

Accounting for regional transmission variability and the impact of malaria control interventions in Ghana: A population level mathematical modelling approach.

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Abstract

Background Assessing the effectiveness of malaria control measures in Ghana will require taking transmission dynamics of the disease into account given the influence of climate variability in the region of interest. The impact of preventative interventions on malaria incidence and the prospects of meeting program timelines in Ghana have been investigated using mathematical models based on regionally diverse climatic zones.

Methods An ordinary non-linear differential equation model with its associated rate parameters was developed incorporating the transitions between various disease compartments for three ecological zones in Ghana. Model parameters were estimated using data captured on the District Health Information Management System in Ghana from 2008 to 2017. The impact of insecticide treated bed nets and indoor residual spraying on the incidence of malaria were simulated at various levels of coverage and protective effectiveness in each ecological zone. To fit the model, Approximate Bayesian Computational sampling approach was adopted.

Results Increasing the coverage levels of both long lasting insecticide treated bed nets or indoor residual spraying activities without a corresponding increase in their proper use or patronage does not impact highly on averting predicted incidence of malaria in Ghana. Improving on the protective efficacy of long lasting insecticide treated bed nets through proper usage could lead to substantial reductions in the predicted incidence of malaria. Similar results were obtained with indoor residual spraying across all zones.

Conclusions Projected goals set in the National Strategic plan for malaria control 2014-2020 as well as WHO targets for malaria pre-elimination by 2030 are only likely be achieved if a substantial improvement in treated bed net usage is achieved coupled with targeted deployment of indoor residual spraying with high efficacy.

Introduction

With the adoption of the 2016–2030 milestones to focus the agenda towards malaria control and elimination, many countries including Ghana, currently classified as a country in the control phase, are making great efforts towards the achievement of these goals [1, 2]. To this end, the National Malaria Control Program (NMCP) is guided by a national malaria strategic plan to reduce the burden of malaria by 75% across Ghana by 2020 partly by scaling up the distribution of Insecticide Treated bednets (ITNs)/Long lasting insecticide treated bednets (LLINs), targeted Indoor Residual Spraying (IRS) and improving monitoring activities [3, 4].

In recent years, NMCP with support from partners such as the United States Agency for International Development (USAID), President's Malaria Initiative (PMI) and The Global Fund to Fight AIDS, Tuberculosis and Malaria have achieved relative reductions in malaria-related mortalities but progress towards substantial reductions in morbidity still remains a challenge [5]. These achievements follow the

deployment of new intervention strategies following the adoption of new national policies on the use of Artemisinin-based combination therapy (ACTs) as first line therapies for uncomplicated malaria between 2002 to 2004, scale up and distribution of ITNs in 2002 and thereafter, Intermittent Preventive Treatment of malaria in pregnancy (IPTp) using Sulfadoxine-Pyrimethamine (SP) between 2003–2004 and Indoor Residual Spraying (IRS) on a small scale in 2005 [5, 6].

Although these interventions are in place, evaluating their effectiveness using mechanistic models based on locally available data still remains largely unexplored [6]. Despite the contributions of earlier mathematical models, developed describing the transmission dynamics of malaria in the country, some gaps such as finding a rational basis for deploying these interventions and evaluating them in different ecological zones of Ghana still persist [7].

The dynamics of malaria morbidity generally follow patterns of ecological factors such as rainfall and temperature [8]. There is evidence supporting this spatial heterogeneity in the ecology of Ghana and therefore the burden of malaria. For this reason, the spatial scale should not be ignored in any malaria investigations of national scale. Due to this diversity, the country was partitioned into zones along three main ecological regions of Ghana, namely the Guinea savannah, Transitional forest and Coastal savannah, as described elsewhere [8].

Examples abound of uses of compartmental models for investigation of diseases with the aim to understanding underlying principles or processes governing dynamics of diseases [9]. Since their introduction into public health by Bernoulli in 1766, several models focused on malaria have been developed through the span of time, building on those formulated by Ross and varying in complexity and diversity specifically to elucidate further understanding into the mechanism of malaria transmission in humans [10]. Currently mathematical models are also being used among others, to support the formulation of policies aimed at controlling diseases, including monitoring and evaluation of disease incidence [11].

The model developed in this study is based on the basic Susceptible Infected Recovered Susceptible (SIRS) model [12, 13] which has been modified to include additional compartments and attributes of the transmission settings in Ghana such as superinfection. The model structure includes a human population model coupled with a vector model with climatic elements adapted from Augusto F.B. et al [14].

The objective of this paper is to present results of the impact of various intervention scenarios of malaria intervention control measures in Ghana, simulated at a sub-population level that represents three main ecological zones [7]. The impact of various levels of protective effectiveness as well as coverage of LLINs and IRS were investigated and prospects of achieving relevant locally and internationally set goals of malaria control and elimination in Ghana were also considered.

Methods

Ordinary differential equations were used to develop compartmental models for malaria transmission dynamics in the three ecological zones of Ghana. The model diagram for both human and vector populations is as illustrated in Fig. 1. Further details and description of the model are presented in S1 Text, the online supplementary files.

Model structure

Human population: S represent the susceptible human compartment (where different probabilities have been applied respectively to recruited naïve or non-immuned children under 6 years of age, adults and pregnant women into the latent stage L. before the onset of gametocytes. Ic, Ia, Is and Ism compartments represents symptomatic infection (clinical infection), asymptomatic infection, severe infection and sub-microscopic infection respectively. Pregnant women attend antenatal clinic (ANC) without an infection, IANCN or progress from L3 into IANCP once infected. Tr1, Tr2 and Tr3 represent the treatment sought for confirmed uncomplicated malaria (Ic), severe malaria (Is) and routine monthly SP prophylaxis for pregnant women at ANC, Trf1, Trf2 and Trf3 represent respective treatment failure due to adherence and possible drug resistance for the three latter treatment options. Vector population: Lv represents larva population and Sm susceptible mosquitos. Exposed mosquitoes are captured in Em compartment. Whereas infectious mosquitoes are in the Im compartment.

The model diagram shown in Fig. 1 above depicts a vector coupled malaria transmission model that includes compartments for various stages of malaria and subsections of the Ghanaian population. The subsections of the population captured are adults, children under 6 years and pregnant women.

The grey compartments represent the populations, which are susceptible, yellow those with latent infection, brown those with a blood stage infection and green members of the population with symptomatic infection that undergo treatment. Compartments for treatment failure are indicated in red colour. The red and blue arrows present the forces of infection from infectious mosquitoes to humans and infectious humans to mosquitoes respectively.

Stages of development of the malaria parasite and the mosquito are captured by four compartments representing the young and adult mosquitoes that can be classified as being susceptible, infected and infectious, once ingested parasite(s) complete the full cycle of development.

Transmission is governed by the forces of infection (λ_{mh} and λ_{hm}) from mosquitoes to humans and human to mosquitoes respectively. The forces of infection in turn are driven primarily by the dynamics of Biting Rate (BR) per person per month (b/p/m) in the various zones [15, 16]. The model also accounts for the possibility of being infected more than once (super infection).

Data and interventions

The data consist of uncomplicated and severe reported malaria cases and reported cases of malaria in pregnancy from 2008 to 2017 [8]. The model parameters used, where were sourced from literature or from the data fitting process to account for zonal transmission diversity. This was done to capture the different

dynamics of morbidity of malaria and to allow for a better evaluation of the effectiveness of the various interventions in these zones.

In this study, the interventions investigated include, impact of elevated coverage levels and protective effectiveness (PE) of Insecticide Treated bed Nets (ITNs) or Long Lasting Insecticide Nets (LLINs) and Indoor Residual Spraying (IRS).

Data fitting and calibration

Data management was undertaken in Stata version 13.1 (StataCorp LP, College Station, Texas, USA). All analyses and computation were performed using R version 3.3.2 Copyright (C) 2018 [17].

Model fitting was carried out using the Approximate Bayesian Computation (ABC) approach (S 1 Text), with a rejection criterion based on the Euclidean distance between summary statistics of predictions arising out of sampled parameter set and summary statistics of observed monthly malaria cases from health facilities in all 216 districts in Ghana from 2008–2017 [18, 19]. All simulations were performed on high performance computing facilities provided for by the ICTS High Performance Computing team (<http://hpc.uct.ac.za>) of the University of Cape Town. To validate parameters, the cv4abc package in R was used [19].

Results

Models were implemented from 1988 to 1997, first to attain a steady state then reported levels of previous interventions incorporated from 1998 to 2017. As shown in Figs. 2a, 2b, and 2c below, the data were fitted from 2008 to 2017 and predictions made from 2018 to 2030, S1 Figs. 4, 5 and 6.

The most populous of the zones is the Transitional forest with a population of 17.1 million, followed by the Coastal savannah 8.1 million while the Guinea savannah accounts for 5.1 million people (using 2017 zonal estimated population from DHIMS2).

Figure 2: Model run time is 1988 to 2030. Steady state period spans from 1988 to 1997, 1998 to 2017 previous interventions implemented and reporting rates on DHIMS introduced. Data fitting from 2008 to 2017 for the (a) Guinea savannah, (b) Transitional forest and (c) Coastal savannah.

Biting intensity seems to be higher in the Guinea savannah compared to the other zones. As captured in S1 Fig. 7, biting rates in the Guinea savannah could be as high as 170(b/p/m) compared to those of the Transitional forest 12(b/p/m) and 10(b/p/m) in the

Coastal savannah during the peak transmission seasons respectively. S1 Fig. 7 suggests that, even though biting (as well as transmission) seems to occur all year around, in all zones, they peak following rising rainfall.

Estimated burden of all clinical cases of malaria (uncomplicated and severe malaria) in the baseline year of 2018 in the Guinea savannah was 219 (95% p.CI [153, 315])/1000 population and 261 (95% p.CI [220,

312]/1000 population, 139 (95% p.CI [117, 154])/1000 population for the Transitional forest and Coastal savannah zones. However, reported cases of uncomplicated and severe malaria in 2018 at the health facilities were however estimated to be 173 (95% p.CI [121, 250])/1000, 199 (95% p.CI [168, 238])/1000 and 104 (95% p.CI [88, 115])/1000 population in the Guinea savannah, Transitional forest and Coastal savannah respectively.

Results of scaled up interventions implemented for 3 years to achieve universal coverage levels with respect to LLINs and 5 years to achieve targeted coverage levels of IRS in the various zones were simulated from 2018 to 2030 under various intervention scenarios as presented in the following sections below.

