New Nets Project Interim Results

Output 3: Evidence of effectiveness and cost-effectiveness of dual-AI ITNs created and disseminated

PATH

2201 Westlake Avenue
Suite 200
Seattle, WA 98121 USA

www.path.org

July 2022

Contents

Partners

Funding partners

Supporting partners

Implementation partners

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Evaluation partners

Burkina Faso

The **Centre National de Recherche et de Formation sur le Paludisme** is the lead technical partner in Burkina Faso. It is responsible for all in-country data collection, management, and reporting. The Centre National de Recherche et de Formation sur le Paludisme collaborates with the study partners on development of protocols, analyses, reporting, and dissemination.

Mozambique

In Mozambique, the New Nets Project pilot evaluation is led by the **Programa Nacional de Controlo da Malária** and **Instituto Nacional de Saúde**, with coordination and technical support from **Tropical Health LLP**.

Rwanda

The **Rwanda Biomedical Centre** is the lead in-country technical partner in Rwanda. It is responsible for data collection, management, and reporting activities. The **University of Rwanda** is the coordinating partner. It is providing administrative support for contract implementation and technical support on the entomological and human behavior study components.

Nigeria

The evaluation in Nigeria is led by the **National Malaria Elimination Programme**, with support from **Ibolda Health International** for the epidemiological and human behavior components, the **Nigerian Institute of Medical Research** for the entomological and durability monitoring components, and **Tropical Health LLP** for the durability monitoring component. **PATH** is providing technical support on standard operating procedures, analysis, and study activities with the other New Nets Project pilots.

Global

Imperial College London is the lead technical partner responsible for developing and interpreting mathematical models of insecticide-treated net impact for all pilot countries. The **Liverpool School of Tropical Medicine** led the development of the methodology for the human behavior component. It also is providing analytic support in Burkina Faso and Rwanda. **Tulane University** is leading the cost and cost-effectiveness work across all pilot countries. The **US President's Malaria Initiative** provides general coordination support and is leading durability monitoring activities in Rwanda and Burkina Faso.

Abbreviations

AI	active ingredient
ANC	antenatal care
CDC	US Centers for Disease Control and Prevention
CDCLT	US Centers for Disease Control and Prevention light trap
CI	confidence interval
COVID-19	coronavirus disease 2019
DHIS2	District Health Information Software 2
FGD	focus group discussion
HLC	human landing collection
HMIS	health management information system
IDI	in-depth interview
IG2	Interceptor® G2
IRS	indoor residual spraying
ITN	insecticide-treated net
LGA	local government area
NMCP	national malaria control program
PBO	piperonyl butoxide
PSI	Population Services International
RDT	rapid diagnostic test
RG	Royal Guard®
s.l.	sensu lato
s.s.	sensu stricto
SMC	seasonal malaria chemoprevention
WHO	World Health Organization

Project overview

The widespread emergence of pyrethroid resistance in malaria vectors has prompted the need to develop new technologies to ensure the continued effectiveness of insecticide-treated nets (ITNs) in the fight against malaria. Dual–active ingredient (AI) ITNs represent some of the most promising new tools. However, the number of products currently available are limited, they cost significantly more than pyrethroid-only nets, and the evidence base demonstrating their efficacy and cost-effectiveness is limited.

The New Nets Project partnership was established with the goal of making the latest dual-AI ITN technology more widely available to malaria programs throughout sub-Saharan Africa. In addition to managing the rapid deployment of new nets to partner countries and negotiating a volume guarantee to reduce prices, New Nets Project partners oversee randomized control trials and pilot studies evaluating the efficacy and effectiveness of dual-AI nets. The evidence gathered from these studies will be used to ascertain the impact and cost-effectiveness of dual-AI nets and support an appropriate ITN policy recommendation from the World Health Organization (WHO). The New Nets Project team is also gathering operational learnings in order to optimize future deployment of new nets.

The New Nets Project is cofunded by Unitaid and the Global Fund to Fight AIDS, Tuberculosis and Malaria, with complementary funding provided by the Bill & Melinda Gates Foundation and US Agency for International Development. The project is led by IVCC, which is responsible for the overall management of the project. Other project partners include the Alliance for Malaria Prevention, Imperial College London, Liverpool School of Tropical Medicine, London School of Hygiene & Tropical Medicine, PATH, Population Services International (PSI), and Tulane University. The New Nets Project will not only result in accelerated access to new nets and updated policy recommendations, but it will also provide critical evidence to help guide countries looking for the best value for money in controlling malaria across a range of transmission settings.

New in this report

Burkina Faso

In Year 2 of the evaluation period, overall trends indicating decreased malaria incidence across all study districts, as reported through passive health facility case surveillance, appeared to be broadly in line with the trends observed in Year 1. Additionally, a comparison of trends from new ITN (i.e., Interceptor® G2 [IG2] and piperonyl butoxide [PBO]) districts with trends from the standard ITN districts indicated that the improved gains associated with the new ITN types were maintained two years after ITN distribution. Compared with the standard ITN district, cumulative 2-year reductions in case incidence were 25% greater in the IG2 study district and 16% greater in the PBO study district.

This report includes updates on:

- Monthly malaria incidence data through December 2021 and adjustments of the year-to-year comparison months.
- 12-month physical durability monitoring summary from the US President's Malaria Initiative.

Northern Mozambique

Twelve months after the mass ITN distribution campaign, comparative trends in passive case incidence indicated that IG2 ITNs in Cuamba and Royal Guard® (RG) ITNs in Mandimba had much greater impact compared with standard ITNs in Gurue. Compared with the standard ITN district, reductions in case incidence were 75% greater in the IG2 district and 64% greater in the RG district.

This report includes updates on:

- Monthly malaria incidence data collected from health facilities and community health workers through December 2021.
- Updated entomological data through November 2021.
- 12-month physical durability monitoring summary.

Western Mozambique

Twelve months after the mass ITN distribution campaign, comparative trends in passive case incidence indicated that IG2 ITNs in Guro had greater impact compared to standard ITNs in Chemba, while PBO ITNs in Changara and standard ITNs in Chemba had similar impact. Compared with the standard ITN district, reductions in case incidence were 26% greater in the IG2 district and 2% greater (though this marginal difference is not statistically significant) in the PBO district.

This report includes updates on:

- Monthly malaria incidence data collected from health facilities and community health workers through December 2021.
- Updated entomological data through November 2021.
- 12-month physical durability monitoring summaries.

Rwanda

In Rwanda, the latest cross-sectional survey results continued to indicate very low levels of malaria burden, with no study district showing all-ages prevalence greater than 1.2%. Passive case incidence rates were also lower in the post-ITN mass-campaign period in each study district through Year 1. Compared with the standard ITN district of Nyamagabe, the reductions in incidence were 29% greater in the standard ITNs + indoor residual spraying (IRS) district of Ruhango and 13% greater in the IG2 district of Karongi.

This report includes updates on:

- Monthly routine health management information system (HMIS) data through December 2021.
- Cross-sectional survey results from November 2021.
- Year 1 (March 2020 to March 2021) entomological results.

Nigeria

This report incorporates results from the Year 1 cross-sectional survey, which indicated a decrease in malaria prevalence among children under 5 years old in all local government areas (LGAs). The largest decreases were observed in Asa (IG2 ITNs) and Moro (RG ITNs), which also received seasonal malaria chemoprevention (SMC). Modeling is in progress to estimate the impact of IG2 and RG ITNs in the theoretical absence of SMC. ITN ownership and use increased across all LGAs compared with baseline. Updated monthly incidence, as calculated from routine data from public facilities reporting to the HMIS, showed an increase in incidence across most LGAs in Year 1, with the largest increase in Asa. Antenatal care (ANC)–based surveillance through December 2021 indicated relatively stable prevalence throughout Year 1. The 12-month physical durability monitoring survey (November 2021) showed that over 95% of campaign ITNs in all LGAs were in serviceable condition.

This report includes updates on:

- Results from the Year 1 cross-sectional survey, which was conducted in from November to December 2021, including prevalence.
- Monthly incidence and prevalence data collected from HMIS- and ANC-based surveillance through November 2021 and December 2021, respectively.
- 12-month physical durability monitoring summaries.

For all countries, some revisions have been made to indicator estimates since the previous report with no impact on previous interpretation.

Methods

Overview

This report presents updated preliminary results from observational evaluations of dual-AI ITNs in Burkina Faso, Mozambique, Nigeria and Rwanda. As part of the New Nets Project, limited numbers of dual-AI ITNs were included in several national malaria control program (NMCP)–led ITN mass distribution campaigns on a pilot basis in 2019 and 2020. Evaluations accompanying these pilot distributions are currently measuring the effectiveness of these ITNs compared to standard, pyrethroid-only ITNs, in real-world implementation scenarios. In each country, the evaluations began the year of ITN distribution and will conclude in 2022 (Table 1). Districts were selected for inclusion in the study based on baseline comparability and whether they received dual-AI ITNs, standard pyrethroid-only ITNs, PBO ITNs, or standard ITNs and IRS. The new dual-AI ITNs in the evaluation were the IG2 ITN (alphacypermethrin and chlorfenapyr) manufactured by BASF and the RG ITNs (alphacypermethrin and pyriproxyfen) manufactured by Disease Control Technologies.

