Evaluating the impact of vector control interventions: Results from the PMI VectorLink Project

BACKGROUND

Remarkable progress in reducing malaria morbidity and mortality has been made over the past two decades, with an estimated 2 billion malaria infections prevented and 11.7 million lives saved.[1] The core vector control interventions—insecticide-treated nets (ITNs) and indoor residual spraying (IRS)—have contributed significantly to this progress and are essential tools in the global effort to end malaria faster. However, progress has stalled worldwide amid a myriad of threats such as widespread resistance to pyrethroid insecticides and emerging resistance to other classes of insecticides among mosquito populations. While both the global malaria case incidence rate and the malaria mortality rate decreased between 2020 and 2021, malaria still caused an estimated 619,00 deaths globally in 2021 with an estimated 247 million cases worldwide.[2] African countries continue to be the hardest hit, accounting for 96 percent of malaria deaths and 95 percent of illnesses.[2]

Delivering insecticide-treated nets in Madagascar.

THE PMI VECTORLINK PROJECT

The U.S. President's Malaria Initiative (PMI) VectorLink Project has worked in 25 countries in Africa as well as Cambodia and Colombia to equip countries to plan and implement safe, cost-effective, and sustainable IRS, ITN, and other life-saving malaria vector control interventions to protect millions of people and reduce the global malaria burden. With the introduction of new vector control products in the context of expanding insecticide resistance, National Malaria Programs (NMPs) increasingly need to make data-driven decisions at the sub-national level. PMI VectorLink, in collaboration with NMPs, prioritized the importance of integrated data analytics, visualization, and evaluation to help inform vector control decisions and strategies. By partnering with NMPs to conduct impact evaluations using routine data, PMI VectorLink generated the localized evidence needed to support these vector control intervention decisions.

Impact Evaluations

Each impact evaluation was designed and tailored for each country, though all aimed to answer the following questions:

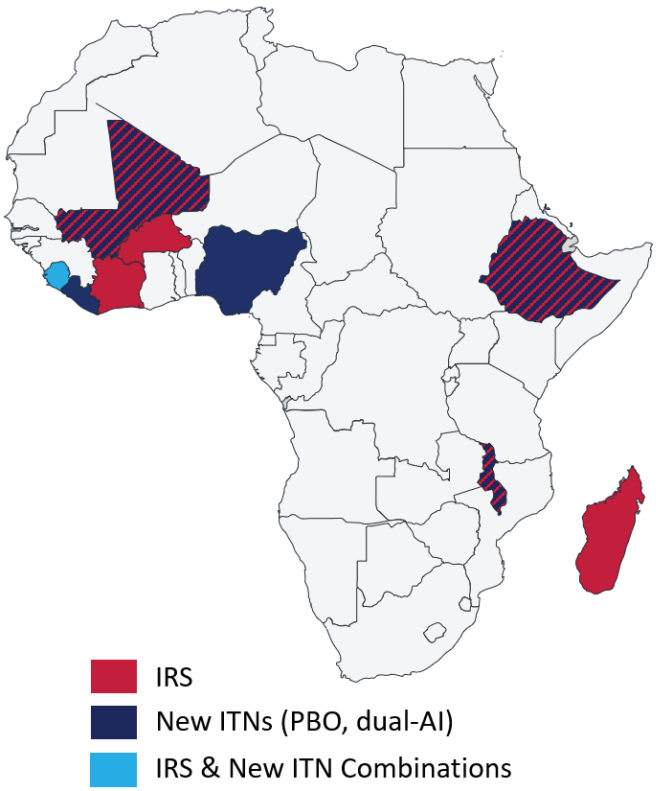
1. What was the **epidemiological impact** of the vector control intervention in the country?
2. When data was available, what was the **entomological impact** of the intervention?
3. How did that **impact compare** to the impact of alternative vector control interventions?

Between 2018 and 2021, PMI VectorLink initiated 12 vector control impact evaluations across 9 countries (Figure 1). Seven of these evaluations were completed while five are still underway and will be completed under PMI Evolve, PMI's new global malaria vector control project.