Impact of LLIN interventions

LLIN coverage of 70% and 90% at baseline usage (56%, 45% and 35% for Guinea savannah, Transitional forest and Coastal savannah)

The impact of increased universal coverage levels of ITNs/LLINs were tested for the various zones and model simulation results shows that, achieving elevated levels of LLIN coverage of 70.0% and 90.0% at baseline level of protective efficacy of LLINs (40.0%) and IRS (30.0%) while keeping the coverage levels of IRS at baseline (0.0%) at 2018, leads to a 2.5% and 8.9% reduction in uncomplicated cases in the Guinea savannah, 8.2% and 17.3% in the Transitional forest and 9.9% and 19.8 in the Coastal savannah respectively, Fig. 3a,3b and 3c (S4 Figs. 1a). Corresponding reductions in reported cases of severe malaria and malaria in pregnancy were observed as in S4 Fig and 1b (S2 & S3 Figs. 1a, 1b and 1c) [20].

For predictions of all reported clinical incidence of malaria (uncomplicated and severe), the corresponding reductions in the in the incidence rates were 169 (p.CI [117, 245])/1000 and 160 (p.CI [108, 245])/1000 population in the Guinea savannah in 2020 and 168 (p.CI [116, 245])/1000 and 155 (p.CI [100, 230])/1000 population by 2030, S5 Table 1.

In the Transitional forest, the incidence rates are 189 (95% p.CI [157, 226])/1000 and 179 (95% p.CI [148, 226])/1000 population in 2020 and 177 (95% p.CI [139, 215])/1000 and 159 (95% p.CI [109, 190])/1000 population by 2030, S5 Table 2.

Incidence rates of 189 (95% p.CI [157, 226])/1000 and 189 (95% p.CI [157, 226])/1000 population for reported cases of all malaria were observed in 2020 while 189 (95% p.CI [157, 226])/1000 and 189 (95% p.CI [157, 226])/1000 population were predicted by 2030 in the Coastal savannah, S5 Table 3.

LLIN coverage of 70% and 90% at baseline usage of 60% across zones

When coverage levels are maintained at 70.0% and 90.0%, in all the zones, reductions in predicted uncomplicated cases by 4.2% and 11.3%, respectively in the Guinea savannah, 20.0% and 32.8% in the Transitional forest and 36.9% and 51.3%, in the Coastal savannah are observed by increasing the level of usage of LLINs to 60.0%, S4 Figs. 1a, 1b and 1c and Fig. 4a, 4b and 4c below.

Corresponding cases of severe malaria and malaria in pregnancy observed are shown on S2 & S3 Figs. 2a, 2b and 2c and S4 Figs. 1b and 1c respectively.

The corresponding incidence rates with an increased LLIN usage to 60% in the Guinea savannah are 166 (95% p.CI [114, 242])/1000 and 156 (95% p.CI [104, 230])/1000 in 2020 and 165 (95% p.CI [112, 241])/1000 and 151 (95% p.CI [94, 225])/1000 population by 2030 respectively for LLIN coverage of 70% and 90%, S5 Table 1.

Rates predicted in the Transitional forest for elevated use of LLIN to 60% respectively for LLIN coverage levels of 70% and 90% were 171 (95% p.CI [139, 206])/1000 and 158 (95% p.CI [126, 191])/1000 at 2020 and 148 (95% p.CI [103, 186])/1000 and 113 (95% p.CI [64, 151])/1000 population by 2030, S5 Table 2.

With respect to an increased level of LLIN usage and coverage levels of 70% and 90% respectively in the Coastal savannah, the predicted rates were 77 (95% p.CI [60, 91])/1000 and 69 (95% p.CI [53, 83])/1000 for 2020 and 51 (95% p.CI [26, 78])/1000 and 31 (95% p.CI [12, 58])/1000 by 2030, S5 Table 3.

LLIN coverage of 70% and 90% at baseline usage 80 across zones

A further proportion of predicted cases of reported uncomplicated malaria are averted when the LLINs usage is increased to 80% as shown in and Fig. 5a, 5b and 5c. The proportion of predicted cases averted in the Guinea savannah, Transitional forest and Coastal savannah are 13.5% and 24.4%, 36.6% and 53.2%, and 55.7% and 69.0%, respectively for LLIN coverage of 70% and 90% across all the zones S4 Figs. 1a, and similarly for predicted cases of severe malaria and malaria in pregnancy as shown in S4 Fig. 1b and 1c and S2 & S3 Figs. 3a, 3b, 3c respectively.

At an 80% proper usage of LLINs in the Guinea savannah could lead to a reduction in the rates of clinical malaria reported to 150 (95% p.CI [97, 223])/1000 and 136 (95% p.CI [84, 206])/1000 population by 2020 and 148 (95% p.CI [91, 222])/1000 and 125 (95% p.CI [62, 196])/1000 population by 2030, S5 Table 1.

Similarly for the Transitional forest, the rates of clinical incidence in all cases of malaria could be reduced to 146 (95% p.CI [115, 179])/1000 and 130 (95% p.CI [100, 160])/1000 population in 2020 and 107 (95% p.CI [57, 145])/1000 and 60 (95% p.CI [22, 93])/1000 population by 2030, S5 Table 2.

When LLIN usage of 80% and LLIN coverages of 70% and 90% are implemented successfully in the Coastal savannah, the incidence rates of reported cases of malaria could possibly be reduced to 62 (95% p.CI [47, 77])/1000 and 53 (95% p.CI [39, 67])/1000 population respectively by 2020 and 27 (95% p.CI [10, 55])/1000 and 11 (95% p.CI [4, 28])/1000 population by 2030, S5 Table 3.

Impact of IRS interventions

IRS coverage of 80% and PE of 30% and 60%, LLIN coverage and usage at baseline levels (66% and 56% in the Guinea savannah, 51% and 45% in the Transitional forest and 50% and 35% in the Coastal savannah respectively)

On average, annual predicted cases of uncomplicated malaria averted close to 90.0% at various levels of PE, if an 80% IRS coverage target were attained in five years and maintained through to 2030 across zones as showed in Fig. 6a, 6b and 6c and S4 Figs. 2a,2b and 2c.

In the Guinea savannah, the potential reported cases of uncomplicated malaria averted by 2030 is predicted to be 25.9% at a baseline protective efficacy of IRS of 30% and 30.5% at a protective efficacy of 60% Fig. 6a,S4 Fig. 2a.

With regards to all cases of malaria reported by program target dates, the predicted rates of incidence in the Guinea savannah could be reduced to 150 (95% p.CI [99, 222])/1000 and 112 (95% p.CI [65, 174])/1000 population for an IRS coverage of 80% and 90% respectively for a protective efficacy of 30% and 60% in 2020. By 2030, rates could be as low as 113 (95% p.CI [48, 183])/1000 and 18 (95% p.CI [2, 44])/1000 population respectively, S4 Table 1.

The corresponding potential uncomplicated cases of malaria averted in the Transitional forest zone as shown on Fig. 6b, S4 Fig. 2a could be 49.3% and 54.4% by 2030 for a coverage level of 80% and PE of 30% and 60% respectively.

These declines could translate into a reduction in the rates of incidence of all cases of malaria reported to 163 (95% p.CI [132, 197])/1000 and 129 (95% p.CI [101, 158])/1000 population by 2020 and 50 (95% p.CI [19, 79])/1000 and 2 (95% p.CI [1, 2])/1000 by 2030 respectively for a 30% and 60% levels of IRS PE, S4 Table 2.

Similar predictions are also observed for the Coastal savannah where the possible proportion of cases averted could be 58.9% and 62.9% for a 30% and 60% IRS PE by 2030, Fig. 6c,S4 Fig. 2a and Figs. 2b and 2c for severe and malaria in pregnancy cases reported.

Possible incidence rates for all cases of malaria (uncomplicated and severe) of 150 (95% p.CI [99, 222])/1000 and 150 (95% p.CI [99, 222])/1000 population could be attained by 2020 and 150 (95% p.CI [99, 222])/1000 and 150 (95% p.CI [99, 222])/1000 by 2030 respectively for IRS PE of 30% and 60%, S5 Table 3.

IRS coverage of 90% and PE of 30% and 60%, LLIN coverage and usage at baseline levels (66% and 56% in the Guinea savannah, 51% and 45% in the Transitional forest and 50% and 35% in the Coastal savannah respectively)

Relatively higher cases of uncomplicated, severe malaria and malaria in pregnancy could be potentially averted with a higher IRS coverage of 90% at the similar levels of PE at 30% and 60% across all the zones, Figs. 7a-7c, S4 Figs. 1a-1c, and 2a-2c and 3a-3 c.

In the Guinea savannah, a possibly 72.0% and 79.0% of uncomplicated cases averted could be attained by 2030. Correspondingly, similarly proportions of severe malaria cases and of malaria in pregnancy

could be averted by 2030 with an 90% IRS coverage and PE of 30% and 60% respectively, Fig. 7a, S 4 Fig. 1a,2a, 3a.

The impact of these declines in cases of malaria on incidence of all malaria cases could be a decline to 146 (95% p.CI[95, 218])/1000 and 105 (95% p.CI[59, 164])/1000 population by 2030 and 102 (95% p.CI[36, 169])/1000 and 6 (95% p.CI[1, 15])/1000 population by 2030 for a 30% and 60% PE and coverage of 90% IRS, S5 Table 1.

Likewise, in the Transitional forest, potentially 75.7%, of uncomplicated (similarly for severe malaria and malaria in pregnancy cases) could be averted with an IRS coverage of 90% and PE of 30% respectively. For an IRS PE of 60%, the reported cases that could be averted is 78.5of uncomplicated cases may be averted by 2030, Fig. 7b, S4 Figs. 2a-2c.

Consequently, the rates of incidence of all cases of malaria may be lowered by to 159 (95% p.CI[128, 192]) and 121 (95% p.CI[94, 149]) for an IRS PE of 30% and 60% by 2020 and 35 (95% p.CI[12, 59]) and 1 (95% p.CI[1, 1]) for an IRS PE of 30% and 60% by 2030, S5 Table 2.

The impact of IRS only, in averting uncomplicated cases, as shown in Fig. 7c S2 & S3 Fig. 4a, 4b and 4c, S4 Figs. 2b and 2c, could be 78.5% versus 80.9% for a 90% IRS coverage with a 30% and 60% levels of PE respectively for uncomplicated malaria by 2030.