Decisions on the brand/type of ITN to distribute and where to distribute them were made by partner NMCPs through consultation with partner institutions and international donors. The NMCPs in Burkina Faso and Rwanda incorporated IG2 into their mass distribution campaigns in 2019 and 2020, respectively. The NMCPs in Mozambique and Nigeria incorporated both IG2 and RG ITNs into their 2020 mass campaigns. Burkina Faso, Mozambique, and Nigeria also incorporated ITNs that contain PBO, an insecticide synergist, in addition to a pyrethroid into their mass campaigns.

A subset of districts that received IG2, RG, PBO, and standard ITNs were selected as study districts. In Rwanda, the districts that received PBO nets were not comparable to those that received IG2 ITNs or standard ITNs; thus, they were not included in the evaluations. Other malaria control interventions, such as SMC or IRS, in the selected study districts will be accounted for in future multivariate analyses.

Table 1. Overview of observational studies.

	Study time period	**ITNs evaluated**	**ITN distribution completed**
Burkina Faso	2019–2022	IG2, PBO	June 2019 (PBO) August 2019 (standard) October 2019 (IG2)
Northern Mozambique	2020–2022	IG2, RG	November 2020
Western Mozambique	2020–2022	IG2, PBO	December 2020
Rwanda	2020–2022	IG2	February 2020 (standard) June 2020 (IG2)
Nigeria	2020–2022	IG2, RG, PBO	November 2020

Abbreviations: IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide; RG, Royal Guard.

This interim report on preliminary evaluation outcomes is organized by country, with two distinct evaluations occurring in Mozambique—one in western Mozambique representing a more southern-Africa context and one in northeast Mozambique representing a more eastern-Africa context. Due to country-specific factors, the timing of the data collection, management, and analysis varies. As this is a preliminary report and evaluations are ongoing, no definitive or final conclusions can be drawn from these pilots at this time.

Epidemiology

Cross-sectional surveys were conducted prior to or during ITN distribution for the baseline year and then annually thereafter for Year 1 and Year 2. During each survey, participants were asked a series of malaria-related questions through a household survey and at least one household resident was tested for malaria by conventional rapid diagnostic test (RDT). In each setting, RDT-positive individuals were provided treatment according to the national malaria program treatment guidelines.

Routine health system data. Passive case surveillance data were collected from routine health information systems, with additional support for data quality assurance provided where needed. In addition, at participating ANC clinics in Nigeria, data on malaria prevalence from RDT results, net use, and care seeking were recorded for women attending their first ANC visit. Routine data were used to calculate malaria case incidence rates. Routine data also will be used to estimate comparative case rate ratios and dual-AI ITN incremental cost-effectiveness ratios.

Entomology

The entomology outcomes included vector species composition, population densities, biting behavior patterns, estimated entomological inoculation rates, and insecticide-resistance profiles. While methods and approaches varied across evaluation countries, a core set of surveillance tools were used to understand the entomological impact of different ITNs. These tools included US Centers for Disease Control and Prevention (CDC) light traps, human landing collection (HLC), larval sampling for insecticide-resistance monitoring, and pyrethrum spray resting catches in Nigeria.

US Centers for Disease Control and Prevention light traps (CDCLTs) were used to monitor indoor and, in Nigeria, outdoor host-seeking *Anopheles* mosquito densities. In each participating household, traps were hung at the foot of one sleeping space where the sleepers were protected by a bednet. Traps were hung approximately one hour before sunset and operated until one hour after sunrise, following standard WHO vector-surveillance procedures [1].

HLCs were used to assess vector biting rates and to estimate malaria transmission by entomological inoculation rates [1]. Paired collectors conducted HLCs, with one collector seated indoors within five meters of the entrance to the home and one collector seated outdoors in the peridomestic environment. Nightly HLCs occurred over 12 hours—approximately 1 hour before sunset until approximately 1 hour after sunrise—with paired collectors alternating locations every 2 hours for two consecutive nights. In Nigeria, indoor human-baited CDCLT collections were paired with similar outdoor human-baited CDCLT collections in lieu of HLCs. Also, in Nigeria, pyrethrum spray catches were used in the morning to collect indoor resting mosquitoes to supplement indoor entomological inoculation rates and blood-feeding rate estimates.

Species identification and molecular methods for identification and detection of sporozoite infections. All *Anopheles* mosquitoes sampled during CDCLT collections and HLCs were identified morphologically to species group [2]. A subsample underwent molecular analysis by polymerase chain reaction for species identification [3,4].

Sporozoite infection. Standard polymerase chain reaction [5] and serology-based [6] assays were conducted to detect sporozoite infection rates among primary and potential secondary vector species.

Insecticide resistance. Field bioassays used to monitor insecticide resistance in local vector populations included the standard WHO tube test [7] and CDC bottle test procedures [8]. Polymerase chain reaction was also used to assess knockdown resistance [9] and ace-1 mutation frequencies [1], as appropriate. Larval sampling for *An. gambiae* s.l. test populations, following WHO Global Malaria Programme recommendations [10], was conducted in each district during peak densities to assist in insecticide-resistance monitoring. Field (wild) populations of *An. funestus* s.l. were collected for resistance testing as adults during resting and/or HLC activities. When considering the effect of PBO pre-exposure on mortality assay results, resistance was “mitigated” if mortality returned to greater than 97% after pre-exposure and “partially mitigated” if mortality rates increased from the standard assay results but did not reach the 97% threshold.

Age grading. A subsample of the vector species was assessed for age using standard parity dissection [10].

Human behavior

The human behavior data collection focused on understanding transmission risk by characterizing when people were at risk (not under an ITN and exposed to biting malaria vectors) and when they were protected (under an ITN). It then explored the drivers behind these behavior patterns.

Structured observation and indirect monitoring. Observations of human activity patterns were conducted in villages by either anthropology or entomology staff. These included quantitative recordings of waking times, daily activities (including travel times), and time spent indoors and outdoors. Structured observations occurred in the same villages as entomological surveillance activities to correlate human and mosquito behaviors. In some contexts, indirect monitoring was used to gather data on time in and out of ITN protection. This included measurement of time spent inside and outside of a net using two stopwatches to track the time participants spent outside of their ITNs before going to bed and time spent outside of the net after getting out of bed.

In-depth interviews (IDIs) were conducted with village residents to explore factors in transmission risk, especially to understand the key facilitators and barriers to ITN use.

Focus group discussions (FGDs) were conducted with predetermined homogenous groups (e.g., heads of households, pregnant women) to explore factors in transmission risk, especially to understand the key facilitators and barriers to ITN use.

Durability monitoring

The primary outcomes of durability monitoring included ITN attrition or survivorship (measured by the loss of campaign ITNs from households), net integrity (measured by the number and size of holes in the nets), and median net survival (estimated by combining the attrition and integrity measures). Additional outcomes included insecticide bioefficacy, as measured by bioassay, and insecticide content, as measured by chromatography and other appropriate methods. Methodologies for this component were adapted from the US President’s Malaria Initiative long-lasting insecticidal net durability monitoring toolkit [11]. Protocols for new chemistries have been being developed in collaboration with other research institutions and will be used to evaluate the insecticidal durability of the new net types for future reports.

Costing and cost-effectiveness

The goal of the costing and cost-effectiveness component is to provide new data on the costs of distributing dual-AI ITNs in varied settings in sub-Saharan Africa and determine if the cost of distribution for dual-AI ITNs is different from the cost for standard ITNs. These costs will be paired with observational data on the effectiveness of dual-AI ITNs compared with standard ITNs, as well as with model-based predictions of effect, to produce cost-effectiveness estimates for each net type. This will bolster the evidence base available to help guide decisions around the deployment and use of various ITN products.

The New Nets Project planned to use cost data from national malaria programs in Burkina Faso, Mozambique, Nigeria, and Rwanda, but the COVID-19 pandemic complicated travel and data collection. Data were collected retrospectively from a selection of sites, including some study sites and some additional sites where dual-AI ITNs were distributed, such as Mali. Separately, the New Nets Project was able to leverage support from the International Federation of Red Cross and Red Crescent Societies to estimate the cost implications of COVID-19 mitigation on ITN distribution campaigns and to complete data collection in several additional sites where dual-AI ITNs were distributed. Cost data were collected from financial and operational records and key stakeholder interviews. These data will be combined with epidemiological outcomes to estimate the incremental cost-effectiveness ratios for IG2, RG, and PBO ITNs in comparison with standard ITNs in each setting where they were studied under the New Nets Project. Additionally, an updated systematic review on the cost of ITN distribution is being conducted. Results of this review will be combined with the outcomes of observational studies and mathematical modeling to make predictions of cost-effectiveness. Results from the observational cost-effectiveness studies will be compared with the predicted cost-effectiveness from mathematical models and systematic review to validate the predictive modeling results. New data on ITN distribution costs have been collected through the New Nets Project in Burkina Faso, Mali, Mozambique, Nigeria, and Rwanda.