Leveraging routine data

A critical component for each of these evaluations was the integration and use of routine health systems data, entomological data, and vector control program data. While cluster randomized controlled trials provide the highest quality of evidence for impact, they are costly and provide limited evidence within specific country contexts regarding the impact of new vector control tools, or the combination of tools, to support national and subnational product choice and targeting decisions. With improved availability and quality of routine malaria case data through countries' health management information system (HMIS), as well as increased availability of entomological and vector control program data, there is a greater opportunity to use these data to help address important malaria control questions. Read more about leveraging routine data and methodological considerations for vector control evaluations here.

Figure 1. Countries where PMI is supporting vector control impact interventions



KEY FINDINGS

Results from the seven evaluations completed under PMI VectorLink found the following key takeaways:

- Newer IRS and ITN products with non-pyrethroid insecticides were effective at reducing malaria burden and entomological indicators of malaria transmission in settings of confirmed pyrethroid resistance.
- Dual active ingredient (dual-AI) and piperonyl-butoxide (PBO) ITNs had a greater epidemiological impact compared to standard pyrethroid-only ITNs.
- The impact of IRS may differ significantly by climate-related transmission setting and patterns of ITN use.
- Sustained implementation of IRS over multiple years and higher levels of IRS coverage may provide additional benefits.

EVALUATION FINDINGS BY COUNTRY: IRS IMPACT EVALUATIONS

Burkina Faso: Differential impact of IRS by malaria transmission setting

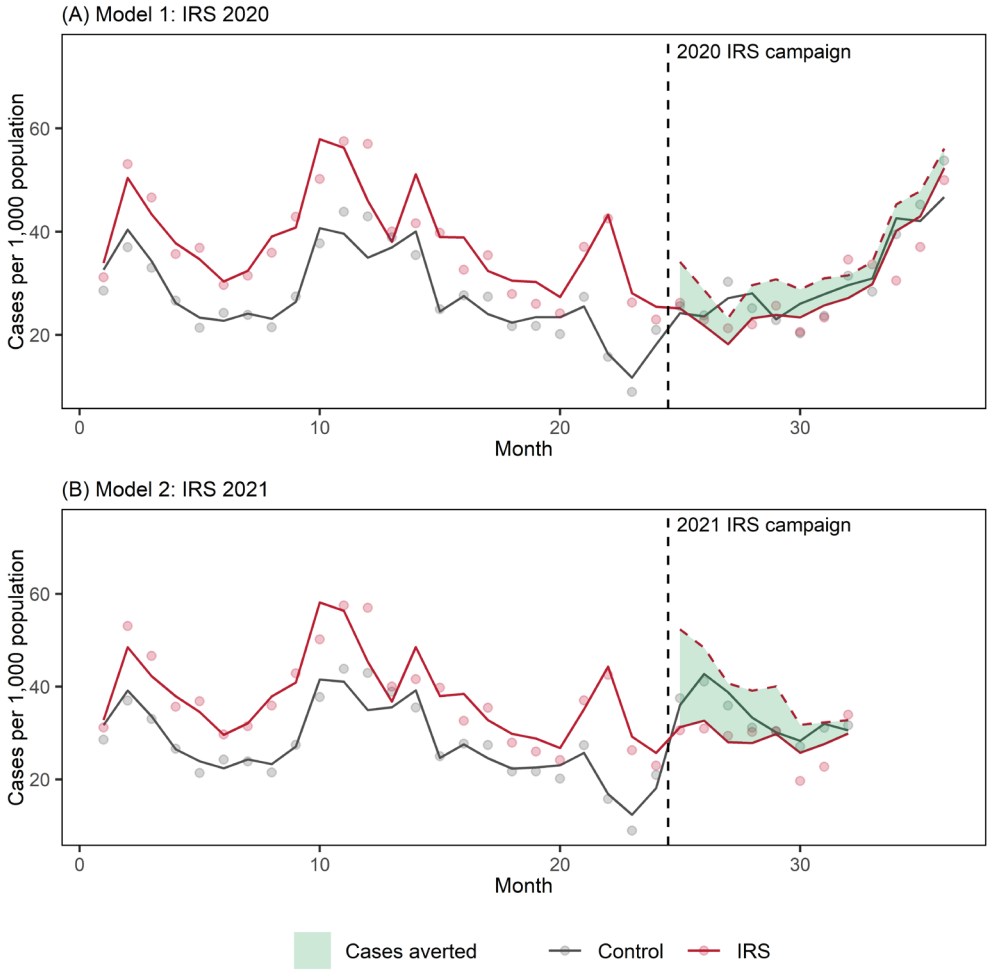
Between 2018 and 2021, PMI VectorLink and the Burkina Faso Permanent Secretary for Malaria Elimination (SP/Palu) implemented IRS with non-pyrethroid insecticides concurrently with annual SMC in two regions. The SP/Palu also implemented a mass ITN campaign of standard pyrethroid nets in 2019 in the same areas. PMI VectorLink used multiple controlled interrupted time series models to detect changes in malaria case incidence rates following IRS campaigns in 2018, 2020, and 2021 compared to the pre-IRS baseline. Analyses found that in Solenzo, a district with a Sudano-Sahelian climate, there was a significant 32% decrease in malaria case incidence after the 2018 IRS campaign compared to control districts, while there was no effect following the 2020 or 2021 IRS campaigns. In Kampti, which has a tropical climate and lower reported ITN use than Solenzo (based on MIS and DHS results),[3,4] malaria incidence rates were significantly lower (between 36-38%) than in the control district following all three IRS campaigns compared to the pre-IRS baseline period.