The incidence rates for all cases of malaria following the attainment of these intervention targets could potentially be 75 (95% p.CI[59, 89])/1000 and 53 (95% p.CI[40, 65])/1000 population for 30% and 60% IRS PE by 2020 and 8 (95% p.CI[3, 20])/1000 and 0 (95% p.CI[0, 0])/1000 population by 2030, S5 Table 3.

Deployment of LLINs and IRS

LLIN coverage at 80% and IRS coverage at 80% or 90% with LLIN usage and IRS PE at baseline settings (56% and 30% in the Guinea savannah, 45% and 30% in the Transitional forest and 35% and 30% in the Coastal savannah respectively)

Achieving 80% LLINs and IRS coverage while maintaining the LLIN usage and IRS PE at baseline respectively in the population potentially results a 30.8%of reported uncomplicated malaria cases averted in the Guinea savannah, Fig. 8a, and S4 Figs. 3a 3b and 3c.

The proportions of malaria cases averted for implementing an 80% LLIN and IRS coverage at baseline LLIN usage and IRS PE result in terms of incidence rates are 144 (95% p.CI[93, 214])/1000 and 103 (95% p.CI[37, 170])/1000 population for all cases of malaria in the Guinea savannah by 2020 and 2030 respectively, S5 Table 1.

Corresponding proportions of cases averted potentially with IRS coverage increased to 90% as shown on Fig. 8a, S4 Figs. 3a, 3b and 3c are 34.4%, for reported uncomplicated. The accompanying incidence rates

for all cases of malaria predicted in 2020 and 2030 are 140 (95% p.CI[90, 210])/1000 and 91 (95% p.CI[27, 156])/1000 population respectively.

In the Transitional forest zone, 58.0% of uncomplicated cases are predicted to be averted and similarly for cases of severe malaria and malaria in, Fig. 8b, S4 Fig. 3a,3b and 3c.

The resulting incidence rates, as shown in S5 Table 2 are 150 (95% p.CI[120, 183])/1000 and a 29 (95% p.CI[9, 51])/1000 population for the Transitional forest respectively for 2020 and 2030. The associated potential proportions of uncomplicated malaria, severe malaria and malaria in pregnancy cases averted under similar intervention scenario as before but with an elevated coverage of IRS to 90% is 60.6%, Fig. 8b, S4 Figs. 3a,3b,and 3c. Corresponding incidence rates for all cases of malaria under this scenario are predicted to be 146 (95% p.CI[116, 178])/1000 and 20 (95% p.CI[6, 36])/1000 population respectively, S5 Table 2.

Under the 80% coverage for both LLIN and IRS and LLIN usage and IRS PE at baseline, the associated potential proportions of uncomplicated, severe and malaria in pregnancy cases averted in the Coastal savannah are predicted to be 64.7% respectively, Fig. 8c, S4 Figs. 3a,3b,and 3c.

Predictions of the incidence rates per 1000 for the Coastal savannah under this intervention scenario are predicted to be 72 (95% p.CI[56, 85])/1000 and a 7 (95% p.CI[3, 18])/1000 population for 2020 and 2030 respectively, S5 Table 3.

When only the coverage levels of IRS is increased to 90% while the other intervention scenarios are maintained, the incidence rates per 1000 population are predicted to be 69 (95% p.CI[54, 82]) and 5 (95% p.CI[2, 12]) in the Coastal savannah by 2020 and 2030 respectively, S5 Tables 3. Shown on S4 Figs. 3a, 3b and 3c are the respective proportions of potential cases (66.3%) of uncomplicated malaria, severe malaria and malaria in pregnancy predicted to be averted.

LLIN and IRS coverage at 90% and 80% versus 90% and 90% respectively with LLIN usage and IRS PE baseline (56% and 30% in the Guinea savannah, 45% and 30% in the Transitional forest and 35% and 30% in the Coastal savannah respectively)

Given that, baseline usage of LLIN and PE of IRS remain in force as in the previous scenario except increasing the coverage levels of LLINs to 90% and maintaining IRS coverage at 80%, the incidence rates per 1000 population are predicted in the Guinea savannah zone to be 139 (95% p.CI[89, 209]) and 94 (95% p.CI[29, 161]) respectively by 2020 and 2030, Fig. 9a and S5 Table 1,

versus 136 (95% p.CI[86, 204])/1000 population by 2020 and 83 (95% p.CI[20, 146]) by 2030 which is less compared to the previous scenario, S5 Table 1 and Fig. 9a. For a scenario with an increased LLIN coverage at 90% and IRS coverage at 90%. The accompanying proportions of the various cases of predicted reported malaria are shown on S4 Figs. 3a,3b and 3c.

The observed rates for the Transitional forest are 146 (95% p.CI[116, 178])/1000 and 142 (95% p.CI[113, 173])/1000 population versus 24 (95% p.CI[7, 42])/1000 and 16 (95% p.CI[5, 29])/1000 population respectively by 2020 and 2030, S5 Tables 2, Fig. 9b.

Related predictions of proportions of uncomplicated malaria, severe malaria and malaria in pregnancy are shown on S4 Figs. 3a, 3b and 3c respectively.

Testing a 90% LLIN and 80% IRS coverage versus 90% LLIN and 90% IRS coverage under baseline prevailing levels of LLIN usage and IRS PE, predicted 70 (95% p.CI[54, 83])/1000 and 67 (95% p.CI[52, 80])/1000 population versus 6 (95% p.CI[2, 15])/1000 and 4 (95% p.CI[2, 10])/1000 population respectively by 2020 and 2030, S5 Tables 2, Fig. 9c. Corresponding cases potentially averted in proportions are shown on S4 Figs. 3a, 3b and 3c, respectively for uncomplicated, severe malaria and malaria in pregnancy.

LLIN and IRS coverage at 80% and 80% versus 80% and 90% respectively maintaining LLIN usage at 60% and IRS PE baseline (30% in the Guinea savannah, 30% in the Transitional forest and 30% in the Coastal savannah respectively)

A scenario with an elevated level of LLIN usage in the presence of IRS at baseline PE and LLIN and IRS coverage levels of 80% versus 80% or 80% versus 90% predicts 33.0% versus 37.7% uncomplicated malaria respectively in the Guinea savannah in 2030, S4 Figs. 3a, 3b and 3c.

Equivalently, the incidence rates for all malaria cases predicted are 140 (95% p.CI([89, 210])) versus 137 (95% p.CI([86, 206])) for 2020 and 98 (95% p.CI([33, 165])) versus 86 (95% p.CI([23, 151])) by 2030 respectively, S5 Table 1 and Fig. 10a. Under the same scenario of interventions, the predictions in the Transitional forest zone by 2020 are 65.6% versus 68.3% for uncomplicated malaria respectively by 2020, S4 Figs. 3a, 3b and 3c.

The rates of incidence for all cases are however respectively 133 (95% p.CI ([103, 163])/1000 versus 129 (95% p.CI ([100, 159])/1000 population by 2020 and 140 (95% p.CI([89, 210])) /1000 versus 140 (95% p.CI([89, 210])/1000 population by 2030, S5 Table 2, Fig. 10b.

In the Coastal savannah, uncomplicated malaria, severe malaria and malaria in pregnancy cases by 2020 under the same scenario of interventions leads to 74.6% versus 76.1 respectively potentially averted, S4 Fig. 3a, 3b and 3c. Correspondingly, 55 (95% p.CI ([41, 68])/1000 versus 53 (95% p.CI ([39, 66])/1000 population by 2020 and 2 (95% p.CI ([1, 6])/1000 versus 2 (95% p.CI ([1, 4])/1000 population by 2030 are the predicted rates of incidence respectively for the two scenarios of LLINs and IRS being tested, S5 Table 3, Fig. 10c.

Discussions

The potential impact of malaria interventions were investigated by simulating various implementation scenarios while taking into account the diversity of morbidity in the three ecological zones across Ghana.

These investigations which were conducted within the period 2018 to 2030 also assessed the prospects of achieving some goals of the National Malaria Strategic Plan, 2014–2020 as well as those of the WHO Global Technical Strategy milestones [1].

The models take into account, the population sizes of the different transmission settings. Differences in transmission potential for young children, adults and pregnant women were also considered. The gradual improvement in the data capture and reporting, through the DHIMS infrastructure, at the district level in government health facilities, faith based private facilities across the country were accounted for by allowing for various levels of reporting and system improvements from 2008 to 2018 while years of improvement of malaria diagnosis was also incorporated [21, 22].

The roll out of LLINs on large scale basis in Ghana begun from 2003 [21]. This has resulted in a substantial improvement in the proportion of households with at least one LLIN as well as at least one LLIN per every two members of a household (universal coverage) across the country [23]. For instance as at 2016, the proportion of households on average with at least one LLIN was 89.0%, 74.8%, and 70.0% compared to 59.0%, 42.5% and 37.6% in 2008 for the Guinea savannah, Transitional forest and Coastal savannah zones respectively [23, 24]. On the other hand, on average, the universal coverage of LLINs in 2016 were 65.7%, 50.5% and 49.9% respectively for the Guinea savannah, Transitional forest and Coastal savannah zones [23]. These achievements have largely contributed to the gradual decline in the prevalence of malaria among children aged 6–59 months of age with the latest (2016) measurement being 21.0%, falling from 27.0% in 2014 [23].

Relatively, ITN/LLIN usage is low across the country. On average 56.0%, 45.0% and 35.2% of the population in the Guinea savannah, Transitional forest and Coastal savannah zones were reported to have slept in an ITN/LLIN in 2016, a marginal increase from 47.1%, 45.6% and 32.5% in 2008 for children under the age of five years respectively [23–25]. These observations follow the results of this study which suggests that, ITN or LLIN usage could be low given the current level of coverage and incidence of malaria across all the zones. The results from the models show that, with elevated levels of usage of LLINs, which improves the protective effectiveness (PE), a significant number of predicted incidence cases could be averted.

For example, as described earlier, the predicted cases averted by increasing the coverage levels of LLINs to targeted levels of 70%, 80% and 90% during a three year implementation campaign leads to only a marginal improvement from the baseline scenario without a corresponding increase in the PE of the LLINs. This observation may explain why the relatively high universal coverage levels of LLINs currently observed (at least 50% across zones as at 2016) may not be impacting very much in reducing the level of predicted cases as would have been expected.

