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Original Article

Reductions in malaria cases after deployment of dual-active ingredient insecticide-treated nets in Ghana—a Bayesian interrupted time series analysis

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Abstract

Background: **Insecticide-treated nets (ITNs) represent a key tool in reducing human vector contact for malaria control. However, increasing insecticide resistance of malaria vectors threatens the effectiveness of pyrethroid-only nets in reducing malaria risk. Next-generation nets, such as those with dual-active ingredients, have been recommended for use in areas with high malaria burden and confirmed pyrethroid resistance. Here, we assessed the impact of the distribution of Interceptor® G2 (IG2) ITNs on malaria cases in the Western North Region of Ghana distributed in 2021.**

Methods: **We analysed monthly numbers of confirmed malaria cases reported by health facilities in the Western North Region from 2018 to 2023. To control for possible confounding effects of climate, monthly mean values of modelled vector habitat suitability and temperature suitability were included. Bayesian Poisson regression time series models were developed to assess the immediate and sustained impact of IG2 ITNs on malaria case trends measured as odds ratio (OR) with their corresponding credible intervals (CrI).**

Results: **Malaria cases reduced by 30% (OR, 0.696; CrI, 0.623–0.778) immediately after the distribution of IG2 ITNs in the Western North Region. This effect was sustained at 6 months up to 30 months post-intervention, where cases reduced by 26% (OR, 0.739; CrI, 0.653–0.837) and 40% (OR, 0.594; CrI, 0.492–0.718), respectively. The intervention was also strongly associated with reductions in malaria cases in seven of the nine districts in the region, after controlling for climatic factors.**

Conclusion: **This study demonstrates the effectiveness of dual-active Interceptor® G2 ITNs in the Western North Region, an area with confirmed pyrethroid resistance. The findings support the scale-up of next-generation nets by National Malaria Programs and highlight the need for further research to explore the utility of these nets in other high-burden malaria areas with region-specific insecticide resistance profiles.**

Keywords next-generation nets, dual active ingredient, insecticide resistance, malaria cases, Bayesian interrupted time series

Key Messages

- We sought to discover what impact the distribution of Interceptor® G2 insecticide-treated nets has on malaria cases in the Western North Region of Ghana.
- Distribution of Interceptor® G2 ITNs caused immediate and sustained impact on malaria case reduction in the Western North Region.
- Dual-active ingredient insecticide-treated nets are effective in field settings and could be deployed at a large scale.

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Introduction

Insecticide-treated nets (ITNs) and indoor residual spraying are two core vector control interventions recommended by the World Health Organization (WHO) to prevent malaria transmission [1]. Pyrethroids are the preferred insecticides for ITNs [2, 3], but widespread resistance in malaria vectors threatens their efficacy [4]. To mitigate this challenge, next-generation nets treated with piperonyl butoxide combined with pyrethroids, as well as dual-active ingredient nets (pyrethroid-pyriproxyfen and pyrethroid-chlorfenapyr) have been introduced to boost the efficacy of ITNs against resistant malaria vectors [5]. Dual active ingredient nets, since their introduction, have averted 13 million malaria cases and 24 600 deaths in 17 endemic countries between 2019 and 2022 [6].

Pyrethroid-only ITNs have been distributed in Ghana since 2003 [7]. Four nationwide ITN distribution campaigns (2010, 2014, 2018, and 2021) have been carried out to make nets accessible to all populations at risk of malaria [8]. In the 2021 campaign, a mix of pyrethroid-only, pyrethroid + piperonyl butoxide, and dual-active ingredient nets were distributed, based on the level of malaria burden [9]. The Western North Region, which was part of the Western Region in 2019 [10], with the highest malaria prevalence, was assigned dual-active Interceptor® G2 nets (IG2) active ingredient nets for the 2021 mass ITN distribution [9]. Remarkable reductions in malaria prevalence and cases were documented in 2022, suggesting possible reductions in malaria burden post-intervention [11].

Guided by such insight, we hypothesized that the distribution of IG2 nets contributed to a decrease in malaria cases in the Western North Region. To assess this, we evaluated the impact of IG2 net distribution on clinical malaria cases in the Western North Region of Ghana from 2018 to 2023 by (i) determining the magnitude of decrease in clinical malaria cases immediately after the ITN distribution in the region and (ii) assessing the sustained effect up to 30 months after the intervention.