These findings suggest that the implementation of IRS, in combination with SMC and ITNs, may differ significantly by climate, and may have higher impact in areas with low ITN use.

Côte d'Ivoire: Clothianidin-based IRS associated with reduction in malaria case incidence

PMI VectorLink worked closely with the Côte d'Ivoire Programme National de Lutte contre le Paludisme (PNLP) to implement IRS using clothianidin-based insecticides in two previously unsprayed districts of Côte d'Ivoire in 2020 and 2021, to complement standard pyrethroid ITNs distributed in 2017 and again in 2021. The project used a controlled interrupted time series model to analyze malaria case data abstracted from health facility registers and reported by community health workers (CHWs) after each IRS campaign. Our analyses found that in the 12 months following the 2020 IRS campaign, an estimated 10,709 malaria cases were averted in the IRS districts, representing an overall 15.7% reduction in cases compared to the baseline period (Figure 2). And in the 8 months following the 2021 campaign, 14,056 malaria cases were averted, representing a 11.6% reduction compared to the baseline period.† Standard pyrethroid ITNs distributed in 2021 may have contributed an additive effect to the 2021 IRS campaign, though in the context of pyrethroid resistance the added impact of the ITNs may be limited. This study, among the first to assess the impact of clothianidin-based insecticides, shows the effectiveness of these IRS products in a setting of increasing resistance to the current chemicals used in IRS.

Figure 2. Monthly all-ages confirmed malaria cases per 1,000 population in IRS and non-IRS districts in Côte d'Ivoire



Solid lines represent model estimates, and points represent observed values. The red dashed line indicates estimated malaria cases under a counterfactual scenario of no IRS implementation.

† A full year of data could not be evaluated following the 2021 campaign since the 2022 campaign started earlier than in previous years.

Ethiopia: Higher IRS population coverage associated with lower malaria case incidence

PMI VectorLink conducted an evaluation to measure the impact of non-pyrethroid IRS on malaria burden in the high burden regions of Benishangul-Gumuz and Gambela in Ethiopia between 2015 and 2019. Due to the limited number of control districts that did not receive IRS, this evaluation explored the dose-response relationship between the proportion of population protected by IRS and malaria case incidence. For every ten-percentage-point rise in the population protected by IRS, there was a corresponding decrease of 7.2% in the malaria case incidence rate. These findings suggest that even at the highest levels of population coverage there is an additional incremental benefit of reaching more people with IRS, and programs should aim to achieve the highest level of coverage feasible.