The promise to averting more predicted cases through LLINs maybe a step up in the campaign to persuade the population to comply to proper LLIN usage while continuous efforts are made to sustain the already achieved coverage. Many factors have been reported for people not sleeping in ITN/LLIN

including an inability to hang them, real or perceived health concerns, difficulty in breathing when sleeping under them and other factors [26–28].

This calls for further and continuous advocacy on the usage of ITNs/LLINs through any means including formal education channels or through community hang-up/social behaviour communication change campaigns on the proper and sustained usage of the LLINs while highlighting the potential biting patterns of mosquitoes to avert unnecessary out-door exposure [15, 16].

Given the proven efficacy of LLINs, and the relatively high coverage levels currently prevailing in the various zones, correspondingly higher reductions in the burden of malaria could have been achieved if patronage to the usage of these LLINs were equally as high as demonstrated throughout the results of various intervention scenarios simulated in this study with increasing levels of PE.

Following the WHO guidelines for vector control, Ghana may have attained a high enough LLINs coverage in selected areas, especially in the Guinea savannah zone where transmission is highly seasonal and coverage is relatively higher, to begin the roll out of IRS on a targeted large scale basis as a complimentary vector control measure [8, 28].

However, relative to LLINs, the coverage of IRS is by far the lowest across the country. Although parts of the Guinea savannah and the Transitional forest zones have had some implementation of IRS on pilot bases, studies are yet to be sited of any such activities rolled out in the Coastal savannah [21, 29, 30].

It was shown in parts of the Guinea savannah that, districts where IRS were deployed compared to non-IRS districts resulted in a reduction of 39.0% on average in malaria incidence during six months after spraying. These gains were however reversed when the IRS activities were not sustained [30, 31].

Results in this study shows that, a potential reduction from 48.9–90.4% of predicted cases of malaria could be attained with an increased deployment of IRS in the various zones for varying levels of PE of a spraying programme that will take up to five years to attain and maintain these coverage levels, S4 Figs. 2a,2b and 2c. At these levels of decline, pre-elimination would be in sight as observed in the incidence rates of 1 (95% p.CI [1, 2])/1000 population or less for attaining a 90% coverage of IRS in three years and maintained up to 2030 across the country S5 Tables 1,2,3. Combining both LLINs and IRS will likely contribute very significantly to not only averting much more predicted cases across Ghana but probably drive the annual incidence of malaria presented at the health facilities down towards pre-elimination levels if the population improved on the sustained usage of LLINs and scaling up of IRS especially in the Transitional and coastal zones S5 Tables 1, 2 and 3.

IRS might hold a greater promise of averting much more cases of malaria compared to LLINs given the relatively low level of dependence on human behaviour to usage. However, the feasibility of rolling out of IRS as an additional intervention to LLNs, even though will have additional benefit to averting more predicted cases, on a large or targeted basis may depend on the level of community acceptability and the considerable additional cost given the limited operational budget space.

Figures 8a-8c and 9a-9c, show the level of the cases of malaria averted following implementation of both LLINs and IRS at elevated coverage levels while maintaining prevailing usage relative to Figs. 10a-10c which shows the impact of increasing the usage of LLINs only. The proportion of predicted cases potentially averted with an elevation of the usage to 60% ,S4 Figs. 1a,2a and 3a are relatively higher than those of maintaining prevailing LLIN usage .Similarly for severe and malaria in pregnancy cases S4 Fig. 1b,2b,3band S4 Fig. 1c,2c,3c respectively across all three zones up to 2030. This seems to suggest that, while high coverage levels of the various interventions are desired, equally important are the uptake of these interventions that ultimately increases the levels of PE which will lead to further reductions of predicted incidence of malaria cases in the various zones.

The investigations for combined LLIN and IRS presented in Figs. 8, 9 and 10 are hypothetical scenarios of deploying IRS in selected districts with relatively high risk at the zonal level as a supplementary intervention to LLIN. For practical and financial considerations, it may be infeasible to achieve universal coverage of both LLINs and IRS. This makes efforts towards improving the effectiveness of LLIN, at the already high coverage levels an imperative otherwise it amounts to not achieving value for money for the investment over the years.

The presence of community water reservoirs such as irrigation dams or dug-outs could potentially adversely affect the burden of malaria particularly a rise in incidence of malaria despite their potential socio-economic benefits to the communities they are situated [32–34]. In this respect, the promise of the Government of Ghana to build community level dams/dag-outs/ponds in various districts of the country, under the one village one dam policy [35–37], could pose a risk to the gains already made in reducing the burden of malaria if appropriate dam management practices are not applied after they are commissioned. It is perhaps not out of place at this time to think of a supplementary vector control strategy such as larva source management as one example of the “best practices” approach for dam management with regards to malaria control interventions to avert any potential rise in the local burden of malaria.

According the WHO guidelines on vector control, Larviciding could be considered as a supplementary intervention once the source of mosquitoes are few, fixed and findable [38].This maybe a viable vector control measure in parts of the Guinea savannah zone ,since most of these dams are proposed to be sited largely in this zone. Larviciding has the potential to avert between 75.0–84.0% cases of malaria and reduce the parasite prevalence by 11.0–42.0% [38].

Therefore, as continuous efforts are being made by the NMCP and other stakeholders to scale up various vector control measures across the country, an even stronger advocacy needs to be made for education of the population through various channels such radio, television messages and programmes and community durbars on the uptake of the various malaria interventions especially LLINs [39, 40].

Given the possible high levels of LLIN non-use in Ghana, 58.0% (2016), which is relatively higher compared to her neighbours, Benin 28.9% (2017), Burkina Faso 33.0% (2014) and Cote d'Ivoire, 49.6% (2016), the community health officers stationed in the various CHPS compounds may be of great

resource to undertaking these additional tasks of educating and mounting hang up campaigns and other means of communication for the uptake of the usage of LLINs [25, 41–43].

From the results thus far, it's unlikely that with the current rate of decline being observed Ghana will achieve the principal target of reducing the burden of malaria by 75% (which translates to 47 cases per 1000 population per year using cases reported in 2012 as baseline) by the 2020 projected by the National malaria strategic plan of 2014–2020, even though large declines have been achieved with malaria attributable deaths [4]. Meeting the goals of the strategic plan by 2030 may require full scale deployment of IRS in targeted districts and communities complementary to LLINs in all the zones to at least 80% coverage using insecticides with high level of protective efficacy or as shown by the predicted incidence rates of reported clinical cases on S5 Tables 1, 2 and 3 per 1000 population year by 2030 respectively for the Guinea savannah, Transitional forest and Coastal savannah zones.

The relatively high treatment seeking (72.0%) and diagnosis (90.0%), respectively for the Guinea savannah, Transitional forest and Coastal savannah were taken into account while testing the impact of the various interventions. Attaining improved coverage levels of vector control interventions across the country may require an unprecedented level of investment and a multi-prong action to roll out interventions such as LLINs and IRS (in targeted districts), to prevent cases and to treat cases concurrently while rallying all the citizenry to improve usage of LLINs and seek treatment promptly while investing in personal protection.

Limitations

To consider the force of infection as dependant on only infectious humans specific to their respective zones is to ignore the possible contributions of migrants from other zones to the local infectious human reservoir. However, given the high level of malaria incidence across all zones and all year round, stand-alone zonal model structure may still be considered valid and not affected significantly by the lack of spatial interaction which allows for movement of various classes of the population of each zone to another.

Even though reported universal coverage of LLINs were used from the various surveys over the years, knowing the detailed number of LLINs distributed by zones would even be more preferred. However, the estimates for both LLIN and IRS historical coverages used were obtained from results of robust national surveys which are considered credible. Additionally, a current country measured levels of protective effectiveness of the LLINs and IRS are also not available and therefore this study relied on published data from studies of meta- analyses which included sub-Saharan African countries which may be reflective of the levels of protectiveness of LLINs in Ghana as well [20].

Regardless of the demonstrated benefit of IPTi among infants in Ghana [44] and elsewhere, not including the impact of IPTi in this study does not diminish the importance of the findings given the relatively low population size of these infants.

Population growth in Ghana was estimated to be 2.5% from 2000 to 2010 but this was not factored into the models [45]. These could be applied to estimates obtained and therefore does not impact negatively on the value of the findings.

Future Work

A similar investigation will be carried out considering the impact of increasing the probability of receiving a diagnostic test when classified as being a suspected of malaria infection at the health facility and a population level treatment on the incidence of malaria. A follow up study of this current investigation will include the development of a meta-population model which will allow for interaction between zones to account for possible contributions to the local infectious reservoir by neighbouring zones. This will require sub-dividing the zones into respective regional blocks that may enable a more detailed investigation of the burden of malaria at the local administration level.

Conclusions

This study has shown that, it's possible to achieve targets set out by the NMCP and those of the Global strategy for malaria using current interventions if compliance to their recommended application are improved. Therefore, any programmes and strategies that would further increase the patronage, proper and continuous usage of ITN/LLIN should be encouraged and supported.

Districts with incidence rates of malaria above zonal averages could be targeted for IRS to complement LLINs as recommended by WHO since the LLIN coverage is relatively high. If desired levels of malaria related morbidity will be attained, as projected by the National strategic policy of 2014–2020 [4], then a rapid and momentous effort needs to be made to improve upon the uptake and sustained usage of the LLINs while consideration is given to targeted IRS especially in high risk districts in the Transitional forest and Coastal savannah zones.

Declarations

Ethical considerations

Ethics approval was obtained from the Institutional Review Board of the Navrongo Health Research Centre, Ghana as well as the University Of Cape Town Faculty Of Science Research Ethics Committee. Permit to use health facility data (DHIMS2 data) was granted by the National Malaria Control Program, Ghana.

Availability of the data and materials

The authors do not have the rights to share the meteorological data which can be obtained from client@meteo.gov.gh. The health facility based malaria data could be requested for at nmcp@ghsmail.org.

Authors contributions

TA and SS conceptualised and developed the research questions and TA developed the models and wrote the manuscript. TA and SS made comments and suggestions for revision and both authors read and approved the final manuscript.

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Consent for Publication

Not Applicable

Competing interests

Neither the sponsors of my PhD studies nor the authors have any competing interests.