Impact modeling

Mathematical transmission models enable the exploration of an intervention's potential effects, while holding explicit assumptions, because they mechanistically capture how *Plasmodium falciparum* malaria is transmitted between human and mosquito populations. The *P. falciparum* malaria transmission model [12–15] that is employed for the New Nets Project has been described comprehensively elsewhere [16,17], and the code is publicly available [18].

The modeling team from Imperial College London will use the pilot data from each country to specifically calibrate the transmission model parameters to reflect current understandings of mosquito ecology, intervention use, and human characteristics (e.g., treatment; other intervention use, such as SMC; and proportion of infectious bites received indoors or in bed) at the cluster or district level (depending on the granularity of the respective data sources). Later reports will include mathematical transmission models.

Table 2 includes baseline prevalence, vector species, and other relevant information. This table has been provided to Imperial College, which will use this information to parameterize the transmission model and project the impact of standard, PBO, and IG2 ITNs in each of the 16 districts. This exercise can be used to validate the model predictions where these different ITN types are deployed. The model makes explicit assumptions on the mechanisms of transmission; this enables comparison of the observed performance of any net in each district with the model's predictions of what the reference nets (standard or PBO) would have achieved in that district, while accounting for ecological and other baseline differences between sites.

Table 2. Information used to parameterize malaria transmission models.

Country	District	ITN type	Dominant vector species	Dominant vector WHO tube test mortality, %*	Dominant vector indoor: outdoor biting ratio	Secondary vector species	Secondary vector WHO tube test mortality, %	Secondary vector indoor: outdoor biting ratio	Baseline malaria prevalence (RDT+), %**	Year 1 malaria prevalence (RDT+), %**	Year 2 malaria prevalence (RDT+), %**	Baseline incidence rate (per 10,000 person-months)	Year 1 incidence rate (per 10,000 person-months)	Year 2 incidence rate (per 10,000 person-months)	Previous ITN distribution	Baseline population ITN access	Year 1 population ITN access (months after deployment)	Year 2 population ITN access (months after deployment)	Other interventions	Proportion of fevers treated with ACT	Proportion of fevers treated with non-ACT medication
Burkina Faso	Gaoua	Standard	*An. gambiae* s.l.	<50	0.86	*An. funestus* s.l.			81.00 July 2019	48.90 June 2020	21.10[§] June 2021	533.2	432.7	611.1	2016	44.4	53.8 (10)	40.5 (22)	SMC	Pending	Pending
	Banfora	IG2	*An. gambiae* s.l.	<50	0.75	*An. coustani*			39.60 July 2019	18.40 June 2020	11.60[§] June 2021	471.1	386.5	358.2	2016	58.9	84.2 (8)	74.9 (20)	SMC	Pending	Pending
	Orodara	PBO	*An. gambiae* s.l.	<50	0.64	*An. funestus* s.l.			28.40 July 2019	3.60 June 2020	2.10[§] June 2021	449.2	347.2	365.7	2016	94.0[†]	87.4 (12)	82.0 (24)	SMC	Pending	Pending
Northern Mozambique	Gurue	Standard	*An. funestus* s.l.	60–100	1.80	*An. gambiae* s.l.	15–89	0.84	64.90 September 2020	52.50 October 2021		352.6	493.8		March 2017	23.1	85.7 (12)			Pending	Pending
	Cuamba	IG2	*An. gambiae* s.l.	54–83	0.50				47.50 September 2020	29.40 October 2021		363.5	236.1		March 2017	21.0	64.8 (12)			Pending	Pending
	Mandimba	RG	*An. gambiae* s.l.	54–83	1.10	*An. funestus* s.l.	60–100	1.20	66.00 September 2020	46.20 October 2021		383.9	290.7		March 2017	16.4	75.5 (12)			Pending	Pending
Western Mozambique	Chemba	Standard	*An. funestus s.l.*	60–100	1.10	*An. gambiae s.l.*	17–53	0.40	44.30 October 2020	39.00 October 2021		531.2	414.4		April 2017	30.4	86.0 (11)			Pending	Pending
	Guro	IG2	*An. gambiae* s.l.	88	0.60				17.10 October 2020	3.80 October 2021		477.0	193.3		April 2017	18.8	88.9 (11)			Pending	Pending
	Changara	PBO	*An. gambiae* s.l.	92	0.94				5.70 October 2020	2.10 October 2021		194.8	139.3		April 2017	26.3	84.2 (11)			Pending	Pending
Rwanda	Nyamagabe	Standard	*An. funestus* s.l.	Pending	0.27	*An. gambiae* s.l.		0.48	2.36 February 2020	2.70 December 2020[‡]	0.31 November 2021	147.6	76.4		2016–2017	81.8[†]	80.7 (10)	65.5 (22)		Pending	Pending
	Karongi	IG2	*An. gambiae* s.l.	Pending	1.10	*An. funestus s.l.*		1.05	2.47 February 2020	2.69 December 2020[‡]	1.23 November 2021	239.5	91.9		2016–2017	82.2	86.1 (7)	78.32 (22)		Pending	Pending
	Ruhango	Standard	*An. gambiae s.l.*	Pending	0.58	*An. funestus s.l.*		1.09	1.33 February 2020	5.24 December 2020[‡]	0.96 November 2021	500.9	115.5		2016–2017	88.1[†]	88.6 (10)	76.39 (22)	IRS	Pending	Pending
Nigeria	Ejigbo	Standard	*An. gambiae* s.l.	73–94	0.92	*An. funestus* s.l.	Pending	Pending	38.40 October 2020	25.60 November 2021		64.5	66.0		September 2017	28.1	58.0 (12)			Pending	Pending
	Asa	IG2	*An. gambiae* s.l.	12–38	9.75				63.10 October 2020	15.80[§] November 2021		106.5	141.1		September 2017	4.4	43.4 (12)		SMC	Pending	Pending
	Moro	RG	*An. gambiae* s.l.	41–57	2.50				49.90 October 2020	21.10[§] November 2021		79.4	52.4		September 2017	17.7	31.2 (12)		SMC	Pending	Pending
	Ife North	PBO	*An. funestus* s.l.	Pending	Pending	*An. gambiae* s.l.	20–71	10.00	48.30 October 2020	40.90 November 2021		54.7	57.8		September 2017	25.4	51.8 (12)			Pending	Pending

Abbreviations: ACT, artemisinin combination therapy; IG2, Interceptor G2; IRS, indoor residual spraying; ITN, insecticide-treated net; PBO, piperonyl butoxide; RDT+, rapid diagnostic test positive; RG, Royal Guard; SMC, seasonal malaria chemoprevention; WHO, World Health Organization.

*Data on resistance were gathered from the latest sources, and the origin of the data was detailed in each country section.

**Prevalence measures from all evaluations are for children <5 years of age, except in Rwanda, where prevalence is for those 6 months of age and older.

[†]Survey occurred right after distribution; therefore, no true baseline measure is available.

[‡]The second prevalence survey is not directly comparable with the February baseline.

[§]Prevalence among children <5 years old is measured after one dose (Burkina Faso) or a four-dose series (Nigeria) of seasonal malaria chemoprevention.

Limitations

These observational evaluations have limitations that are important to consider when interpreting results. Though district-level observations were matched in time and, to the greatest extent possible, ecology and geography, there were challenges in generating the supportive datasets needed to account for fundamental differences that may exist between study districts and for potential confounding and/or covariable factors. This was especially challenging because the unit of analysis for these studies was the district level, though the procurement, delivery, and distribution of specific ITN types were determined at the provincial level (regional or state level in some countries) so that all districts within a single province received the same ITN type. As such, it was necessary to limit these pilot evaluations to contiguous and/or nearby districts from neighboring provinces. This approach to selecting study districts meant that baseline malaria burden and vector ecology and bionomics varied substantially both within and across the different evaluation settings. This captured real-world diversity in transmission settings but also complicated the interpretation of the observational results.

An additional source of variability that will be important to consider when interpreting results is other malaria control activities in each study district. While these were matched at baseline, they were not consistent for the duration of the study period in several situations. This was the case in Burkina Faso, where annual SMC campaigns targeted the same population used to monitor malaria prevalence—namely, children younger than 5 years of age. The first two surveys were timed to precede the first round of SMC, which limited the temporary effect of the mass treatment on infection prevalence in the target population. However, prior to the third survey, the national campaign was expanded from four to five doses. This complicated the timing of the survey relative to the mass drug administration and necessitated additional testing of older children to help account for potential confounding. Similarly, in Nigeria, SMC for children under 5 years old was introduced in some study districts prior to the 2021 survey. The surveys for 2021 and 2022 therefore were expanded to include children ages 5 to 15 years in addition to children under 5 years old.

Routine health facility data provide real-time insight into malaria cases and trends at the district level. However, routine data are often limited by variable data integrity, limited capacity for quality control, and periodic commodity supply shortages (diagnostic test and drug stockouts, which may affect both case ascertainment as well as health facility attendance), which could lead to an underestimation of true malaria case incidence rates. In addition, use of routine data for evaluations can be limited by systematic differences between districts prior to and during the study. Districts with consistently lower attendance in government health facilities and low use of ITNs could impact estimations of case incidence and limit comparisons across districts. To address these shortcomings, initial standardized data quality assessments were conducted in select community- and district-level health facilities to assess the quality, completeness, and timeliness of reported data. Additional study personnel assisted in data quality assurance procedures where reporting was found not to be strong. Nonetheless, case incidence rates estimated from routine health data reflect only symptomatic cases among those who actively choose to engage with the public health sector; therefore, these case incidence rates represent only a proportion of all malaria infections.