Madagascar: Sustained implementation of IRS over 3 years conferred additional impact

In Madagascar, where IRS and ITNs are cornerstone malaria prevention methods, nine districts received non-pyrethroid IRS from 2017 to 2020, and standard pyrethroid ITNs in 2015 and 2018. PMI VectorLink conducted an analysis using multilevel negative binomial generalized linear models fit to evaluate the overall impact of IRS and sustained exposure of IRS over multiple years. This study found that IRS reduced case incidence by an estimated 30.3% from an estimated 165.8 cases per 1,000 population had no IRS been implemented, to 114.3 in the 12 months after the IRS campaign. When considering multiple years of IRS campaigns, it was found that a third year of IRS reduced malaria cases 30.9% more than a first year and 26.7% more than a second year. This study demonstrated that non-pyrethroid IRS appeared to substantially reduce malaria incidence, and that sustained implementation of IRS over three years conferred additional benefits.

Mali: Differential impact of IRS on all-age and under five malaria case incidence

In 2017, four districts in Mopti Region of Mali began IRS to address the high malaria burden documented in the region. Prior to conducting IRS in these districts, the malaria prevalence in children under five in Mopti was 55% compared to 31% nationally. PMI VectorLink used a difference-in-difference approach to assess the epidemiological impact of three annual IRS campaigns between 2017 and 2019 compared to the baseline year. Analyses controlled for annual changes in precipitation, vegetation, and SMC coverage, as all as for the 2017 ITN mass campaign where standard pyrethroid ITNs were distributed. While there was not a statistically significant decrease in all-age malaria case incidence, sub-analyses assessing the impact of IRS on children under five showed that IRS was associated with a statistically significant 32% decrease in malaria case incidence. There was no observable impact in 2018 and 2019 during the high transmission period. The lack of evidence suggesting an impact in 2018 may be due to the operational challenges experienced during the campaign, including delays due to security risks and disruptions due to higher-than-expected insecticide consumption. While spray coverage (structures sprayed out of structures found) remained high, spray progress (structures sprayed out of structures targeted) and the estimated percentage of the population protected was lower in 2018 compared to other years. There is no clear explanation for the lack of impact observed in 2019.