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Figures

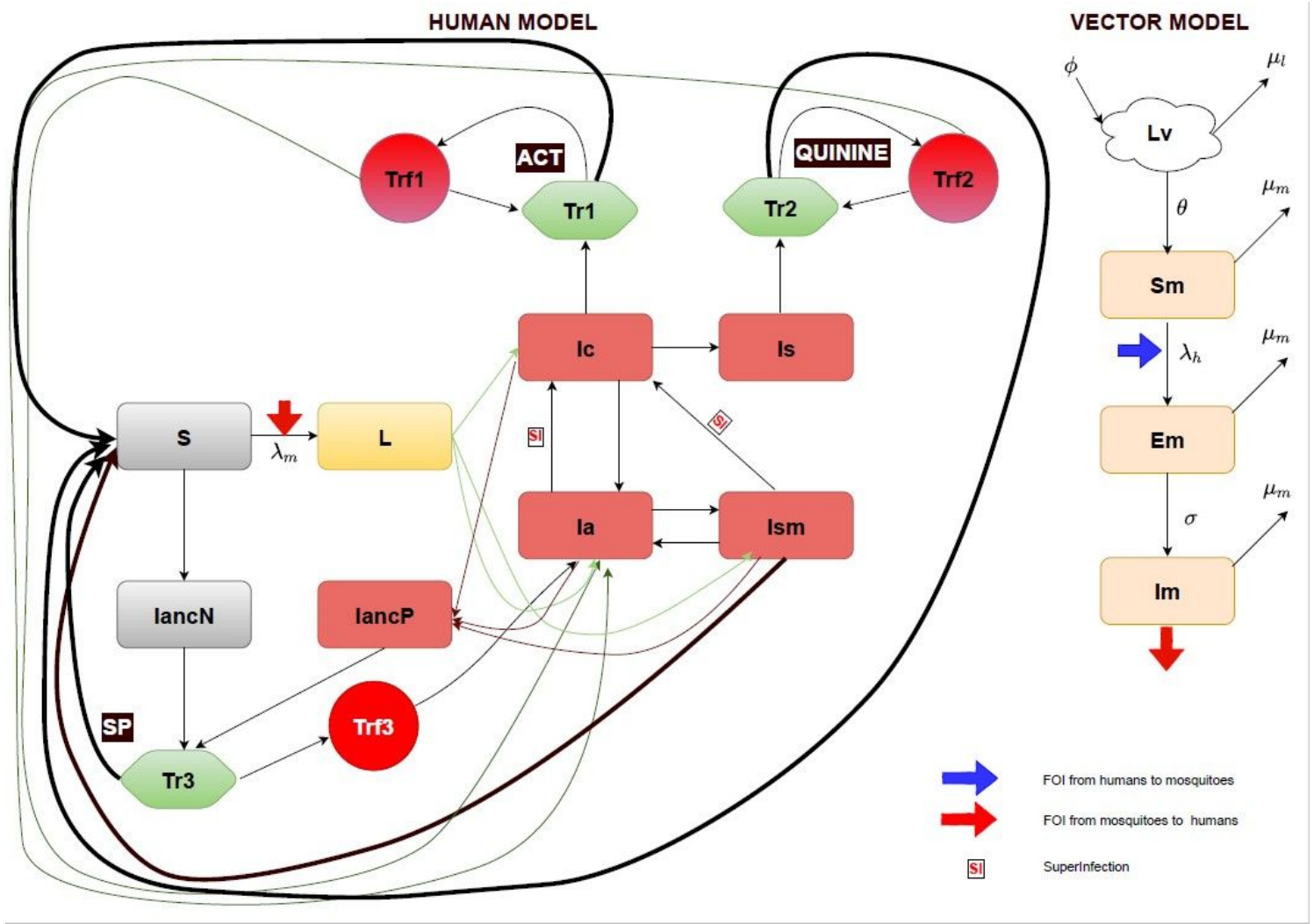


Figure 1

Malaria transmission model showing various compartments of both human and vector populations. Human population: S represent the susceptible human compartment (where different probabilities have been applied respectively to recruited naïve or non-immuned children under 6 years of age, adults and pregnant women into the latent stage L. before the onset of gametocytes. Ic, Ia, Is and Ism compartments represents symptomatic infection (clinical infection), asymptomatic infection, severe infection and sub-microscopic infection respectively. Pregnant women attend antenatal clinic (ANC) without an infection, IancN or progress from L3 into IancP once infected. Tr1, Tr2 and Tr3 represent the treatment sought for confirmed uncomplicated malaria (Ic), severe malaria (Is) and routine monthly SP prophylaxis for pregnant women at ANC, Trf1, Trf2 and Trf3 represent respective treatment failure due to adherence and possible drug resistance for the three latter treatment options. Vector population: Lv represents larva population and Sm susceptible mosquitos. Exposed mosquitoes are captured in Em compartment. Whereas infectious mosquitoes are in the Im compartment.

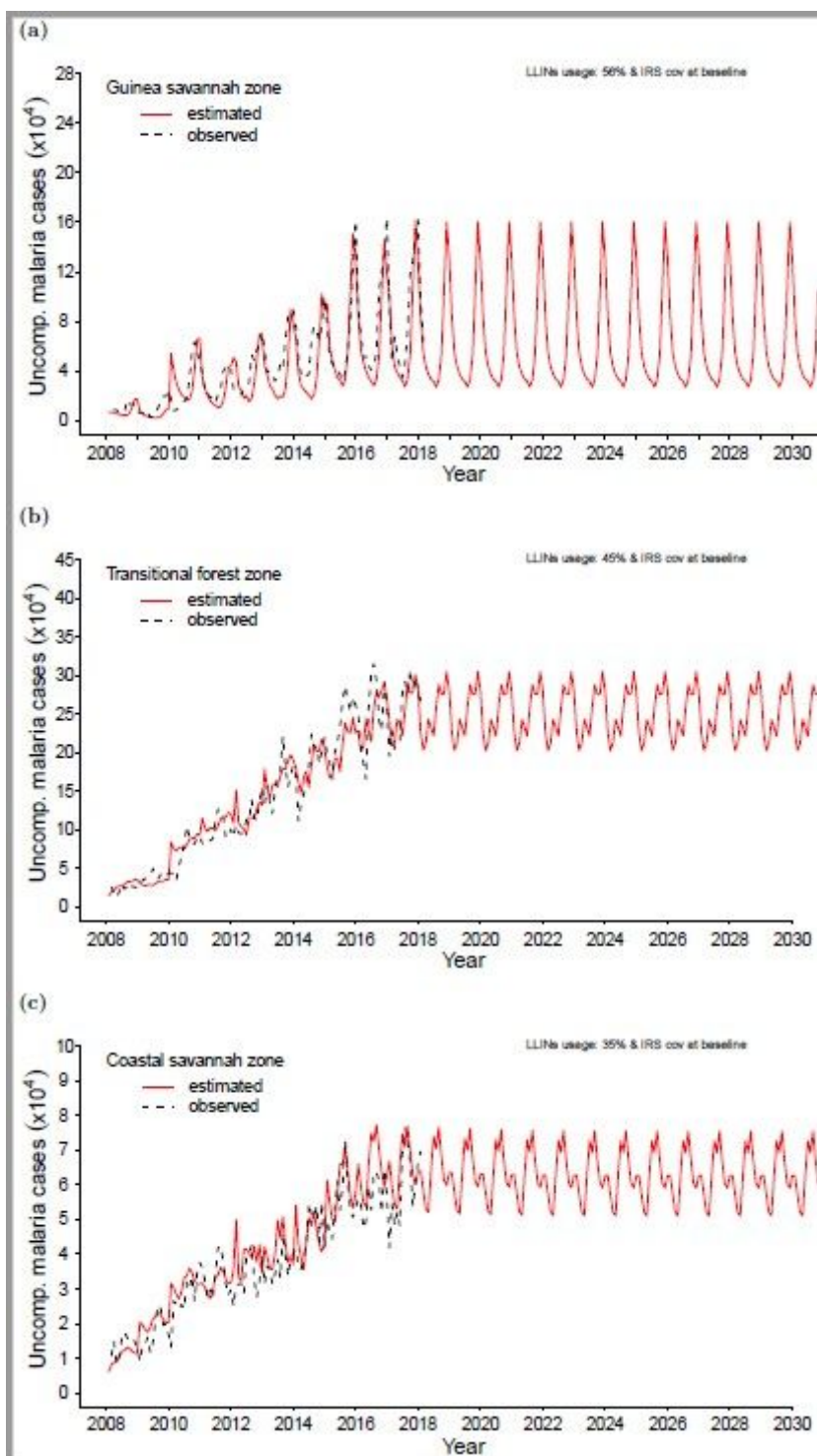


Figure 2

Model run time is 1988 to 2030. Steady state period spans from 1988 to 1997, 1998 to 2017 previous interventions implemented and reporting rates on DHIMS introduced. Data fitting from 2008 to 2017 for the (a) Guinea savannah, (b) Transitional forest and (c) Coastal savannah.