Methods

Study region

The Western North Region of Ghana was created out of the Western Region and inaugurated in 2019 [12–14]. The region is divided into nine [9] administrative districts (Fig. 1). Malaria control interventions implemented in the region include case management, limited larviciding, distribution of ITNs through routine channels, and periodic mass ITN campaigns (Supplementary Fig. S1) [15]. Insecticide resistance data show high pyrethroid resistance intensity to malaria vector populations in the region.

See Supplementary Methods for details about the study region and Supplementary Table S1 for changes in some malaria indicators before (2019) and after (2022) the distribution of IG2 ITNs in the region in 2021.

Data

We sourced aggregated malaria data from the District Health Information Management System of the Ghana Ministry of Health [16]. The District Health Information Management System is the primary data reporting platform for health facilities rendering clinical and public health services in the country. See Supplementary Methods for further details on the data.

For this study, we extracted data on suspected, tested, and confirmed malaria cases from January 2018 to December 2023 for all nine districts in the region. The primary outcome variable used in the analysis was the number of confirmed malaria cases.

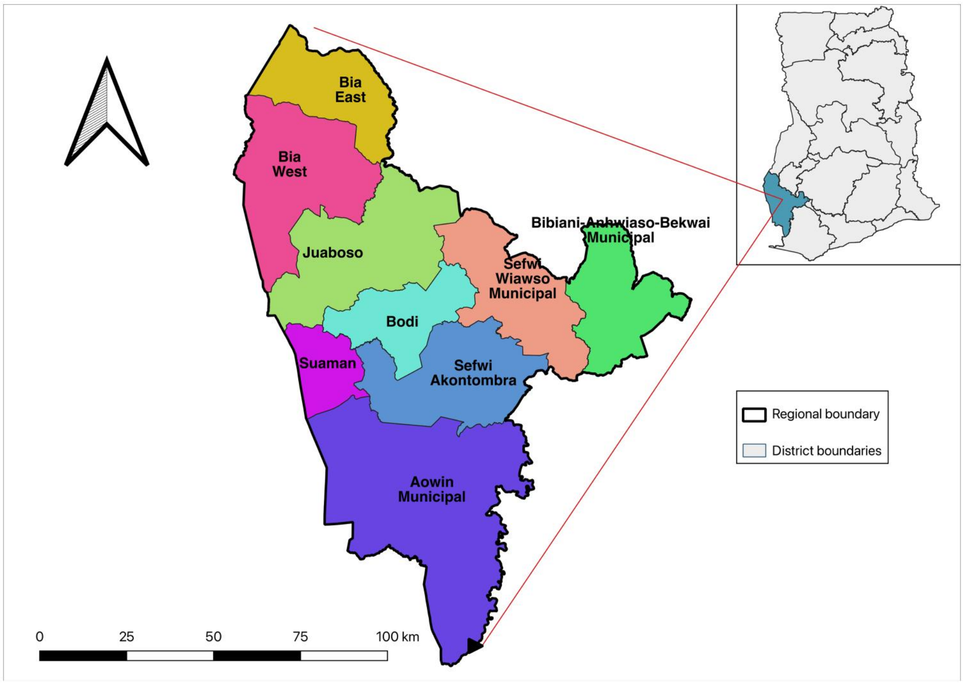


Figure 1 Map of study location.

Intervention—mass ITN distribution campaign

The "intervention" in this study refers to the deployment of dual-active ingredient ITNs (that is, IG2 ITNs) in the Western North Region. In July 2021, approximately 700 000 IG2 ITNs were distributed to approximately 260 000 households in the region (see Supplementary Methods for more information on the distribution). In the subsequent sections of this paper, we use the term "dual-active ingredient" to represent "IG2 nets."

Confounding/potential bias variables

We considered habitat suitability—a proxy for rainfall, and temperature suitability as confounding climatic factors that affect malaria in the region. The Habitat Suitability Index (HSI) assesses the ability of a natural habitat to support the development of an organism [17]. The Temperature Suitability Index (TSI), on the other hand, quantifies the impact of air temperature on mosquito survival and development of sporozoite in the mosquito after it bites an infected person [18]. We extracted the climatic covariates at 5-km resolution for all nine districts in the region from January 2018 to December 2023. The two climatic covariates were standardized using the scale() function in R [19] prior to model fitting. See Supplementary information for details about the covariates considered.