Another source of variability when considering these interim results is the brief periods that were available for baseline, pre-intervention data collection given the need to align study activities with existing regional- and national-level universal coverage campaigns timelines. The timing of different campaign activities across study districts also varied, which resulted in variations in the length of time that each intervention has been deployed to date.

Due to the complexity of national malaria programming and each unique net distribution campaign, the study protocols were not identical; however, key indicators were harmonized across the four countries. A single data analysis framework also was codeveloped by study partners. This framework accounted for local variations for each individual analysis, including possible differences in total duration of net ownership, delays in hanging campaign nets, and data gaps. Any deviations from the main analysis plan will be described in country-specific sections of this report. In this way, the standardized protocols aimed to ensure that the breadth of information and replication of similar analyses in each pilot country will strengthen conclusions on the cost-effectiveness of these interventions across a variety of settings in a way that a single evaluation or single measure could not.

It is also worth noting that these New Nets Project pilot studies are not able to estimate the general impact of any (or all) ITNs relative to no ITNs, as there are no such comparator areas. Instead, the New Nets Project approach is to quantify the incremental impact of dual-AI ITN types relative to standard pyrethroid-only ITN varieties that still provide protection from malaria—particularly when access and use are high.

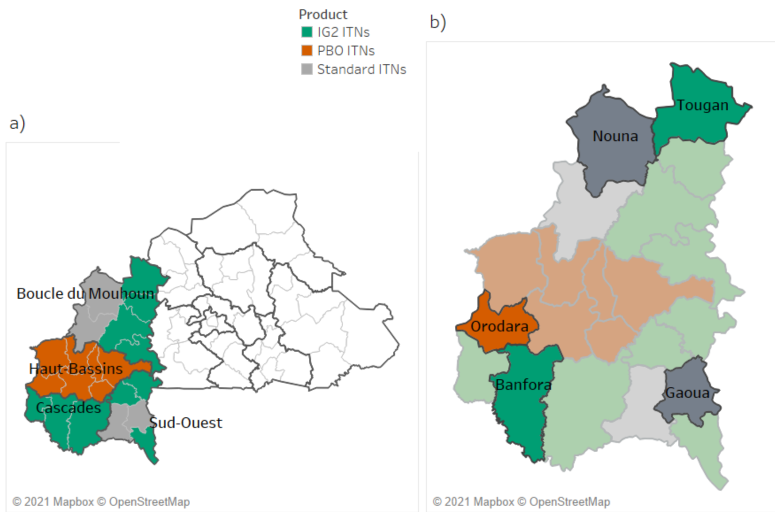
Finally, all these operational challenges were exacerbated by the ongoing COVID-19 pandemic response. Steps to account for these changes will be contextualized during final analysis.

Burkina Faso

The evaluation in Burkina Faso started in July 2019. Evaluation activities have taken place in three districts: Banfora (IG2), Orodara (PBO), and Gaoua (standard). Routine surveillance data from two additional districts, Nouna (standard) and Tougan (IG2), have been included in the case incidence calculations to strengthen comparisons across net types, but pilot activities have not taken place there (Figure BF1). High-transmission season typically occurs from June or July through October.

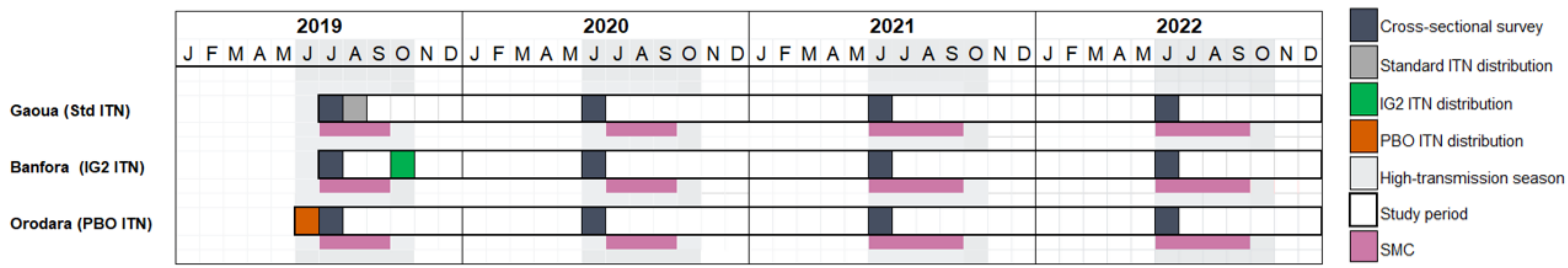
ITNs were distributed during the high-transmission season: PBO ITNs were distributed in June 2019; standard ITNs were distributed in August 2019; and IG2 ITNs were distributed in October 2019 (Figure BF2). The NMCP in Burkina Faso, in consultation with partners, used malaria incidence and insecticide-resistance data to document regions and districts with high pyrethroid resistance, which the NMCP targeted to receive either PBO or dual-AI ITNs. These regions and districts mainly were in the western part of the country; hence, this distribution concentrated mainly on western districts. Other districts in the region also benefited from IRS campaigns; those are not included in this study.

Figure BF1. Map of study districts in Burkina Faso.



a) ITN distribution across four regions of Burkina Faso; b) the three study districts and two comparison districts (Nouna and Tougan).
Abbreviations: IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide.

Figure BF2. Insecticide-treated net distribution and transmission timeline.



Abbreviations: IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide; SMC, seasonal malaria chemoprevention; Std, standard.

Epidemiology

Cross-sectional survey

This section has not been updated since the previous report (published in December 2021). The next round of data collection will take place from June to July 2022.

The baseline cross-sectional survey was conducted in July 2019; the Year 1 survey was conducted from June to July 2020; and the Year 2 survey was conducted from June to July 2021. The baseline and Year 1 surveys were conducted before SMC campaigns and during the onset of the high-transmission season. A minimum sample size of 190 households with an eligible child (under 5 years of age) in each study district was selected. In each household, one child within the ages of 6 to 59 months was selected for prevalence testing and the head of household or primary caregiver responded to the household survey. The Year 2 survey was conducted at the onset of the high-transmission season, as the previous two surveys had been however, when data collection began in June 2021, children aged 6 to 59 months in study districts had already benefited from the first round of the SMC campaign. The SMC campaign began early because study districts had gone from the previous four rounds of SMC to five rounds in 2021, hence the overlap in timing. The first round of SMC (coverage reported to be above 100%) was expected to have biased the prevalence measure of the Year 2 survey, especially because SMC in Burkina Faso targets children under 5 years old, similarly to the cross-sectional survey. To allow for adjustments in the analysis, children 5 to 10 years of age were added to the sample so that their prevalence could be used to model prevalence among children under 5 years old without SMC.

Table BF1 shows household demographics in the study districts from 2019 to 2021. These demographics in general did not vary significantly from year to year except for the average household size. The districts continued to be typically rural, with most of the heads of households having no formal education. Children under 5 years old still represented about a quarter of the population. However, average household size in Gaoua, for example, went from 6.5 members in 2019 to 4.8 in 2020. In Banfora, there was a similar change from 2019 to 2020 and 2021. A further look into the data and field notes showed that these differences can be explained by the type of clusters randomly selected each year. In Gaoua, for example, it appeared that in 2020 and 2021, a few small agricultural villages were randomly selected. Generally, these villages were temporary settlements for the agricultural seasons; hence, the households were smaller than average. Banfora on the other hand, had a few large households (over 20 usual members) randomly selected in 2021, leading to a higher household average size for the district.

Table BF1. Participant/household demographic characteristics, 2019–2021.