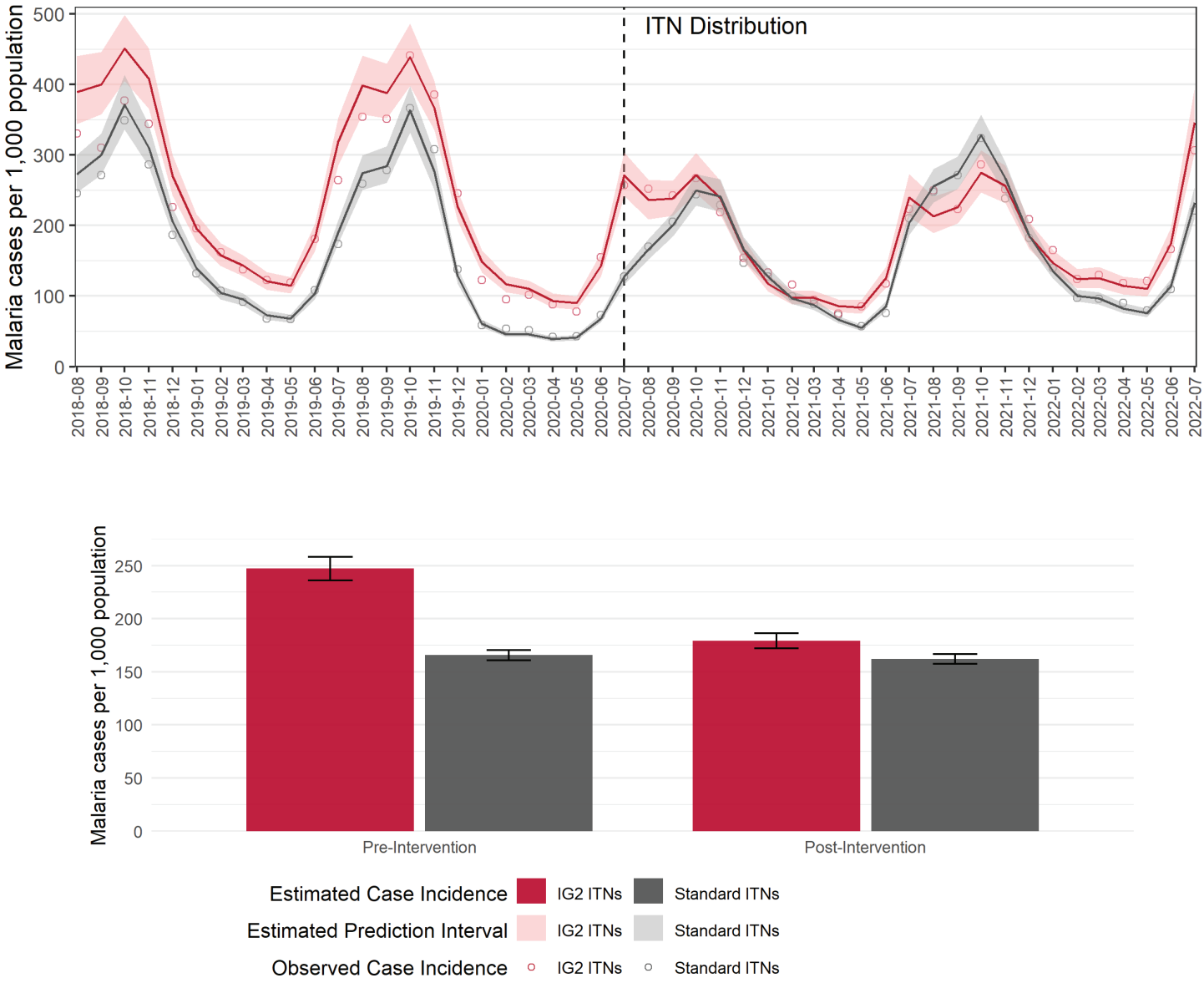
EVALUATION FINDINGS BY COUNTRY: ITN IMPACT EVALUATIONS

Mali: Greater epidemiological impact of dual-AI ITNs compared to standard pyrethroid ITNs

To address growing resistance to pyrethroids among local vector populations in Mali, the NMCP distributed Interceptor® G2 (IG2) ITNs, a new dual-AI ITN containing alpha-cypermethrin and chlorfenapyr, in four districts of Sikasso Region in July 2020. To assess the epidemiological impact of IG2 ITNs compared to standard pyrethroid ITNs, PMI VectorLink used a controlled interrupted time series with comparison model to

evaluate malaria case incidence two years before and two years after the 2020 ITN mass campaign in Sikasso (August 2018 to July 2022). There was a 28% decrease in estimated malaria case incidence among those facilities that received IG2 ITNs compared to a 2% decrease among those facilities that received standard pyrethroid ITNs. The impact was greatest in the first year following the campaign in both groups, while only the IG2 ITN facilities observed a reduction in incidence in the second-year post-campaign (Figure 3). These findings suggest a greater epidemiological impact of IG2 ITNs compared to standard pyrethroid ITNs in an area of moderate to high intensity pyrethroid resistance. However, additional research is needed on a potential waning efficacy of these nets that may hinder further impact.

Figure 3. Modeled malaria case incidence by intervention in Mali, August 2018-July 2022



Nigeria: PBO ITNs associated with reduction in epidemiological and entomological outcomes

