ITN, IRS and standard housing in this epidemiological zone.

Discussion

This study demonstrates that using already available MIS data; we can model targeted coverage levels for control interventions to reach the elimination threshold. This tool is useful for planning of national malaria control. Key findings indicate that the effects of interventions like ITN, IRS and standard housing are more pronounced in the high malaria epidemiological zones. That there is a need for increased coverage

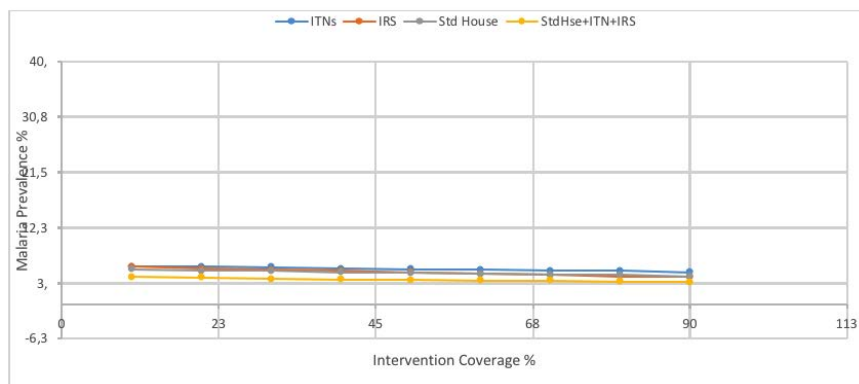**Figure 3. Varying ITNs, IRS and Standard house while keeping all other variables constant at 2015 for Low Prevalence Provinces.**

Table 2. Observed 2015 prevalence *vs* predicted 2015 malaria prevalence.

	Province	Observed	Predicted (95%CI)	P-value	No. of Children
1	Central	13.8	15.9 (7.5 - 24.2)	0.386	203
2	Copper-belt	15.2	17.8 (8.6 - 27.1)	0.198	316
3	Eastern	12.7	13.6 (5.1 - 22.1)	0.683	229
4	Luapula	32.5	30. 2 (16.9 - 43.5)	0.244	562
5	Lusaka	2.4	8.9 (3.9 - 14.0)	<0.000	198
6	Muchinga	31.4	24.1 (11.5 - 36.7)	0.034	181
7	Northern	27.6	27.3 (14.3 - 40.3)	0.909	293
8	North-Western	22.6	27.0 (14.2 - 39.9)	0.113	227
9	Southern	0.6	15.0 (6.1 - 23.8)	<0.000	281
10	Western	15.6	17.9 (7.8 - 28.0)	0.329	237
	National	19.4	19.3 (9.6 - 29.2)	0.895	2727

of primary interventions such as ITN and IRS to at least 90%. Introduction of improving housing structures to standard housing would augment the fight against malaria.

Studies have shown that global malaria is declining, mainly due to interventions, even though not all the decline can be explained.[17] Models have been developed for forecasting malaria, some of which are based on climatic conditions like temperature, rainfall and vegetative indices.[18,19] These models are resource-intensive and require a lot of technical equipment and expertise. They are also helpful in mapping malaria transmission. The model in this publication offers a less resource-intensive approach focusing on average estimates generating targets for malaria control that can guide programmatic activities. The model also controls for the effect of rainfall and temperature, but currently does not include humidity.[20]

Other models use historical data from routine surveillance sources and apply some versions of time series, such as Autoregressive Integrated Moving Averages (ARIMA). Such models have been shown to help in forecasting malaria burden, including seasonal variations even in high burden areas. Programs can then prepare for ongoing malaria transmission and adequately prepare inputs to avoid stock-outs of drugs, test kits, and other supplies.[21,22] The model used in this study combines age, sex, environmental and sociodemographic variables and also includes a constant, which encompasses the unaccounted for residuals that have been generated using data from the recent three Malaria Indicator Surveys in Zambia. This model can be useful in strategic planning for target setting where multiple interventions are used in malaria programs. For example, if a malaria program wants to reduce prevalence by 50%, it can estimate the coverage in predictor variables that would result in the desired 50% reduction in prevalence by changing coverage levels in the model.