	Gaoua (standard ITNs)			Banfora (IG2 ITNs)			Orodara (PBO ITNs)		
	2019	**2020**	**2021**	**2019**	**2020**	**2021**	**2019**	**2020**	**2021**
Households enrolled (clusters)	195 (10)	190 (10)	190 (10)	197 (10)	190 (10)	190 (10)	190 (10)	190 (10)	191 (10)
Average number of household members (95% CI)	6.47 (5.97–6.97)	4.76 (4.48–5.04)	4.38 (4.16–4.61)	6.02 (5.57–6.45)	5.66 (5.37–5.95)	6.85 (6.35–7.35)	5.28 (5.02–5.54)	4.95 (4.70–5.20)	5.09 (4.90–5.27)
Age, % of total (n)									
<5 years old	30.7 (388)	29.8 (270)	26.3 (219)	27.2 (322)	24.3 (261)	23.4 (305)	24.3 (244)	26.2 (246)	23.5 (228)
≥5 years old	65.8 (874)	70.2 (635)	73.7 (614)	70.0 (863)	75.7 (815)	76.6 (997)	73.4 (759)	73.8 (694)	76.5 (744)
Gender, % of total (n)									
Male	46.3 (584)	44.0 (398)	44.3 (369)	47.0 (557)	48.0 (517)	51.6 (672)	49.0 (491)	47.8 (449)	48.8 (474)
Female	53.7 (678)	56.0 (507)	55.7 (464)	53.0 (628)	52.0 (559)	48.4 (630)	51.1 (512)	52.2 (491)	51.2 (498)
Education status of head of household, % of total (n)									
None	85.6 (167)	92.6 (176)	91.1 (173)	76.1 (150)	87.4 (166)	88.4 (168)	77.4 (147)	81.6 (155)	83.8 (160)
Primary	6.7 (13)	2.6 (5)	2.1 (4)	13.2 (26)	6.3 (12)	6.8 (13)	13.7 (26)	10.0 (19)	6.8 (13)
Post-primary	4.6 (9)	2.6 (5)	2.1 (4)	7.1 (14)	3.7 (7)	1.1 (2)	3.7 (7)	2.1 (4)	2.1 (4)
Secondary/superior	3.1 (6)	2.1 (4)	4.7 (9)	3.6 (7)	2.6 (5)	3.7 (7)	5.3 (10)	6.3 (12)	7.3 (14)

Abbreviations: CI, confidence interval; IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide.

Table BF2 shows ITN coverage, access, and use in the study districts from 2019 to 2021. ITN indicators across the three districts remained constant throughout the years, with Gaoua having the lowest ITN ownership, use, and access from 2019 to 2021. Both Banfora and Orodara continued to have relatively high ownership, use, and access after the ITN distribution in 2019. All three districts saw a decrease in access. Data on ITN ownership, use, and access also were collected at baseline and at the 12-month follow-up during ITN durability monitoring that was supported by the US President's Malaria Initiative. Although the cross-sectional survey methodology for collecting and calculating these indicators was different in many aspects, in general, the durability monitoring found similar results: ITN use increased from baseline to the 12-month follow-up in all three districts because, at baseline, campaign ITNs were typically still packaged [19]. The durability monitoring also found that some campaign ITNs had been lost, damaged, or given away 12 months postcampaign. The use given access indicator increased from Year 1 to Year 2 in all three districts, possibly due to continuous behavior change communication to support improved ITN use.

Table BF2. ITN coverage, access, and use, 2019–2021.

	Gaoua (standard ITNs)			Banfora (IG2 ITNs)			Orodara (PBO ITNs)		
	2019	**2020**	**2021**	**2019**	**2020**	**2021**	**2019**	**2020**	**2021**
Average number of ITNs per house (95% CI)	1.52 (1.31–1.74)	1.42 (1.25–1.58)	1.71 (1.56–1.87)	1.87 (1.69–2.06)	2.59 (2.43–2.76)	2.87 (2.66–3.09)	3.59 (3.38–3.80)	2.57 (2.40–2.75)	2.40 (2.26–2.54)
Households with at least one ITN, % (95% CI)	68.7 (61.8–74.8)	74.7 (68.0–80.4)	56.8 (49.7–63.7)	87.8 (82.4–91.7)	99.5 (96.3–99.9)	96.3 (92.5–98.2)	100.0 (–)	100.0 (–)	99.5 (96.3–99.9)
Population that slept under a net last night, % (95% CI)	20.8 (18.6–23.1)	44.2 (40.9–47.5)	37.0 (30.5–42.5)	67.7 (64.9–70.3)	90.4 (88.5–92.1)	82.8 (79.0–86.6)	78.8 (76.1–81.2)	84.8 (82.3–87.0)	83.5 (79.9–87.1)
Population ITN access, % (95% CI)	44.4 (42.4–46.2)	53.8 (51.4–56.2)	40.5 (37.9–43.1)	58.9 (57.1–60.7)	84.2 (83.1–85.3)	74.9 (73.5–76.2)	94.0 (93.1–94.9)	87.4 (86.3–88.5)	82.0 (80.7–83.3)
Use given access*	0.47	0.82	0.91	1.15	1.07	1.11	0.84	0.97	1.02

Abbreviations: CI, confidence interval; IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide.

*Use given access is calculated by dividing use (population that slept under a net last night) by access. Values over 1 are possible given that the calculation is a ratio.

Despite the use of all available incidence, prevalence, and climate data to choose comparable areas for the evaluation, malaria prevalence was significantly different in Gaoua District at baseline and the confidence intervals overlapped for Banfora and Orodara (see Table BF3). The malaria prevalence rates in Gaoua, Banfora, and Orodara at the time of the baseline survey were 80.1%, 39.6%, and 28.4%, respectively. While there was a significant reduction in prevalence in the under-5-year-old population for all net types from Year 1 to Year 2, this was partly due to one round of SMC implemented a few weeks before the Year 2 survey.

The modeling of the likely prevalence in 2021 for children under 5 years old without SMC, using the observed prevalence in children 5 to 10 years old, is forthcoming. For the modeling, a series of systematic reviews were conducted to collate data on key parameters (e.g., human immunity, heterogeneity in biting, drug treatment impact, seasonal patterns in transmission, and mosquito bionomics) that inform malaria parasite transmission between people and mosquitoes in the presence of vector control. Together with the data recorded during the pilot study in Burkina Faso, these parameters will be used to inform and calibrate the model simulation to the baseline situation in Gaoua, Banfora, and Orodara. The model will initiate the SMC on July 20, to simulate SMC just after the prevalence surveys each year. The model also will assume 90% coverage of children in each region given that the reported coverage indicates complete coverage, but there may be unknown individuals in the community.

Table BF3. Malaria prevalence among children <5 years old by study district, 2019–2021.

	Gaoua (standard ITNs)			Banfora (IG2 ITNs)			Orodara (PBO ITNs)		
	2019	**2020**	**2021***	**2019**	**2020**	**2021***	**2019**	**2020**	**2021***
Total tested	195	190	190	190	190	190	190	190	191
Malaria prevalence (RDT+), % (95% CI)	81.0 (74.9–86.0)	48.9 (41.9–56.1)	21.1 (15.5–27.5)	39.6 (33.0–46.6)	18.4 (13.5–24.6)	11.6 (7.4–17.0)	28.4 (22.4–35.3)	3.7 (1.8–7.5)	2.1 (0.57–5.3)
Percent prevalence reduction from baseline to Year 2, %	74.0			70.7			92.6		

Abbreviations: CI, confidence interval; IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide. RDT+, rapid diagnostic test positive.
*Prevalence among children <5 years old in 2021 is measured after a first dose of seasonal malaria chemoprevention.

Routine health system data

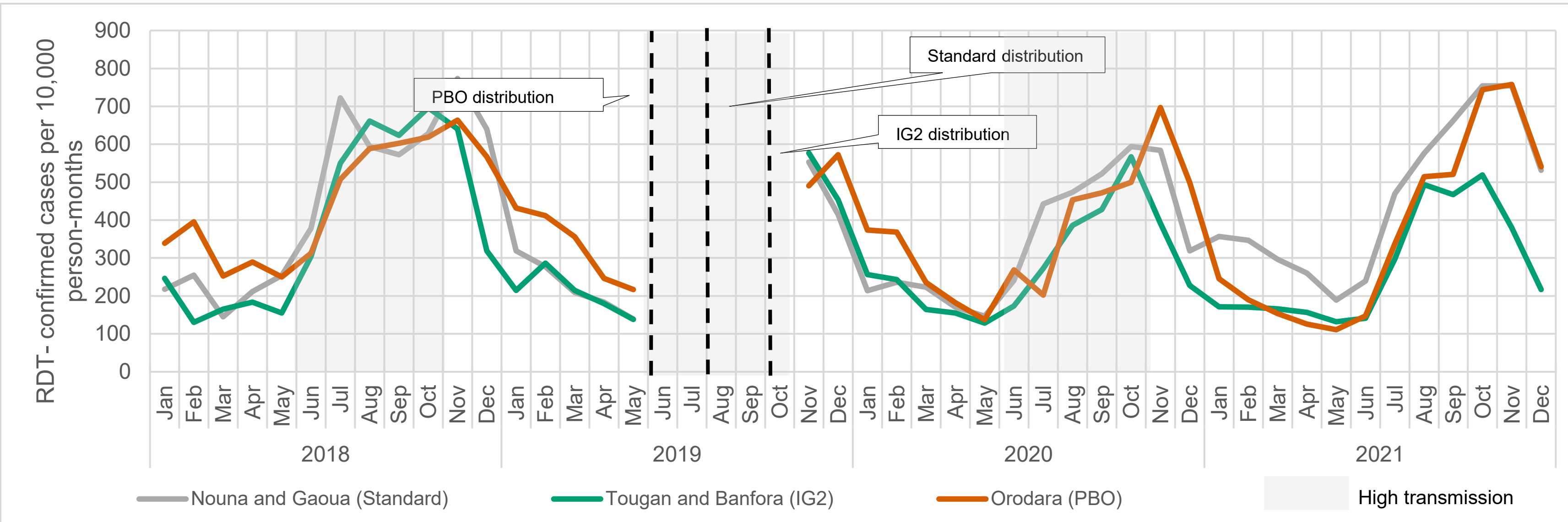
These analyses have been updated from the previous interim results to include malaria incidence from the second half of 2021 (July to December 2021). In addition, the time frame used for the year-to-year comparisons has been adjusted to full calendar years, with January to December 2018 as the baseline year.