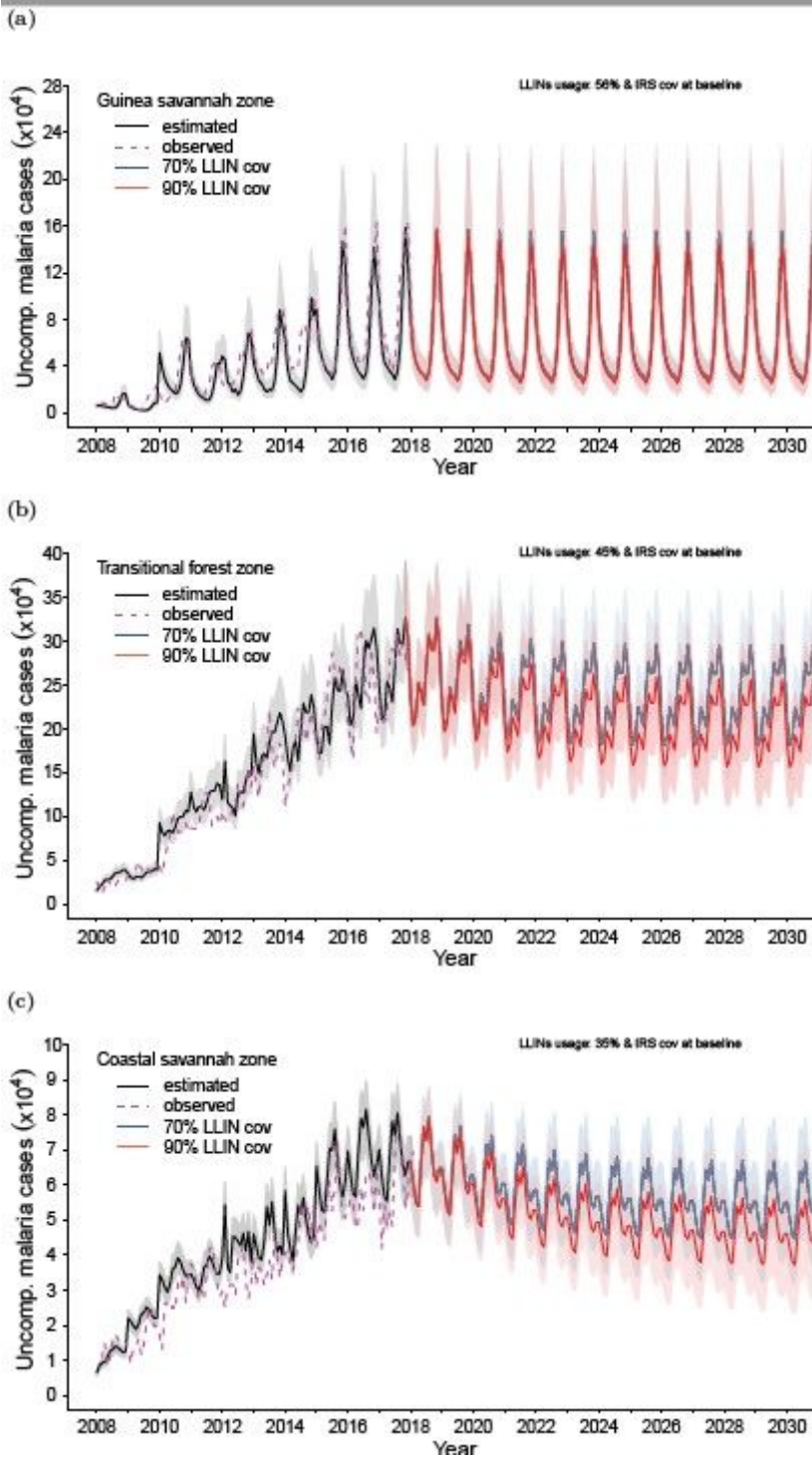


Figure 3

Impact of attaining various levels of LLINs coverage within a 3 year implementation programme at a usage level of 40% while maintaining IRS coverage and PE at prevailing baseline levels in the (a) Guinea savannah, (b) Transitional forest and (c) Coastal savannah.

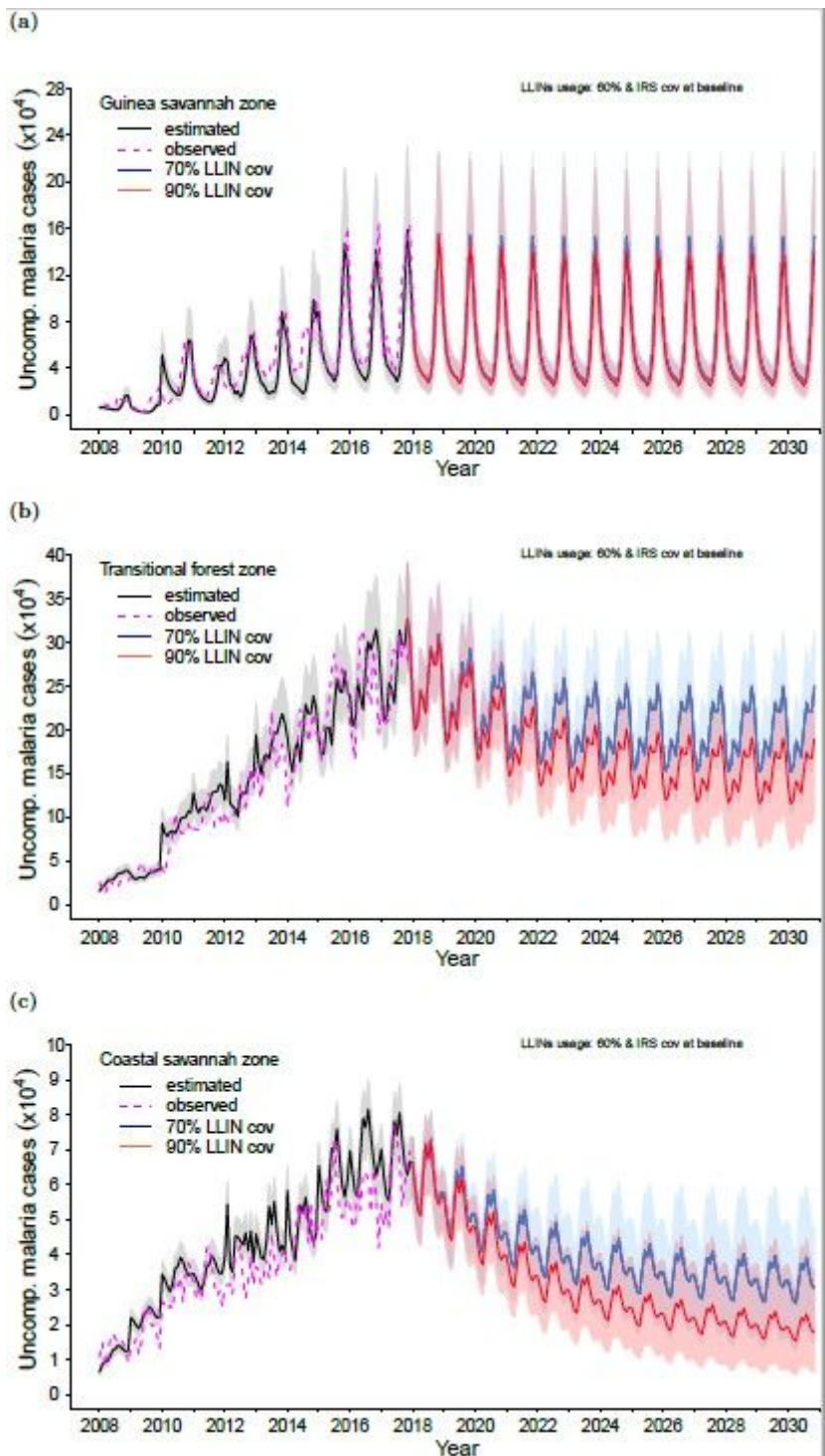


Figure 4

Impact of attaining various levels of LLINs coverage within a 3 year implementation programme at a usage level of 60% while maintaining IRS coverage and PE at prevailing baseline levels in the (a) Guinea savannah, (b) Transitional forest and (c) Coastal savannah.

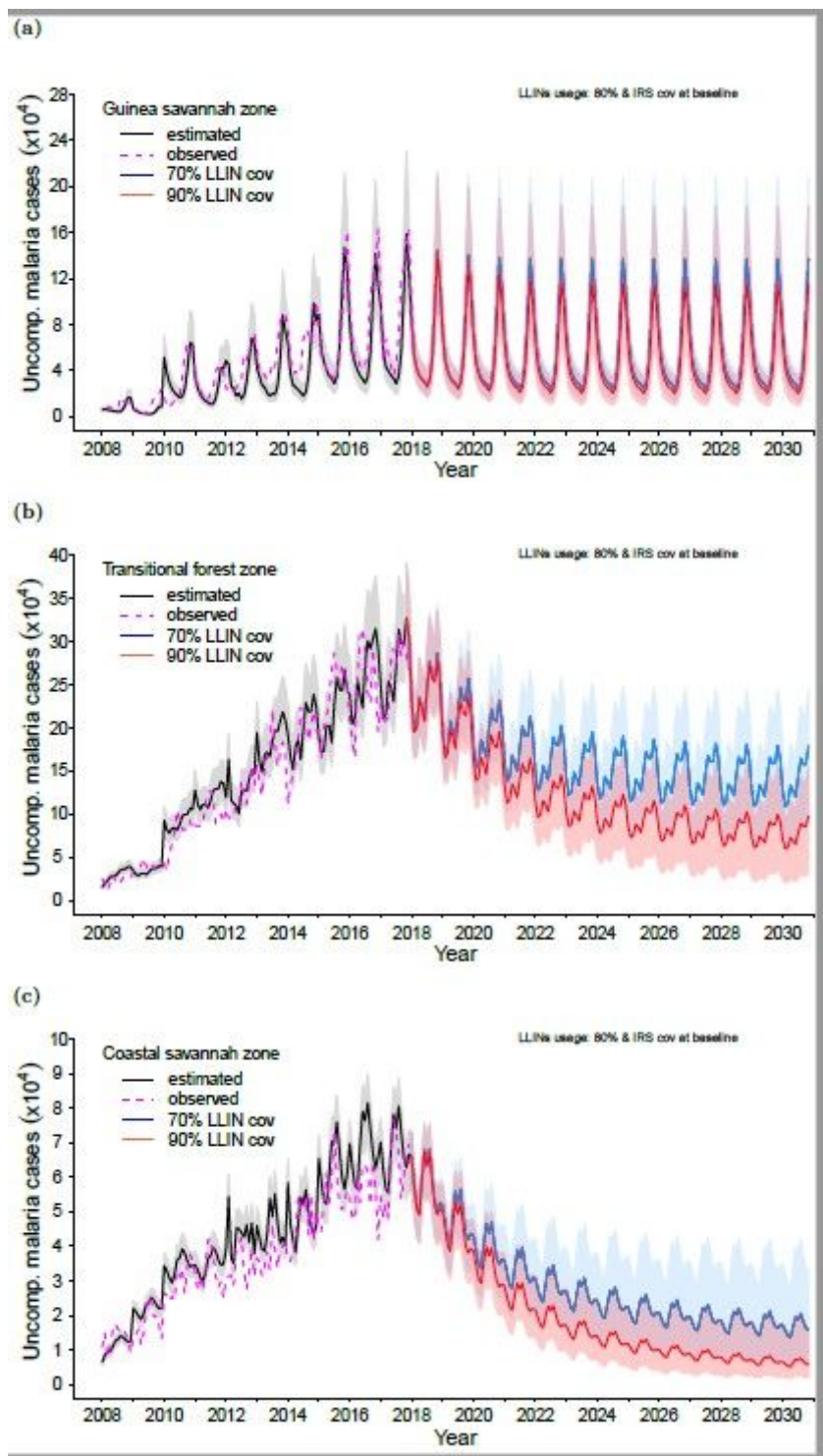


Figure 5

Impact of attaining various levels of LLINs coverage within a 3 year implementation programme at a usage level of 80% while maintaining IRS coverage and PE at prevailing baseline levels in the (a) Guinea savannah, (b) Transitional forest and (c) Coastal savannah.