To remain realistic, only variables that can feasibly be changed using program implementation such as IRS, ITNs and Housing were varied while keeping variables that cannot be feasibly changed in a malaria program constant at 2015 levels. For example, urban/rural residence location: one cannot move people from rural areas to urban areas just because urban areas have less risk of malaria compared to rural areas. Similarly, one cannot change temperature, altitude or people's wealth status in a malaria intervention program. A malaria program can, however, spray people's houses, distribute nets and promote

policies for the building of standard houses and installation of fly screens in dwellings. The advantage of this tool is that it uses existing data such as Malaria Indicator Surveys (MIS) and weather conditions data from the satellite-generated climate database called Climate Explorer (https://clime.xp.knmi.nl), which are not domiciled in Zambia, to predict malaria reductions at provincial and national levels. Its shortcoming is that it relies on household surveys data such as MISs, which are only done periodically and therefore cannot be used for short term monitoring of progress. It can be used for strategic planning to plan certain levels of coverage of interventions that would bring down malaria. Then as a complementary tool some time series like Autoregressive Integrated Moving Averages (ARIMA) models that use routine data from them for monitoring progress in

between surveys. Zambia can benefit from this modelling approach, especially in high endemic, where most of the malaria cases occur.

Out of the five hypothetical scenarios that were created in the counterfactual analysis where ITNs, IRS and standard housing were varied using the dataset for the whole country; no situation was able to predict the desired prevalence of less than 5%. Even when ITNs and IRS were fixed at 80% and standard housing was varied up to 90%, which predicted the lowest prevalence of 10%. Based on the WHO Global Technical Strategy (GTS) for malaria elimination, level four (prevalence >15%) where most of Zambia was in 2015. Elimination activities may not be implemented as there was still a need to bring down the prevalence first using vector control and facility case management. When prevalence gets to level
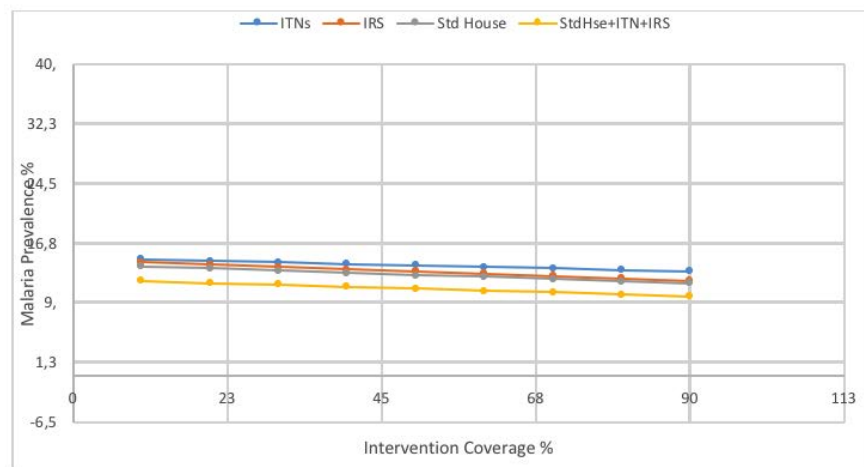

Figure 4. Varying ITNs, IRS and Standard house while keeping all other variables constant at 2015 for Medium Prevalence Provinces.
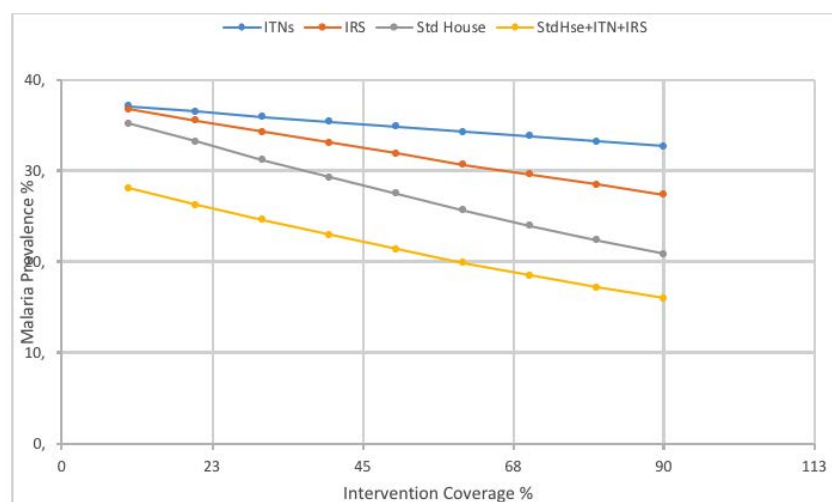

Figure 5. Varying ITNs, IRS and Standard house while keeping all other variables constant at 2015 for High Prevalence Provinces.

three, where it lies between 15% and 5%, accelerator activities such as Mass Drug Administration (MDA) and community case management targeted at hotspots of transmission may be implemented in areas that have the capacity. Otherwise, these are recommended when prevalence is at levels two or below, where prevalence is lower than 5%. In Zambia, only two provinces had prevalence below 5% namely Lusaka and Southern provinces as of 2015. Accelerator interventions such as MDA and reactive case detection have been implemented in these areas to drive the elimination agenda at the subnational level.[23] The primary challenge to subnational elimination efforts is contamination through the importation of malaria cases within regions. There are no restrictions or malaria screening in the mobility of persons across provinces within the country. For example, one study found that 94% of malaria cases at health facilities in Lusaka district were imported from other provinces. The frequency of travel and duration of stay in malaria areas were found to be significant risk factors among residents.[24] Due to the high risk of continual contamination because of human mobility within the country, the authors perceive that a subnational approach to elimination is not sustainable. Instead, bringing down prevalence in all provinces and implementing the accelerator interventions to drive down local transmission further while screening people entering at borders and airports may be a more feasible approach.