The malaria incidence rate was calculated using passive confirmed malaria case data from two additional districts, Nouna and Tougan. The district of Nouna received standard ITNs; hence, its cases were aggregated with Gaoua. Tougan received IG2 ITNs; its cases were therefore aggregated with Banfora. Population estimates from 2017 were used for the 2018 incidence calculation, and updated estimates from 2019 were used for 2019 to 2021. Malaria case data were extracted from the national health data repository in June 2021 and updated in March 2022. A labor strike at the health facility level led to the disruption of data reporting from June to October 2019. It has been confirmed that these data gaps will not be filled, therefore 2019 has excluded from the analysis at this point, considering that the data gap falls right into the high malaria transmission season. The country has only been able to get modeled estimates at the regional level.

As shown in Figure BF3, in 2018, case incidence started to peak around June and July. In 2020, this did not happen until around September, and no peak was visible in 2021 until October. These patterns were possibly due to a slowdown in malaria transmission.

Incidence rate ratios were used to compare the incidences in IG2 districts and the PBO district against standard districts for the baseline year to provide baseline incidence differences across the districts (Table BF4). The 2018 incidence rates for both the IG2 districts and PBO district started slightly lower than Gaoua's, one of the standard districts, in line with the prevalence measures at baseline. In Year 1, case incidence rates declined across all study districts, but they declined by a slightly larger magnitude in both the PBO and IG2 districts. The incidence rate ratio was slightly lower for IG2 ITNs compared with standard ITNs than for PBO ITNs compared with standard ITNs. This trend strengthened in Year 2, possibly indicating a more prolonged incremental effect for IG2 compared with PBO.

Figure BF3. Average monthly incidence rate (per 10,000 person-months) per net type, 2018–2021.



Abbreviations: IG2, Interceptor G2; PBO, piperonyl butoxide; RDT, rapid diagnostic test.

Table BF4. Malaria incidence rates and incidence rate ratios by ITN and year, 2018–2021.

		Incidence rate (per 10,000 person-months)							**Incidence rate ratio (95% CI)**	
Period*	Months	**Orodara (PBO)**	**Banfora (IG2)**	**Tougan (IG2)**	**Overall IG2**	**Gaoua (standard ITNs)**	**Nouna (standard ITNs)**	**Overall (standard ITNs)**	**Overall IG2 vs. standard**	**Overall PBO vs. standard**
Baseline	Jan 2018–Dec 2018	449.2	471.1	308.1	**402.1**	533.2	364.8	**433.2**	0.93 (0.92–0.93)	1.04 (1.03–1.05)
Year 1	Jan 2020–Dec 2020	347.2	386.5	179.2	**300.3**	432.7	298.8	**353.0**	0.85 (0.85–0.86)	0.98 (0.98–0.99)
Year 2	Jan 2021–Dec 2021	365.7	358.2	193.7	**289.8**	611.1	294.9	**423.1**	0.68 (0.68–0.69)	0.86 (0.86–0.87)

Abbreviations: CI, confidence interval; IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide.
*Data are missing for June–October 2019; therefore, the year 2019 was excluded from the routine data analysis.

The difference-in-difference analysis of standard ITNs versus IG2s and standard ITNs versus PBO ITNs using incidence rates compared differences from 2018 (baseline year) with differences from 2020 (Year 1) and 2021 (Year 2). The comparisons assessed if any additional protection was provided either by IG2s or PBO ITNs compared with standard ITNs (Table BF5). The unadjusted model found that IG2 ITNs were about 25% more effective and PBO ITNs were about 16% more effective than standard ITNs two cumulative years after distribution; these results were statistically significant.

Table BF5. Difference-in-difference comparison of next-generation ITNs to standard ITN, Years 1 and 2.

	Year 1 (Jan 2020–Dec 2020) change from baseline (95% CI)	**Year 1 DiD relative to standard ITNs**	**Year 2 (Jan 2021–Dec 2021) change from baseline**	**Year 2 DiD relative to standard ITNs**
Gaoua and Nouna (standard ITNs)	−18.51% (−18.53% to −18.49%)		−2.35% (−2.36% to −2.33%)	
Banfora and Tougan (IG2 ITNs)	−25.31% (−25.39% to −25.23%)	6.8% (6.8% to 6.9%)	−27.93% (−28.01% to −27.85)	25.6% (25.5% to 25.7%)
Orodara (PBO ITNs)	−22.71% (−22.73% to −22.68%)	4.2% (4.2% to 4.2%)	−18.59% (−18.60% to −18.57%)	16.2% (16.2% to 16.3%)

Abbreviations: CI, confidence interval; DiD, difference-in-difference; IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide.

Entomology

This section has not been updated since the previous report (published in December 2021).

In Burkina Faso, entomological surveillance included indoor CDCLT collections one night per week at six sentinel houses in each of the three villages in study districts (totaling 72 collection nights per district per month). It also included paired indoor-outdoor HLCs at two houses per study district (totaling 48 paired collections per district per month), which were performed concurrently with the CDCLT collections but at different houses. Mosquito larval sampling was performed annually in each district to support insecticide-resistance monitoring.

Entomological surveillance activities began in July 2019 and are ongoing. The preliminary analytical dataset through January 2021 has been cleaned and validated. Updated results through Year 1 are presented here.

The most abundant vector species group across all study districts in Burkina Faso was *An. gambiae* s.l. However, *An. gambiae* s.s. was dominant in Gaoua and Orodara, and *An. coluzzii* was dominant in Banfora (Table BF6). *An. funestus* was also present in significant numbers in Gaoua and was collected more often indoors than outdoors. Ongoing sporozoite screens will help clarify which of these species are the dominant vectors.

Insecticide susceptibility patterns in local vector populations are currently being assessed. Historical data indicate that *An. gambiae* s.l. populations from these regions of Burkina Faso are highly pyrethroid resistant. (WHO tube tests from 2019 and 2020 showed mortality rates less than 50% with evidence of multiple resistance mechanisms [15,16].)

Table BF6. Entomological characteristics of the study sites in Burkina Faso, baseline and Year 1.

	Gaoua (standard ITNs)		Banfora (IG2 ITNs)		Orodara (PBO ITNs)	
	Baseline	**Year 1**	**Baseline**	**Year 1**	**Baseline**	**Year 1**
Most abundant vector (% of likely vector species collected)	*An. gambiae* s.l. (67.9%)	*An. gambiae* s.l. (83.7%)	*An. gambiae* s.l. (97.7%)	*An. gambiae* s.l. (99.7%)	*An. gambiae* s.l. (92.9%)	*An. gambiae* s.l. (99.6%)
Second most abundant vector (% of likely vector species collected)	*An. funestus* s.l. (23.4%)	*An. funestus* s.l. (15.6%)	*An. coustani* (0.5%)	*An. funestus* s.l. (0.3%)	*An. funestus* s.l. (0.5%)	*An. funestus* s.l. (0.4%)
***An. gambiae* molecular IDs**						
An. gambiae s.s.	93.30%	Pending	35.10%	Pending	81.10%	Pending
An. Coluzzii	5.20%	Pending	64.70%	Pending	18.90%	Pending
An. Arabiensis	1.50%	Pending	0.20%	Pending	0.00%	Pending
HLC nightly landing rates (*An. gambiae* s.l.)						
Indoor:outdoor ratio	0.86	1.22	0.75	0.99	0.64*	0.83
Pyrethroid-resistance profile	**HIGH resistance: Partially mitigated by PBO**					
WHO tube test morality	Less than 50%					