Exploratory analysis

We reviewed the extracted surveillance data for missingness and consistency. We plotted line graphs of suspected, tested and confirmed cases to visualize and identify if any of the following scenarios were present: tested cases greater than (>) suspected cases; confirmed cases > tested cases or suspected cases; treated cases > suspected cases. We also visualized monthly testing rates to examine whether there had been any systematic changes in the testing of suspected cases over the period. Testing rate was defined as

$$\text{Testing rate} = \frac{\text{Suspected cases tested parasitologically (mRDT or microscopy)}}{\text{Suspected malaria cases}}$$

We checked for overdispersion in our data by finding the ratio of the variance of confirmed cases to the mean of confirmed cases. A ratio >1 suggests overdispersion.

Bayesian interrupted time series model

We used the R-INLA package to build Bayesian interrupted time series models, with monthly confirmed malaria cases as the outcome. To find the appropriate model that deals with overdispersion in our data, different candidate models were assessed. The Poisson model with covariates and month as a random effect was selected based on its relatively low Watanabe–Akaike Application Information Criterion (WAIC) value (see Supplementary model comparison).

We built two models to enable us to assess the immediate effect of the intervention differently from the sustained effect of the intervention. In the first model, we included time trend, HSI, and TSI as regression terms. The relationship between the exposure (treatment) and outcome after the intervention was modelled as a "step change" impact: an indicator coded as zero before the exposure and one afterwards.

In the second Bayesian interrupted time series model, the monthly count of confirmed malaria cases was the outcome, with time trend, time-since-treatment—a 6 monthly multi-factor variable for months with five levels, HSI and TSI as explanatory time series. This was to evaluate the magnitude of impact at each time point independently by modelling the changing relationship between the outcome at 6 monthly time points after the intervention as "slope change" impact. Each time point was coded as zero at the time of intervention or after that time point, and one at that time point (see Supplementary BITS Model file for details).

In both models, we included month as a random effect to handle temporal and secular trends and modelled it as independent and identically distributed (iid) to absorb any unexplained variations. We chose priors such that the coefficients of the covariates shrank to zero—a penalized complexity prior was chosen to control for overfitting (see Supplementary Methods). The change in cases due to the intervention is presented as odds ratios (OR) with its corresponding 95% credible intervals (CrI).