This study was able to predict a coverage that would bring prevalence to at least level three using the dataset for the whole country. In one scenario; ITNs and IRS were kept constant at 2015 levels, standard housing had to reach at least 60%, which in the view of the authors may not be very feasible, given that Zambia is a resource-limited country. In 2015, standard housing was at only 13% of the surveyed households. On the other hand, when mainstream interventions such as ITNs and IRS are increased to 80% from 2015 levels of 49% and 29% respectively, level three was reached when standard housing reached only 20% which is more feasible from the 13% of recorded in 2015. Keeping other variables constant and varying either ITNs or IRS alone did bring prevalence below 15% neither did increase both ITN and IRS at the same time to 80%.

To address effect modification; the country was divided into three epidemiological zones based on the WHO GTS framework. While ITNs, IRS and standard housing were shown to bring down malaria prevalence as coverage was increased, the effects were not statistically significant in low and medium malaria epidemiological zones, but were significant in the high malaria epidemiological zone. To the best of the knowledge of the authors, this is the first time this finding has been demonstrated in Zambia. However, it is in agreement with one study done in Uganda, which also found that the effects of interventions varied within regions.[25] While Zambia had carried out nationwide ITN mass distribution campaigns in 2014[26] and 2017, this study brings to light at least a need to review this approach. One study recommended a prioritization approach to the allocation of resources at the subnational level to achieve efficiencies.[27]

The results from the present study seem to suggest that in all epidemiological zones, standard housing had more effects on bringing down malaria prevalence followed by IRS and least was ITNs. It may not be feasible to construct standard houses for all people in a resource-constrained country like Zambia. However, it could be possible to modify housing structures towards insect-proofing. It may not also be efficient to spray all housing structures with residual insecticides as it has been shown to work better on painted walls compared to rough walls.[28] ITNs, on the other hand, have been shown to have little or no effect on malaria prevalence, particularly in low malaria epidemiological settings.[29] But other interventions such as MDA and community case management are effective in low endemicity settings.[30,31] ITNs work by either killing or repelling invading vectors. If the ITNs are repelling than killing, it has been demonstrated elsewhere that this may pose an increased risk to non-users[32] or change in behaviour to biting at dusk and dawn.[33]

Conclusions

The present study has shown that malaria prevalence can be predicted using different levels of coverage of control interventions while controlling for Age, Sex, rainfall, temperature and Socioeconomic variables such as type of housing and wealth index, and the results were comparable to the actual field data from the National Malaria Indicator Survey of 2015. This modelling approach can help the country as it predicts within acceptable precision in the moderate and high endemic areas. As of 2015, only two out of the ten provinces were in the low endemic zones, where the model was not accurate.

Among critical interventions, IRS, ITN and standard housing at appropriate coverage levels have been shown to have potential to reduce malaria prevalence from current high levels in most parts of the country to at least moderate levels where accelerator interventions for elimination may be implemented. The effects of reducing malaria prevalence were noted to be more pronounced in high prevalence zones of the country compared to low burden areas implying that there might be a need for intervention prioritisation at least at provincial level based on what works locally.

Recommendations

There is a need to increase coverage of mainstay interventions such as ITNs and IRS from 2015 levels, especially in the high prevalence epidemiological zones.

Current mainstay interventions such as ITN and IRS alone are effective but have not been shown to bring down malaria to at least moderate levels. There is a need to complement them with housing infrastructure improvements from improvised housing structures that allow free entry of vector mosquito to standard housing structures that are mosquito proof. In line with the WHO GTS recommendations, it can be possible then to implement accelerator interventions such as enhanced vector control, Mass Drug administration, community case management and surveillance once prevalence is brought down to at least moderate levels.

The modelling approach used in this study can be used by malaria programs to inform target setting and intervention selection for locally effective programs.

Limitations

Due to inadequate numbers of respondents who received treatment in the two weeks preceding the surveys, prompt treatment on malaria prevalence could not be included in the model.

The model used in this study was able to predict malaria prevalence accurately within 95% confidence intervals for moderate and high endemic areas. It was not accurate for low endemic areas with prevalence below 5% in children aged below five years.

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