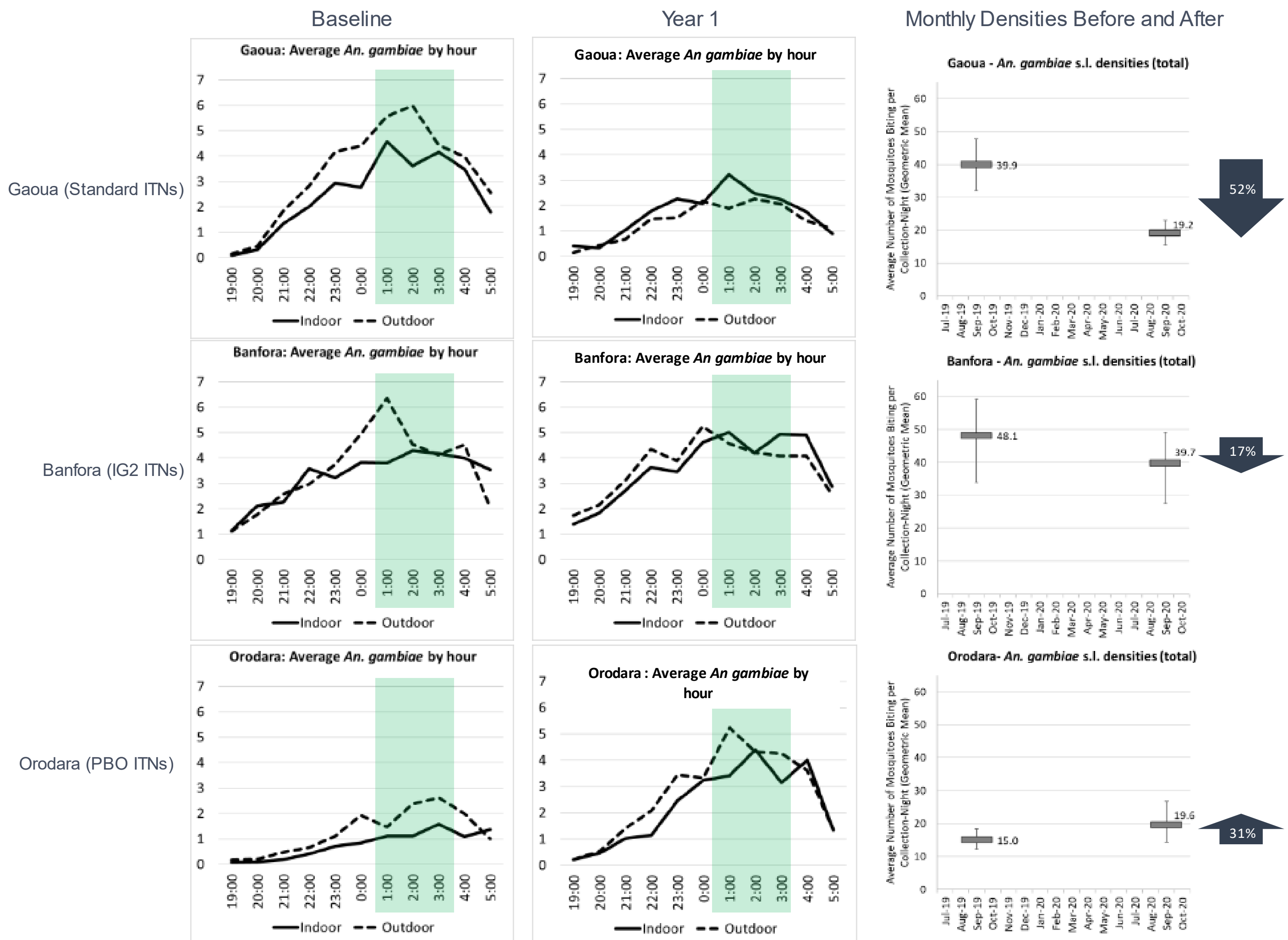
Abbreviations: HLC, human landing collection; ID, identification; IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide; WHO, World Health Organization.

*A ratio that is significantly lower than 1.0 (95% confidence interval on the ratio excludes 1) indicates a strong preference for feeding outdoors.

Data on nightly biting patterns of *An. gambiae* s.l. (Figure BF4) showed a slight preference for outdoor biting at baseline before the ITN distribution campaigns. This tendency was not consistent in Year 1, when mosquitoes were equally likely to be collected indoors as outdoors in all three districts. Regardless of host-seeking location, a peak in biting behavior between the 1:00 and 3:00 hours was noted, though significant biting did occur outside this window in all districts as well.

Also shown in Figure BF4 are total monthly biting rates for *An. gambiae* s.l. at baseline and approximately one year after the ITN distribution campaigns. Total biting rates declined significantly by 52% in Gaoua (standard ITNs) and slightly by 17% in Banfora (IG2s). In Orodara, the PBO district, mosquito biting rates increased slightly. However, Orodara was also the district where prevalence among children under 5 years old fell by the greatest proportion—from 28.4% in 2019 to 3.7% in 2020. The opposite trends of increasing vector biting rates and decreasing malaria prevalence are somewhat paradoxical at first glance. It should be noted, however, that even after the increase in *An. gambiae* biting rates from 2019 to 2020, Orodara still reported the lowest indoor biting rate and an outdoor biting rate on par with the substantially reduced rate in Gaoua.

Figure BF4. Nightly biting patterns by district, baseline and Year 1.



Note: The green shading represents the hours of peak biting.

Abbreviations: IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide.

Finally, preliminary, one-year changes in the mosquito parity rate suggest that *An. gambiae* s.l. in Gaoua District—where malaria prevalence was highest—may be more likely to live long enough to reproduce compared with the *An. gambiae* s.l. populations in Banfora and Orodara. However, this trend was consistent in both the years before and after the ITN distribution campaigns. Additionally, preliminary evidence suggests that none of the ITN types decreased the crude age structure of the vector populations from year to year.

Human behavior

This section has not been updated since the previous report (published in December 2021).

Four rounds of human behavior data collection occurred from 2019 to 2021. Research participants were recruited from nine villages in three districts. A total of 368 IDIs and 100 FGDs were conducted with a total of 1,292 participants (Table BF7). Coding and analysis of Rounds 1 to 3 have been completed; Round 4 coding and analysis are currently in process. After two rounds of data collection, saturation was reached from IDIs. The IDI and FGD guides were revised before Round 4 began, which included both IDIs and FGDs. Data collection for Round 5 was completed in May 2022. Data entry and cleaning are in progress.

Table BF7. Number of participants by human behavior data collection activity, 2019–2021.

	Number of households or participants				
	Round 1 (high-transmission season, 2019)	**Round 2 (high-transmission season, 2020)**	**Round 3 (low-transmission season, 2021)**	**Round 4 (high-transmission season, 2021)**	**Total**
Indirect monitoring	—	—	—	189	189
In-depth interview	144	152	0	72	368
Focus group discussion	342	338	64	180	924

Drivers of ITN use and non-use

Malaria-prevention options. Although participants overwhelmingly reported sleeping under ITNs, they also took several additional measures to prevent malaria, with some expressing preference for other options over ITNs. These options included spraying inside and outside the house with insecticides (e.g., Timor insecticide), using mosquito coils, covering the body with clothing, using anti-mosquito ointments, controlling diet, and reducing mosquito breeding grounds by removing stagnant water and keeping the area around the home “clean.”

> *“Malaria starts with freshness, then the dirty water that we pour in front of our concessions and the garbage near the courtyards.”*

—FGD participant, Tengrela, Banfora

Some participants described using leaves to prevent mosquitoes from entering the house in years past, but they noted that this method was no longer effective. A few participants also expressed a preference for using mosquito coils over ITNs when spending time outside in the evenings.

> *"In the dry season, because it is very hot at this time, [we rest outside at night]. During this time, you cannot sleep because of the mosquitoes. But we light up the mosquito coils.... Some members of my household do not use [nets] during the dry season and prefer to buy mosquito coils, but it is when they have no money that they use the mosquito net."*
>
> *—Interviewee, Dieri, Orodara*

Other participants expressed a preference for spraying insecticides (Timor) while socializing during the day and evening before retiring to bed.

> *"During the day like this, you can spray Timor. Timor can hunt flies and mosquitoes. The mosquito net can be used for the night, but during the day, when talking like we are now, mosquitoes can bite us."*
>
> *—FGD participant, Panga, Banfora*

Access. There was divergence across participants regarding accessibility and ownership of ITNs. The majority of participants used nets received through government distribution campaigns or ANC visits. Others described not having any or having an insufficient number of ITNs for their household.

> *"If you have money, you buy another [net]. If you don't have money, you're out of luck."*
>
> *—FGD participant, Panga, Banfora*

Use. Many participants reported using nets every day and throughout the year in both the dry and rainy seasons. However, some reported not using nets when sleeping outside or when there were not many mosquitoes.

> *"All the time, there's not even a day that I don't sleep under a mosquito net. Even children."*
>
> *—Interviewee, Tengrela, Banfora*

Maintenance. Participants reported washing nets but not mending them. When nets started to show wear or tear, they got rid of them or used them for other purposes.

> *"If mosquito nets start to wear out, people get rid of them because other households have backup nets, which is why others use those that are worn for their garden fence. Otherwise, no one is going to use a new mosquito net to make a fence. Once someone uses a mosquito net for [an]other activity, it is that it is worn out and that he has had a new one."*
>
> *—Interviewee, Dieri, Orodara*

Benefits. Besides protecting against malaria, participants reported that nets were comfortable and kept flies and other insects away.

Challenges. Some participants commented that they themselves or others did not use ITNs because they were “hot,” caused skin irritations, and “prevent[ed] them from breathing.” A few participants also described having issues with setup, including difficulty attaching the mosquito net and not having enough space in the home for each member of the household to attach a mosquito net. Some participants perceived the nets that had been distributed in the latest campaign to be less effective than previous nets.

> *“The mosquito nets of the previous year, when they are tied in the room even if it has been washed, no mosquitoes approach. They are still effective even after laundry.”*
>
> *—Interviewee, Tiefora, Banfora*

Further analysis will consider differences by age and gender, where these data are available, and will probe into the drivers of use of alternatives to ITNs and noncampaign ITNs. It also will analyze the time participants are protected by ITNs compared with the times that mosquitoes are biting. This will give a better indication of indoor and outdoor exposure times.