Results

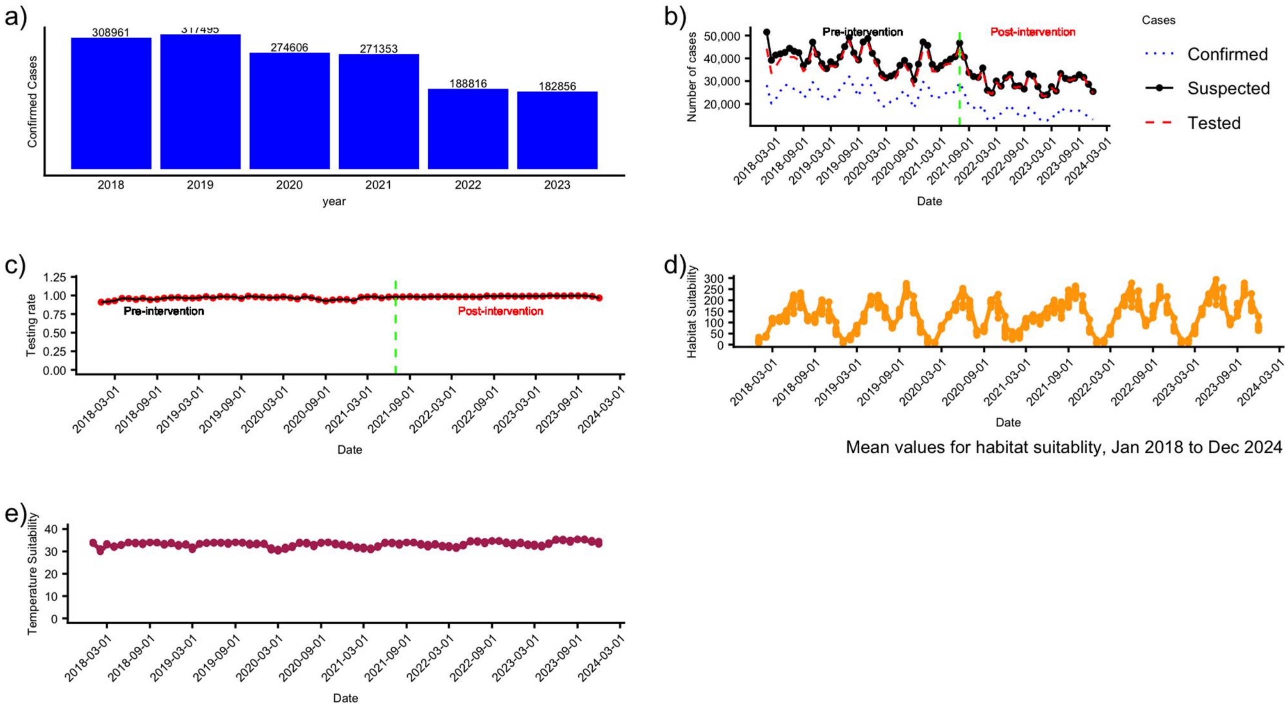
Descriptive analysis

The total number of confirmed cases reported by the region ranged from 308 961 in 2018 to 182 856 in 2023. Confirmed cases reduced slightly from 317 495 in 2019 to 274 606 in 2020 but drastically from 271 353 in 2021 to 188 816 in 2022 (Fig. 2a). There was a remarkable reduction in the monthly number of suspected malaria cases and number of confirmed cases after the intervention, with almost all suspected cases receiving a parasitological test (Fig. 2b). Testing rates increased from 90% in January 2018 to almost 100% during the periods dual active ingredient nets were deployed (Fig. 2c). The time series trends of habitat suitability and temperature suitability show profound variations in monthly estimates of habitat suitability, while estimates for temperature suitability were stable over time (Fig. 2d and e).

Among the districts, Bibiani–Anhwiaso–Bekwai reported most of the cases in the region, with Bia East reporting the least number of cases (Supplementary Fig. S3). In all districts, there was a reduction in cases in 2022 compared to 2021. The monthly trend of cases shows a reduction after the intervention in all but one (Suaman) of the nine districts in the region (Fig. 3). The highest declines were observed in Juaboso, Bia West, Sefwi–Wiawso, and Bibiani–Anhwiaso–Bekwai districts.

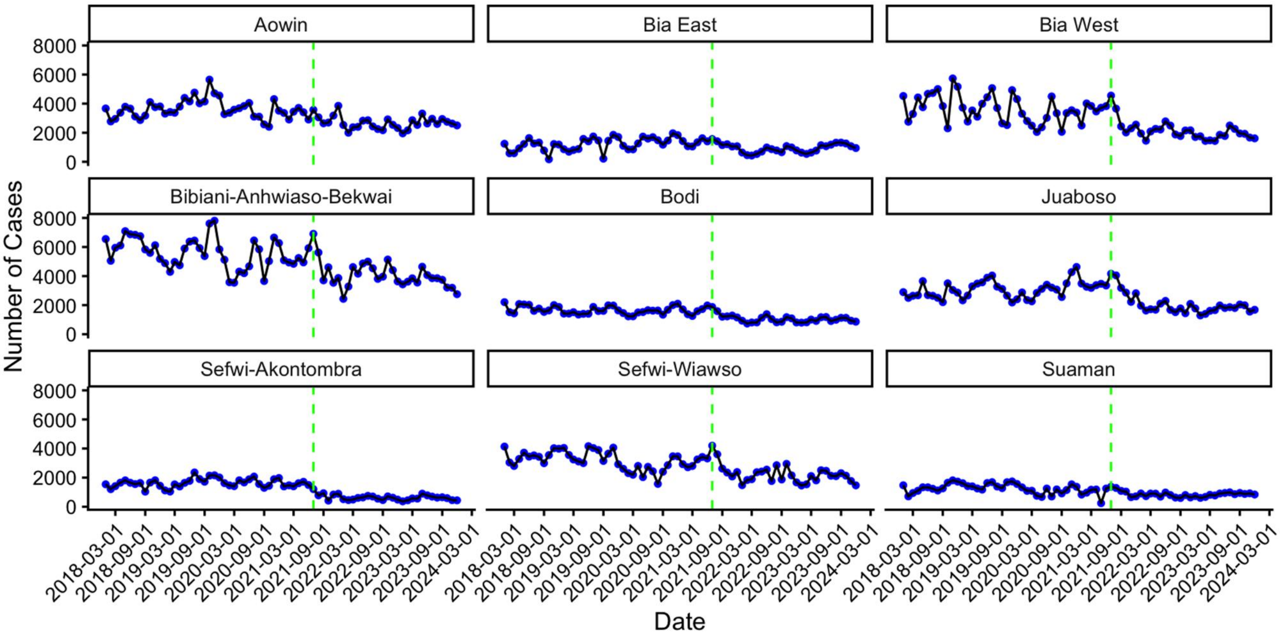
Bayesian interrupted time series model results

The baseline number of confirmed cases (intercept) before the intervention was 26 950 (Table 1). The intervention was associated with an immediate reduction of confirmed malaria cases by 30% (OR, 0.696; CrI, 0.623–0.778). The time parameter, which



Mean values for habitat suitablity, Jan 2018 to Dec 2024

Figure 2 Trend of annual (a) and monthly (b) malaria cases, testing rates (c) and monthly covariate values (d, e).