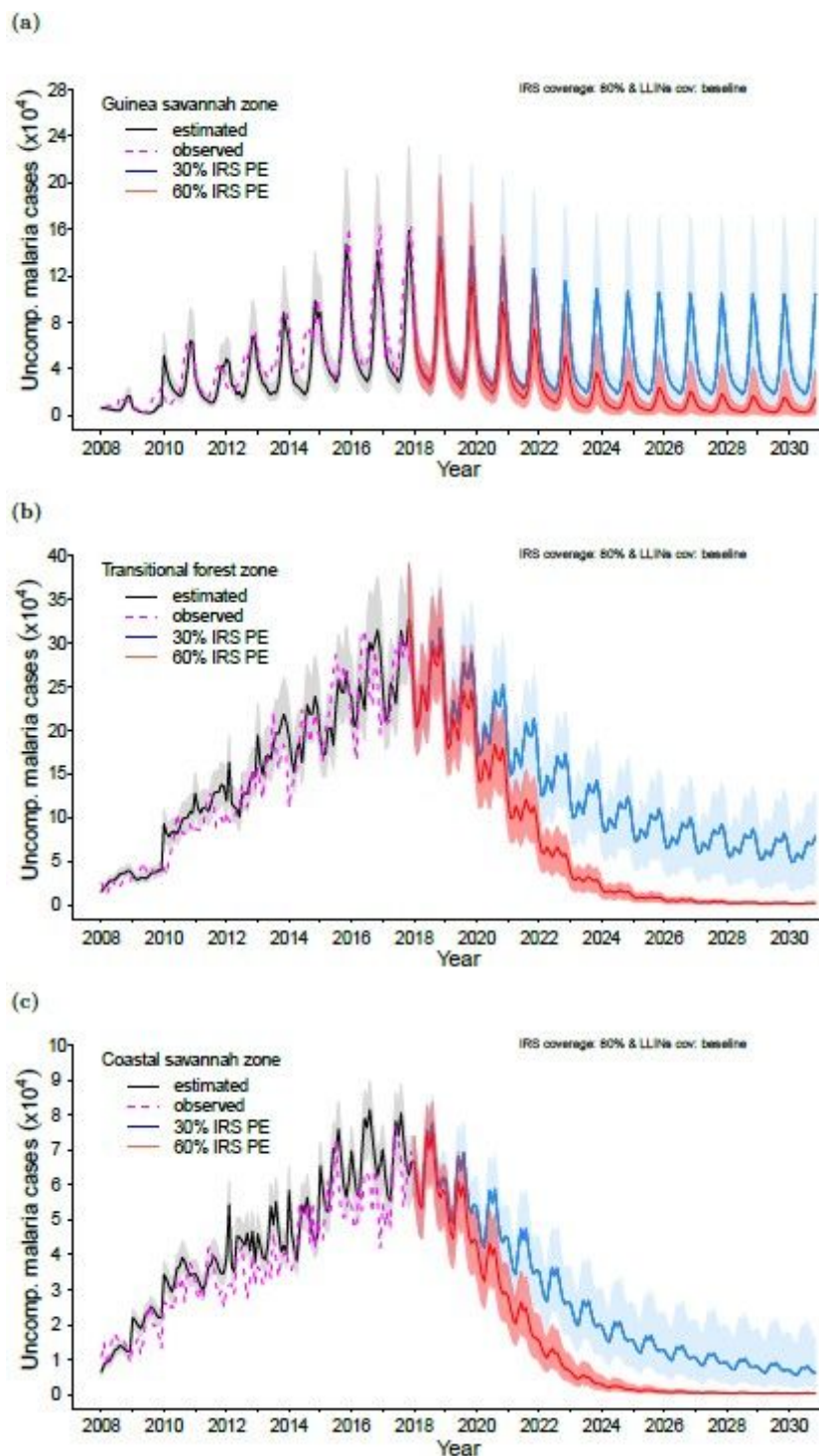


Figure 6

Impact of attaining various levels of IRS coverage within a 5 year implementation programme at various Protective Efficacy (PE) while maintaining IRS coverage at 80% and PE and coverage level and usage of LLINs at prevailing baseline levels in the (a) Guinea savannah, (b) Transitional forest and (c) Coastal savannah.

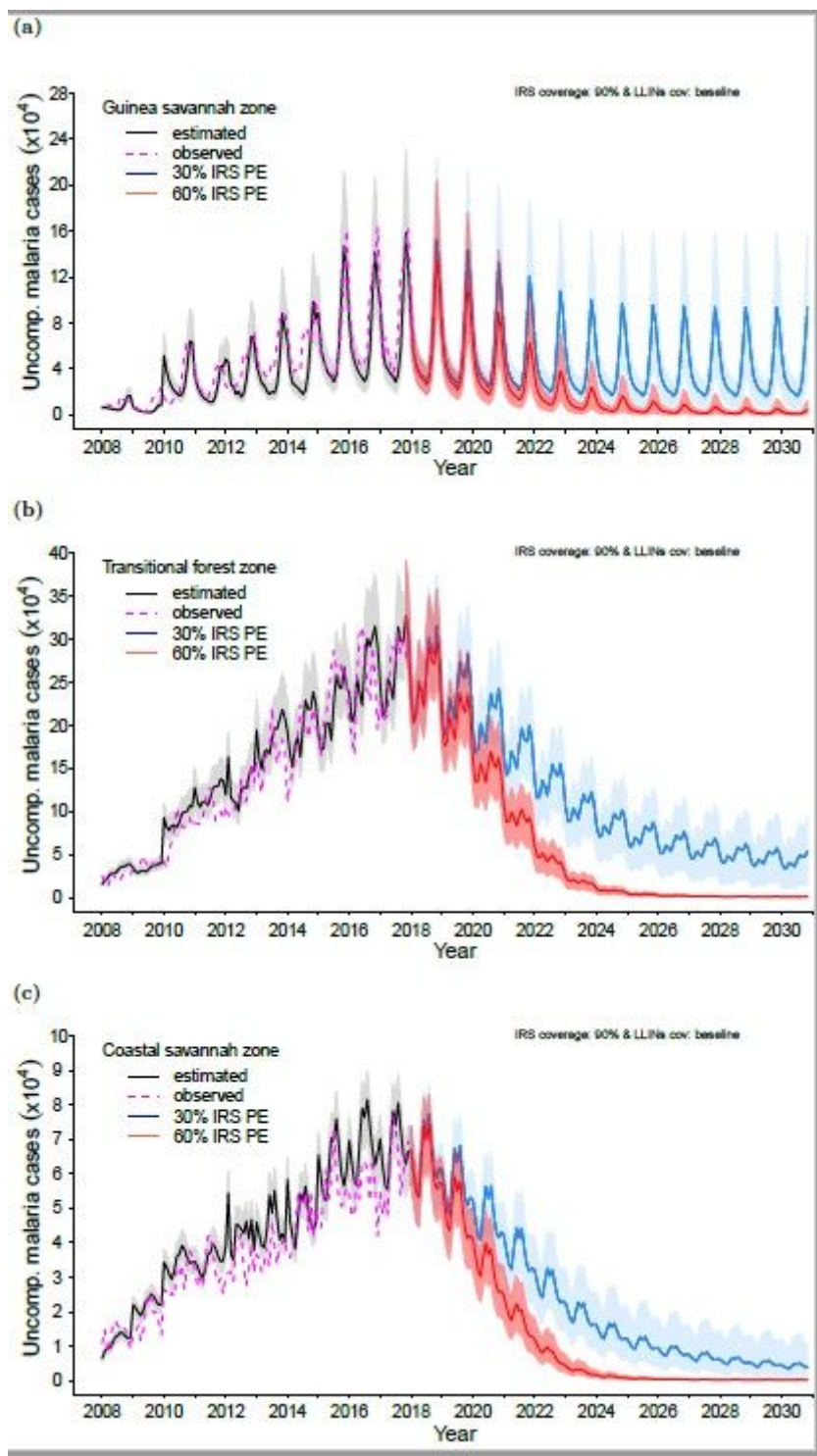


Figure 7

Impact of attaining various levels of IRS coverage within a 5 year implementation programme at various Protective Efficacy (PE) while maintaining IRS coverage at 90% and PE, coverage levels and usage of LLINs at prevailing baseline levels in the (a) Guinea savannah, (b) Transitional forest and (c) Coastal savannah.