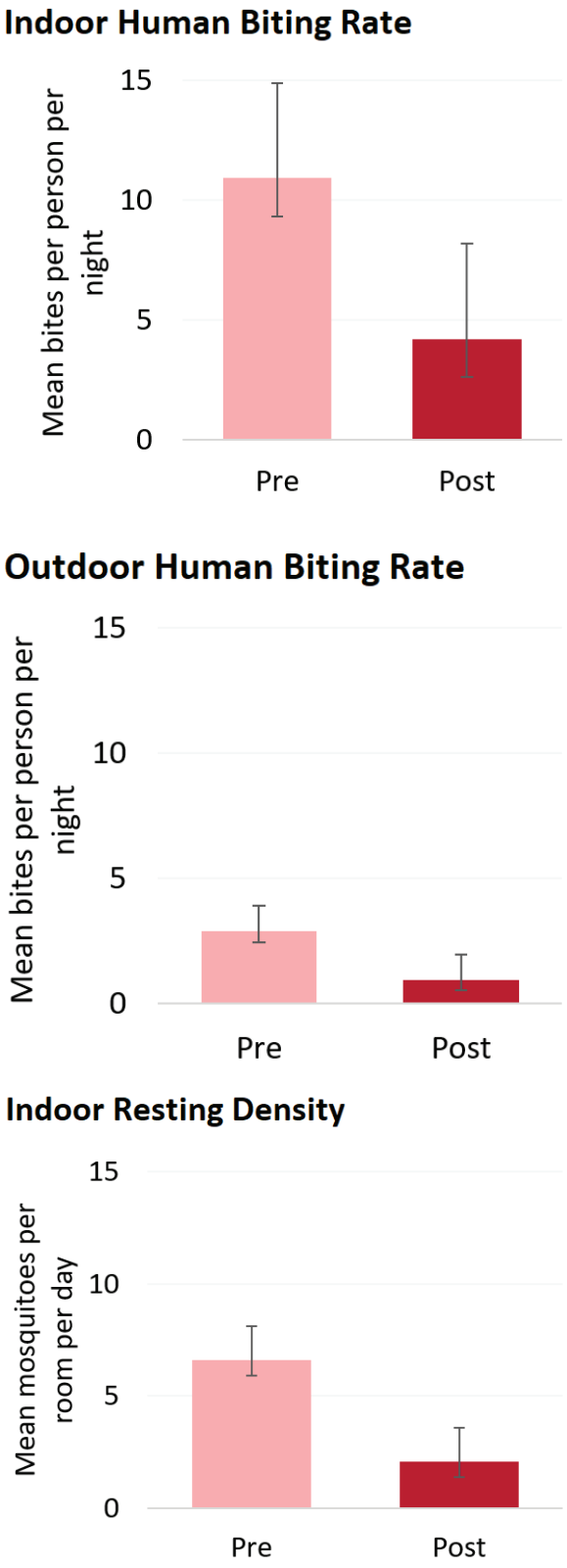
Based on entomological data showing high intensity resistance to pyrethroids in Ebonyi State, the Nigeria National Malaria Elimination Programme distributed PBO ITNs for the first time in Ebonyi in November 2019. An interrupted time series with comparison model was used to evaluate the epidemiological impact of this new type of net and compared this impact to neighboring Cross River State, where standard pyrethroid ITNs were distributed in the same year. A pre/post analysis using two negative binomial models was also conducted to evaluate the entomological impact in Ebonyi only, as entomological monitoring was not done in Cross River. In Ebonyi, PBO ITNs were associated with a 46.7% decrease in malaria case incidence in the two years after the PBO ITNs were distributed compared to if there had been no ITN distribution. In Cross River, there was a significant 28.6% increase in incidence. Additionally, in Ebonyi, the human biting rate was 72% lower and indoor resting density was 73% lower after the PBO ITNs were distributed (Figure 4), underscoring the impact of PBO ITNs in areas where PBO is able to restore susceptibility to pyrethroids.

CONCLUSION

These findings from the evaluations conducted by the PMI VectorLink Project in collaboration with NMPs found a positive impact of the vector control interventions implemented in multiple countries. These results suggested (1) new types of IRS and ITN products, which use active ingredients other than pyrethroids, were effective at reducing malaria burden and entomological indicators; (2) these newer products were effective in settings of confirmed pyrethroid resistance; and (3) new ITNs, such as dual-AI and PBO ITNs, had a greater epidemiological impact compared to standard pyrethroid ITNs.