Confirmed Malaria Cases from Jan 2018 to Dec 2024, by District in Western North

Figure 3 Trends of malaria cases by districts.

signifies the underlying trend or pattern of cases before the intervention, showed no influence on the change. The HSI was positively associated with reported confirmed malaria cases (OR, 1.076; CrI, 1.041–1.112), while temperature suitability was not. The small value of the precision relative to the magnitude of the cases indicates less variation in the data within the months.

There were some observed variations in the effect of the intervention in the nine districts in the region (Fig. 4). In seven out of these nine districts, the intervention was associated with a reduction in malaria cases.

The greatest effect was observed in the Sefwi–Akontombra district, where there was a 61% (OR, 0.39; CrI, 0.33, 0.47) reduction in the number of confirmed cases immediately after the intervention. Bia East, Juaboso, and Bodi districts showed reductions of 49%, 38%, and 32%, respectively. The intervention was further associated with 27%, 22%, and 17% reductions in malaria cases in Bia West, Aowin, and Bibiani–Anhwiaso–Bekwai districts, respectively. However, in the Sefwi–Wiawso and Suaman districts, no associated reduction in malaria cases was observed. At district levels, habitat suitability was positively associated with confirmed malaria cases in four districts, while temperature suitability was negatively associated with confirmed malaria cases in five districts, respectively (see Supplementary Table S3).

In assessing the potential sustained effect of the intervention, we found a reduction in malaria cases up to 30 months after the intervention (Table 2). While the reduction in cases was estimated as 26% when deployed 6 months after the intervention (OR, 0.739; CrI, 0.653–0.837), there was an associated 34% (OR, 0.660; CrI, 0.578–0.755), 39% (OR, 0.607; CrI, 0.521–0.708), 37% (OR, 0.628; CrI, 0.534–0.738) and 40% (OR, 0.594; CrI, 0.492–0.718) reduction in confirmed cases at 12, 18, 24, and 30 months after the intervention, respectively. Habitat suitability was, again, associated with a 7% (OR, 1.066; CrI, 1.032–1.102) increase in malaria cases in the region.

The relationship between the observed and simulated trend of confirmed cases for the region is shown in Fig. 5. We observed a slight declining trend in monthly confirmed malaria cases

Table 1 Results of Bayesian interrupted time series model of the effect of the intervention accounting for effects of exogenous variables.

Parameter	Posterior mean odds ratio (OR)	95% lower credible interval (LCrI)	95% upper credible interval (UCrI)
Baseline	26 949.760	25 162.354	28 864.126
Time	0.997	0.994	0.999
Intervention	0.696	0.623	0.778
Habitat	1.076	1.041	1.112
Temperature	1.023	0.989	1.059
Random field	68.555	47.319	93.691

Baseline parameter denotes the average number of cases prior to the intervention. Time parameter is the underlining trend of cases prior to the intervention. The intervention is the time when the ITNs were deployed whiles habitat suitability and temperature suitability are the environmental covariates associated with malaria in the region. Precision values explain the level of variation in the monthly data.

Table 2 Results of Bayesian model analysis assessing the sustained effect of the intervention months after the distribution.

Parameter	Mean (OR)	LCrI	UCrI
Baseline	25 938.730	24 136.057	27 876.009
Time	0.999	0.996	1.002
6 months	0.739	0.653	0.837
12 months	0.660	0.578	0.755
18 months	0.607	0.521	0.708
24 months	0.628	0.534	0.738
30 months	0.594	0.492	0.718
Habitat	1.066	1.032	1.102
Temperature	1.041	1.004	1.080
Random field	74.292	50.623	102.475

Baseline parameter denotes the average number of cases prior to the intervention. Time parameter is the underlining trend of cases prior to the intervention. The parameters 6, 12, 18, 24, and 30 months are 6 monthly time points after the intervention was deployed while precision explains the level of variation in the monthly data.