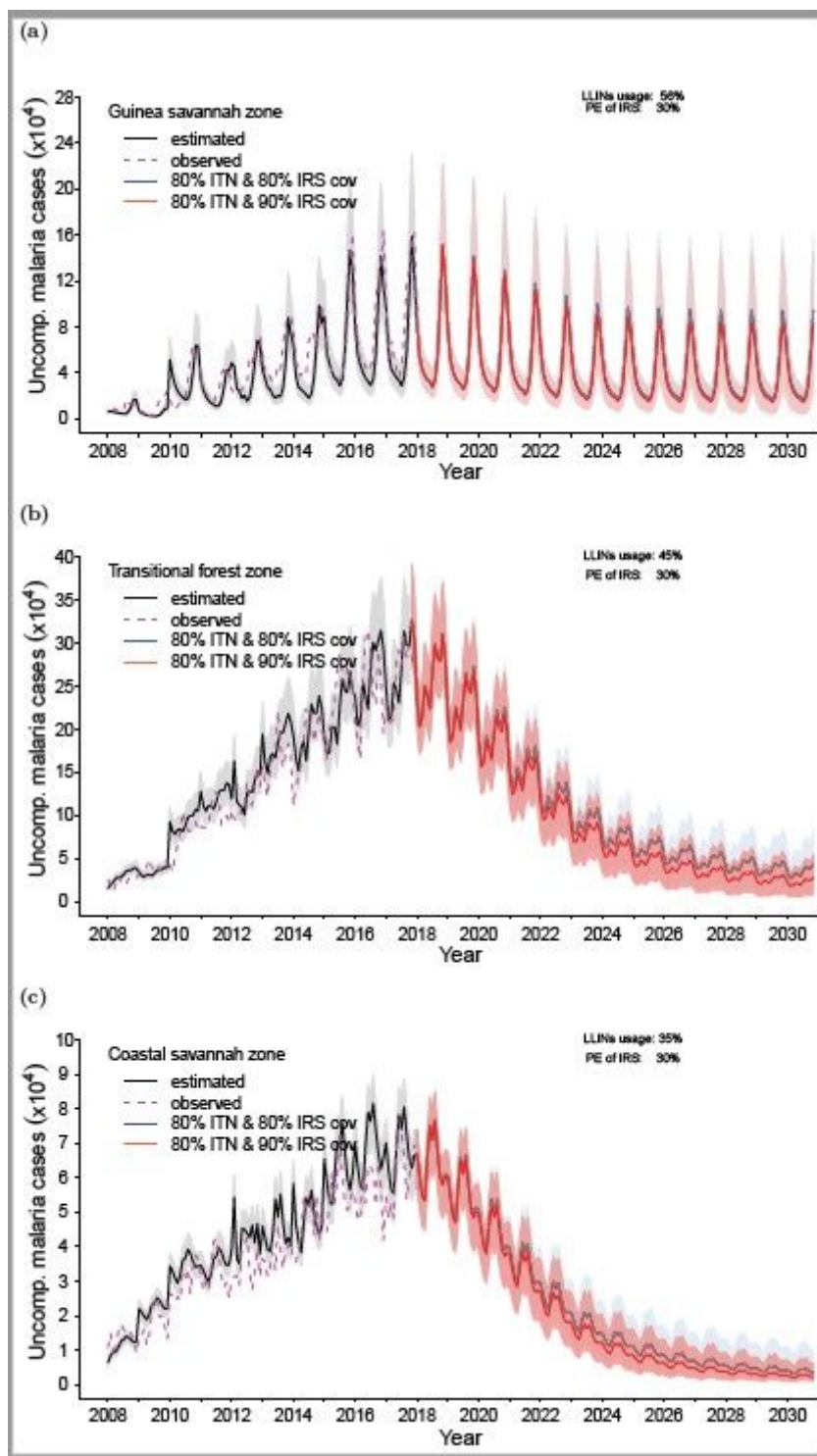


Figure 8

Impact of attaining a combination of various levels of LLINs and IRS coverage within 3 and 5 year implementation programme respectively at baseline Protective Efficacy (PE) of IRS (30%) and LLINs (40%) and usage in the (a) Guinea savannah, (b) Transitional forest and (c) Coastal savannah.

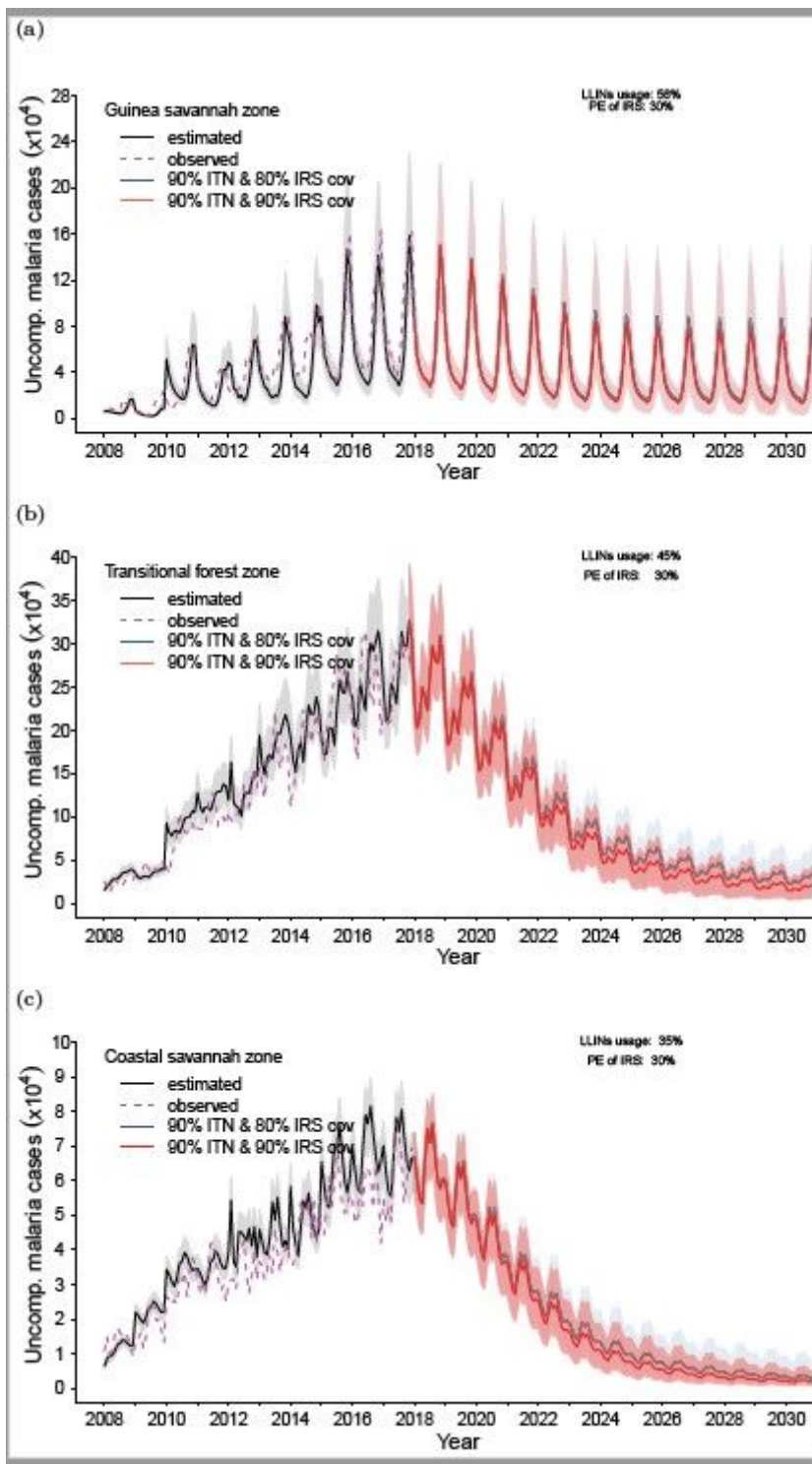


Figure 9

Impact of attaining a combination of various levels of LLINs and IRS coverage within 3 and 5 year implementation programme respectively at baseline Protective Efficacy (PE) of IRS (30%) and LLINs (40%) and LLIN usage in the (a) Guinea savannah, (b) Transitional forest and (c) Coastal savannah.

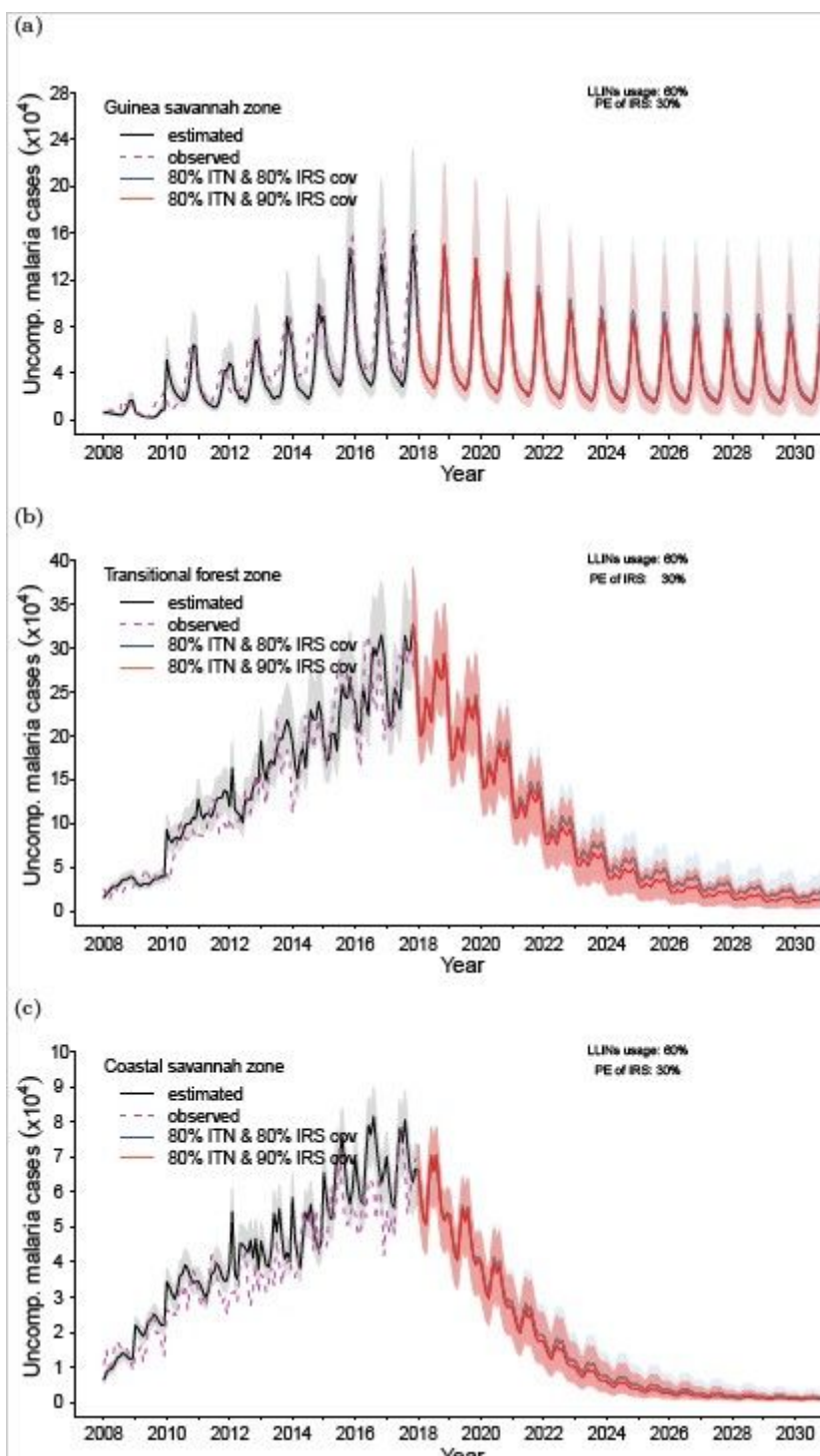


Figure 10

Impact of attaining a combination of various levels of LLINs and IRS coverage within 3 and 5 year implementation programme respectively at baseline Protective Efficacy (PE) of IRS (30%) and elevated level of LLINs (60%) usage in the (a) Guinea savannah, (b) Transitional forest and (c) Coastal savannah

Supplementary Files

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