Randomized controlled trials remain the gold standard for providing high quality evidence of intervention effectiveness; however, these trials are costly and are often completed in only a few countries. These observational evaluations demonstrate that well-designed quasi-experimental evaluations that leverage routine epidemiological, entomological, and programmatic data sources can further our understanding of vector control in different malaria transmission settings. When conducting observational evaluations, evaluators should look for natural 'experiments'—interventions that have a clear before and after period and a comparison group that is similar to the intervention group before the intervention. Evaluators

Figure 4. Directly observed indoor and outdoor human biting rates and indoor resting density in Ebonyi State, June-October 2019 and June-October 2020



should also assess the completeness and quality of the data before conducting the evaluation, to ensure that quality data sources are available. Finally, analysts should increase the potential for evaluation findings to inform decision-making by collaborating with decision-makers early on and throughout the evaluation process. This can be accomplished through co-designing and co-implementing evaluations with key stakeholders, facilitating ongoing discussions throughout the evaluation, documenting how and when evaluation results will be used to guide policy, and effectively communicating the results to target audiences.

As challenges continue to emerge and new vector control interventions are developed, continuing to evaluate the epidemiological and entomological impact of these interventions will be critical. Five of the evaluations initiated under PMI VectorLink are ongoing and will be completed under PMI Evolve (Table 1). These studies will continue to advance our knowledge on the impact of different vector control tools. Known evidence gaps that should be considered for future evaluations include:

- What is the epidemiological and entomological impact of complementary vector control tools, such as larval source management (LSM)?
- What combinations of vector control tools are most effective in reducing malaria burden? And is there a differential impact of these combinations between high burden, low burden, and pre-elimination settings?
- Which interventions or combinations of interventions are the most cost-effective?

PMI Evolve aims to strengthen the capacity of local institutions to conduct future impact evaluations, building on the lessons learned from PMI VectorLink. The project will continue to work closely with NMPs to identify opportunities to answer these critical questions and highlight findings for the global community. These findings will be crucial to helping NMPs, PMI, the Global Fund, and other key stakeholders make strategic programming decisions and effectively target interventions sub-nationally to ensure effective and equitable malaria services in the long term.

Table 1. PMI VectorLink and PMI Evolve Evaluation Portfolio

Country	Evaluation Focus	Completion Date
Burkina Faso	IRS (2018-2021)	2022
Côte d'Ivoire	IRS (2020-2021)	2022
Ethiopia	IRS (2015-2019)	2020
	IRS + Standard ITNs vs. PBO ITNs (2021)	Early 2024*
Liberia	IG2 ITNs (2021)	Early 2024*
Madagascar	IRS (2017-2020)	2021
Malawi	IRS vs. IG2, RG, & PBO ITNs (2021)	Mid 2024*
Mali	IRS (2017-2019)	2020
	IG2 ITNs vs. Standard ITNs (2020)	2022
Nigeria	PBO ITNs vs. Standard ITNs (2019)	2022
	IG2 ITNs vs. PBO ITNs (2022)	Late 2025*
Sierra Leone	IRS + PBO ITNs vs. PBO ITNs (2021)	Early 2024*

**Evaluation is ongoing and will be completed under PMI Evolve*

Abbreviations: IRS, indoor residual spraying; PBO, piperonyl butoxide; IG2, Interceptor® G2; RG, Royal Guard; ITNs, insecticide-treated nets.

An IRS spray operator working in Ethiopia.

ADDITIONAL RESOURCES

- **Journal Article:**
  - Burnett, SM (2023). Process and methodological considerations for observational analyses of vector control interventions in sub-Saharan Africa using routine malaria data. *The American Journal of Tropical Medicine and Hygiene*.
  - Hilton, ER (2023). Using routine health data to evaluate the impact of indoor residual spraying on malaria transmission in Madagascar. *BMJ Global Health*.
- **PMI Technical Document:** Vector Control Integrated Data Analytics & Visualization: Best Practices Guide (English, French)
- **PMI VectorLink Evaluation Case Studies:**
  - Leveraging Routine Data to Drive Targeting of New Vector Control Interventions in Malawi
  - Data-based Vector Control Decision Making in Sikasso Region, Mali
  - Evaluating the Epidemiological and Entomological Impact of Nigeria's First PBO ITN Campaign

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