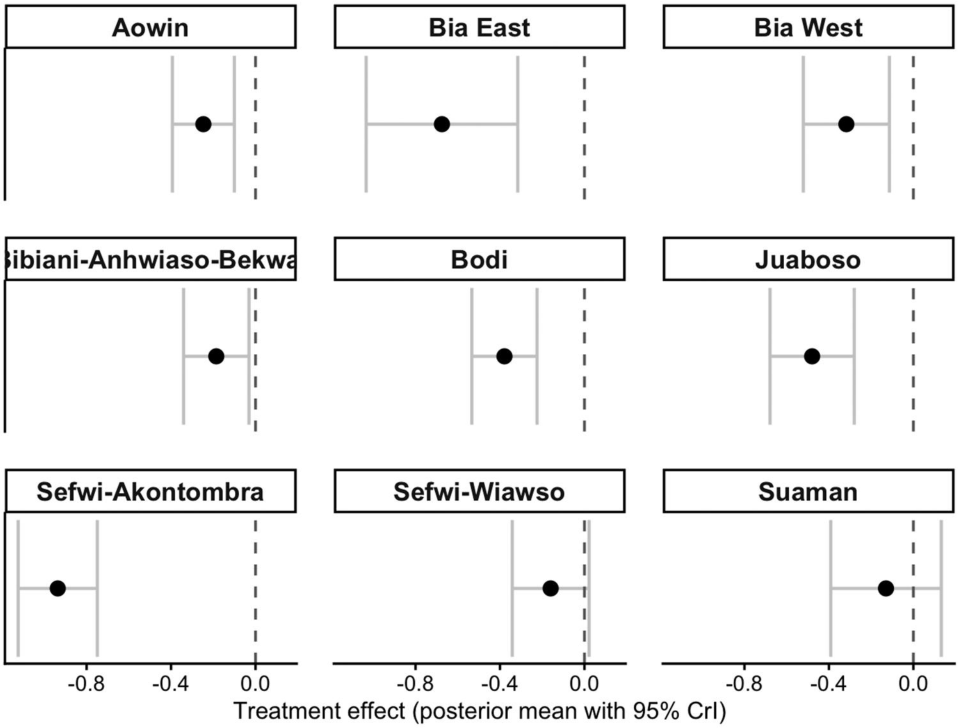


Figure 4 Effect of intervention of malaria cases in all the nine Districts of Western North.

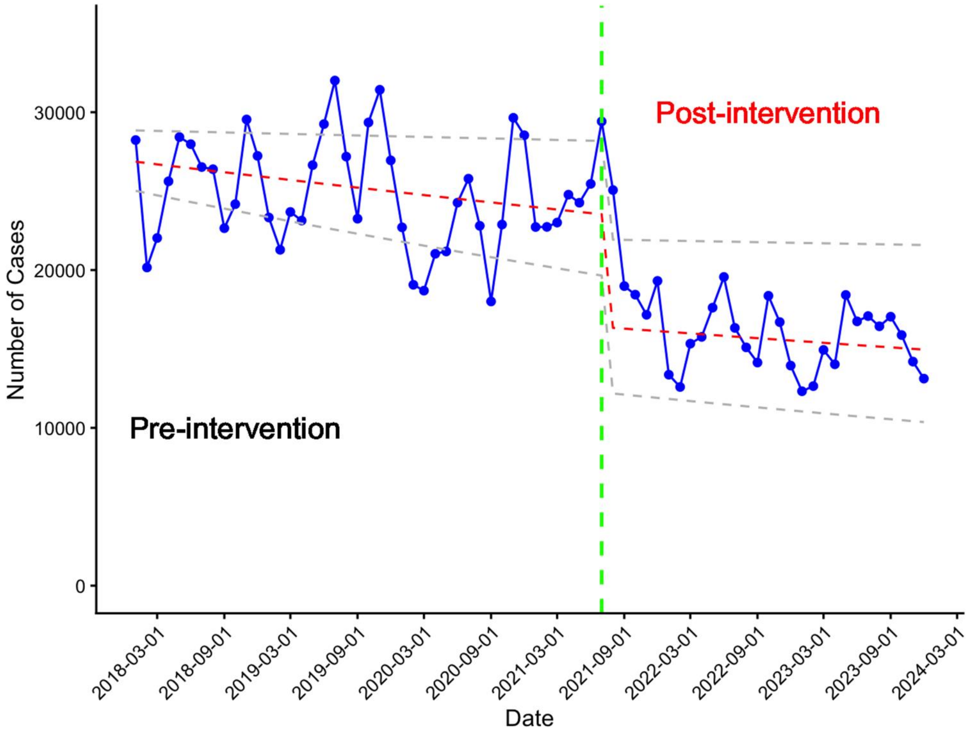


Figure 5 Observed and simulated trends of confirmed malaria cases.

before the intervention and a drastic step change in the trend post-intervention with corresponding 95% CrIs.

The intervention resulted in a steep level change in the trend of confirmed malaria cases in the region.

Discussion

This work has explored the changes in reported confirmed malaria cases following the mass deployment of dual active ingredient ITNs (IG2 ITNs) to households in the Western North Region of Ghana. We conducted the analysis using a Bayesian interrupted time series approach that allows for easy inclusion of covariates and generates the levels of uncertainties around our estimates of the effect of the intervention on confirmed malaria cases in the study area. We were also able to estimate the impact the intervention had on confirmed cases up to 30 months after deployment.

We observed a slight increase in the number of confirmed malaria cases between 2018 and 2019 although a mass ITN campaign was conducted in 2018, where standard pyrethroid-only nets were distributed. However, a reduction of 82 537 cases was observed between 2021 and 2022 when dual-active ingredient ITNs were distributed (Fig. 2a). This suggests that dual-active ingredient ITNs had a much more pronounced effect on malaria cases in the region than the preceding standard ITNs. The high, stable trend in testing rates in the region indicates that confirmed cases were not affected by changes in diagnostic practices of clinicians in the region (Fig. 2c). The reductions in the number of suspected malaria cases after the intervention also suggest that malaria is a major cause of febrile illness in the region (Fig. 2b). This assertion is supported by results of the 2019 Malaria Indicator Survey and the 2022 Ghana Demographic and Health Survey, where the prevalence of fever among children <5 years was found to have reduced from 40.4% in the then Western region to 12.3% and 14.3% in the Western and Western North Regions, respectively (Supplementary Table S1) [10, 11]. Nationally, the prevalence of fever from all causes reduced from 29.6% in 2019 to 15.1% in 2022. The declines in the number of cases between 2019 and 2020, as shown in the time series plot (Fig. 2b) and the exploratory plot (Fig. 2a), can be attributed to COVID-19 pandemic disruptions in the health system. This trend was observed in most health systems across the country, as reported in previous studies [20, 21]. However, cases surged in 2021 as COVID-19 cases declined and structures within the health system recovered from the disruptions (Fig. 2b).

Our results suggest that the intervention reduced confirmed malaria cases by 30% immediately after deployment after adjusting for the effect of climatic factors (Table 1). In acknowledging the lack of a control group and other unmeasured confounding effects, we included the time parameter and month as iid as proposed by Batomen, B. *et al.* (2024) [22]. The non-significance of the trend parameter (time) in the model suggests that the 30% reduction was associated with the intervention and was not influenced by other underlying interventions in the region. In Ghana, ITN usage has been found to reduce deaths from malaria in children under 5 years, where the under-five mortality rate was found to be 18% lower among users compared with non-users [23]. The use of ITNs in areas with high insecticide resistance to pyrethroids has also been found to be associated with a reduction in clinical incidence and infection prevalence [24]. This assertion may, however, be in contrast to a study in Ghana where malaria infection prevalence was reported to be relatively higher among ITN users compared with non-users [25]. Although evidence to date has not consistently demonstrated an association between level of insecticide resistance and malaria incidence or prevalence, there is credible evidence to suggest that dual active ingredient nets have a greater killing effect on *Anopheles gambiae* than pyrethroid-only nets [26]. Guided by this insight, we conclude that the observed reductions were due to the distribution of the dual active ingredient nets, and the same effect would not have been achieved if standard pyrethroid-only nets were distributed.

The varied effectiveness of IG2 ITNs observed across the different districts likely reflects a combination of entomological, epidemiological, and biochemical as well as anthropological factors. While the intervention led to significant reductions in malaria cases in seven of the nine districts, no associated impact was detected in Sefwi–Wiawso and Suaman. Differences in baseline malaria burden may explain the varying impact of dual active ingredient ITNs across districts. Indeed, malaria risk is understood to be generally lower in urban areas [27, 28], and this perceived risk may reduce net use as reported in other studies [29], potentially contributing to the limited impact observed in Sefwi-Wiaso, for example. The intradistrict difference in the impact of the intervention may need to be investigated in future studies.

Different levels of positive association were observed between habitat suitability and malaria cases at the regional level and in three districts, while temperature suitability was negatively associated with confirmed malaria cases in five districts. The reasons accounting for these phenomena are outside the objectives of this study.

Results of the second model to assess the sustained effect of IG2 ITNs on malaria cases showed a consistent decline in malaria cases over the five periods (Table 2). Confirmed malaria cases reduced by 26% 6 months after deployment and 40% 30 months after. Some studies have reported a 35% reduction in malaria incidence between clusters that received dual-active ingredient ITNs and piperonyl butoxide and a 33% reduction among clusters that received dual active ingredient ITNs compared with their pyrethroid-only counterparts, 2 years post-intervention [30]. Typically, ITNs are intended to last 3 years, but factors such as frequency of washing and handling can reduce their durability and potency [31]. To the best of our knowledge, there is currently no published peer-reviewed study that evaluates the effectiveness of dual-active ingredient nets on malaria risk throughout the lifespan of the nets. Though Mosha, JF. *et al.* (2022) reported that the insecticide effects of dual-active ingredient nets continue to be effective after 24 months [32], other studies suggest the median useful life of dual active ingredient nets to be 2.6 years. Therefore, our results indicate that dual active ingredient ITNs could offer protection to the population throughout the lifespan of the net.

There are limitations to our current study and findings. Our study has been designed to identify the impact of the dual-active ingredient bednet distribution, and, accordingly, our findings are contingent on being able to account for the possible effects of other factors on reported malaria incidence. While some, such as climatic factors, were able to be included explicitly in the analysis, others could not be. These included (i) potential changes to health provider practices (e.g. due to training or supervision); (ii) changes to health-seeking behaviour, including use of informal facilities and not reporting to the District Health Information System; and (iii) changes in ITN use, in response to perceived effectiveness of new nets as well as other unmeasured confounders. We do not anticipate that the possible magnitude or timing of any such factors would confound the dual active ingredient impacts, considering the fact that such factors cause gradual changes and not sudden ones, as identified via the interrupted time series analysis.

This study suggested that dual active ingredient ITNs remain effective up to 30 months after distribution. Future work could extend this analysis, such as through a comparative study in similar areas that received other types of ITNs and accounting for some of the factors identified in our limitations. This would improve our understanding of the effects of these nets on malaria cases under uncontrolled settings. The findings of such a future study will enhance decision making process of National Malaria Programs on where to deploy which type of nets. For the Ghana National Malaria Elimination Programme in particular, the findings of this work may support decisions in expanding dual-active ingredient ITN deployment to areas with a high burden of malaria and confirmed pyrethroid resistance.

Conclusion

This study demonstrated that dual active ingredient nets were effective in reducing malaria cases in the Western North Region of Ghana under non-clinical trial settings. Dual-active IG2 nets could reduce malaria cases by 40%, 30 months after distribution. As the Ghana National Malaria Elimination Program plans to expand dual active ingredient ITNs to other high-burden areas with high insecticide resistance, we anticipate further reductions in malaria risk and success in the program to achieve its goals of reducing malaria incidence and mortality towards malaria elimination in Ghana.

Ethics approval

The data used in this study are anonymized and aggregated, and do not include any personal identifiers. Ethical approval for this project was granted by the Ethics Committee of Curtin University (HRE2021-0734). Permission to use the data was granted by the National Malaria Elimination Program of Ghana.

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Author contributions

S.O., O.O.A., C.A.O., K.L.M., and P.W.G. conceptualized the study. S.O. did the analysis and drafted the manuscript. S.O., P.A., K.A.A., P.W.G., reviewed the analysis and interpreted the data and results. S.C., O.O.A., C.A.O., N.Y.P. contributed to the interpretation of the data and results and edited the manuscript. All authors reviewed and approved the final version of the manuscript.

Supplementary material

Supplementary material is available at *IJE* online.

Conflicts of interest

None declared.

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This work is part of the PhD work of the corresponding author who holds a Higher Degree by Research (HDR) full scholarship from the Curtin University.

Data availability

Data for this study can be provided to interested persons upon formal request to the Program Manager of the National Malaria Elimination Programme and completion of a data request form. Enquiries should be directed to nmep@ghs.gov.gh

Use of artificial intelligence (AI) tools

AI tools were used to refine R codes to add aesthetics to the plots.

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