Durability monitoring

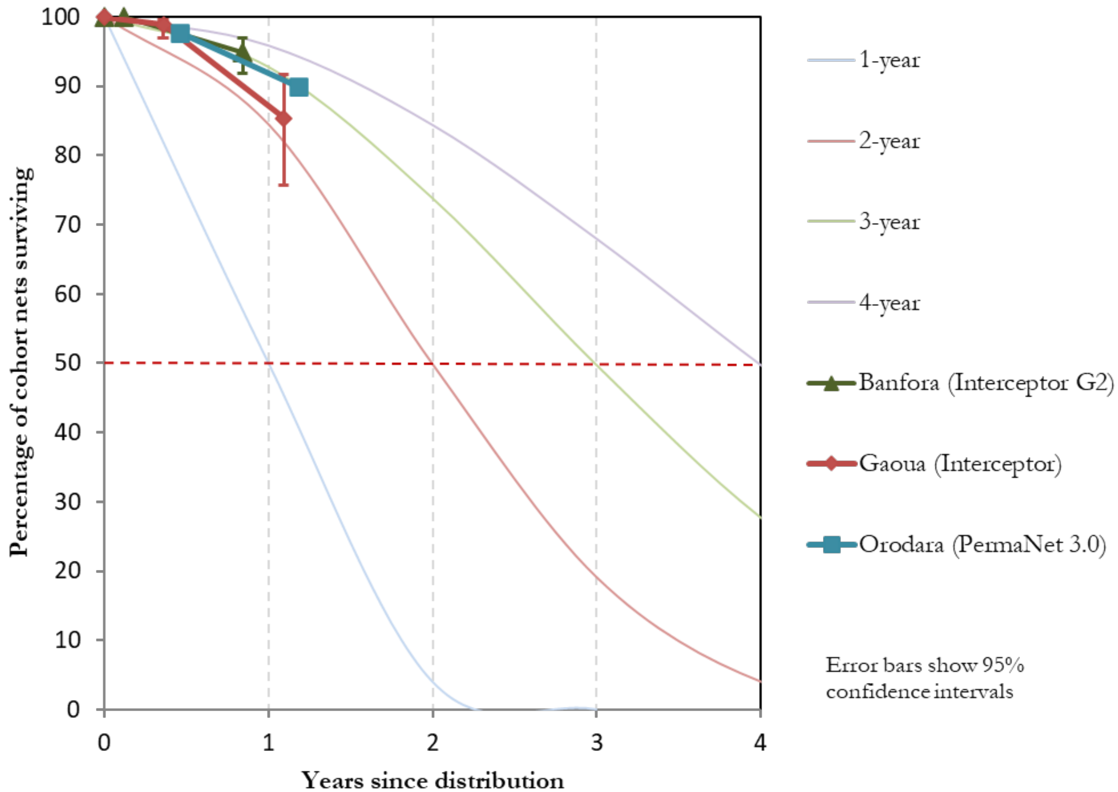
Durability monitoring activities in Burkina Faso are led by the US President’s Malaria Initiative. This section provides a summary update from the following 12-month report: The PMI VectorLink Project. *The PMI VectorLink Burkina Faso ITN Durability Monitoring 12-Month Study Report.* Washington, DC: The PMI VectorLink Project, Population Services International (PSI); 2020.

Baseline data collection was conducted from December 9 to 20, 2019, and the first follow-up survey (hereafter referred to as the 12-month follow-up) was conducted between August 31 and November 12, 2020 (10 to 16 months after the campaign). Data collection was conducted by the *Institut de Recherche en Sciences de la Santé* (Institute of Research on Health Sciences), which is based in Bobo-Dioulasso, under the guidance of VectorLink Burkina Faso.

At the 12-month follow-up, the proportion of campaign cohort nets reportedly used the previous night was 68% in Banfora, 78% in Gaoua, and 86% in Orodara. Fewer than 1.0% of all nets were still in their packages at the 12-month follow-up, down from 7.4% at baseline. Hanging rates were 63% in Banfora, 75% in Gaoua, and 81% in Orodara. Nets from other sources continued to be limited at the 12-month follow-up. The most common other sources were previous campaigns or ANC visits.

At the 12-month follow-up, 91.8% of nets in Banfora, 90.3% in Gaoua, and 81.8% in Orodara were determined to be “in good condition” based on the proportionate Hole Index. Very few nets were too torn to be useful: 3.5% in Banfora, 2.9% in Gaoua, and 4.3% in Orodara. Combining these results with the attrition rate produces estimates of the survival of campaign nets in serviceable condition after 12 months of 94.9% in Banfora, 85.4% in Gaoua, and 88.9% in Orodara (Figure BF5).

Figure BF5. Estimated net survival in serviceable condition with 95% error bars plotted against hypothetical survival curves with defined median survival.



Summary

Malaria prevalence continued to decrease in the study districts two years after ITN distribution. Prevalence among children under 5 years old was 81%, 40%, and 28% in the 2019 baseline survey and 21%, 12%, and 2% in 2021 in Gaoua, Banfora, and Orodara, respectively. The 2021 prevalence was biased by SMC implementation; modeled estimates will better evaluate the impact of the ITNs on prevalence two years after distribution. ITN access and use also decreased slightly in all districts.

An analysis of the changes in malaria incidence rates from 2018 (baseline year) to 2020 (Year 1) and 2021 (Year 2), as well as of standard ITNs versus IG2s and standard ITNs versus PBO ITNs, found that IG2 ITNs were about 25% more effective and PBO ITNs were about 16% more effective than standard ITNs two cumulative years after distribution. These results suggested that the gains in preventing malaria transmission were sustained two years postcampaign.

The entomological and survey data showed that total biting rates declined in Gaoua (standard ITNs) and Banfora (IG2s). In Orodara, the PBO district, mosquito biting rates increased slightly. However, Orodara was also the district where prevalence among children under 5 years old fell by the greatest proportion—from 28.4% in 2019 to 3.7% in 2020. Households from Orodara also reported the highest levels of population ITN access and use.

These findings highlighted the multiple mechanisms by which an ITN can help provide protection from malaria. Even though a community mosquito-killing effect in Orodara was not evident, high rates of ITN access (close to 100% all years) and use (about 80% all years) likely provided high levels of personal protection to the population exposed to the lowest baseline transmission pressure. This complemented the SMC, universal test and treat, and other malaria control strategies in the district to nonetheless help achieve a sharp reduction in malaria prevalence among children under 5 years old.

The incidence of malaria appeared to be similar for the two years after the campaign. Although a full year-to-year comparison was not feasible due to incomplete 2019 data (due to a data strike), the unadjusted model found that IG2 ITNs were about 26% more effective and PBO ITNs were about 16% more effective than standard ITNs for two cumulative years after distribution; these findings were statistically significant.

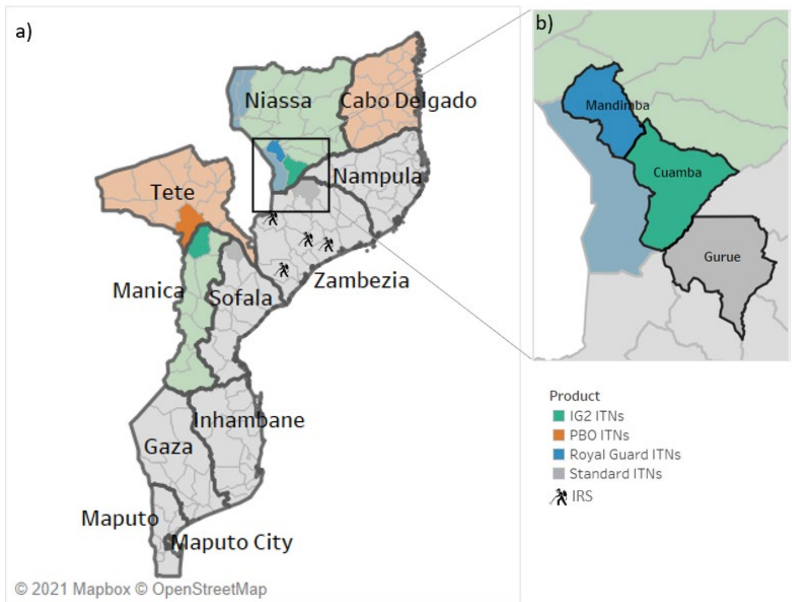
The thematic analysis of the second round of IDIs and FGDs showed that almost all participants reported sleeping under ITNs every day throughout the year, though some also took additional measures or preferred other options. Heat, skin irritation, and sleeping/sitting outside at night were reported as drivers of non-ITN use. Some participants reported insufficient or delayed distribution of nets.

Northern Mozambique

The northern Mozambique evaluation began in August 2020. It has been conducted in Gurue District (standard ITNs) in Zambezia Province, as well as Cuamba (IG2 ITNs) and Mandimba (RG ITNs) districts in Niassa Province (Figure MN1). The high-transmission season occurs in northern Mozambique from January through June. Baseline activities were scheduled to begin in March 2020; however, the NMCP suspended activities and study preparations due to COVID-19. Pandemic mitigation policies and procedures were in place by June 2020, and all critical activities resumed in July 2020. ITN distribution in pilot study districts in the north was completed in October 2020 (Figure MN2). Final reports on the distribution campaign results are expected from project partners in 2022.

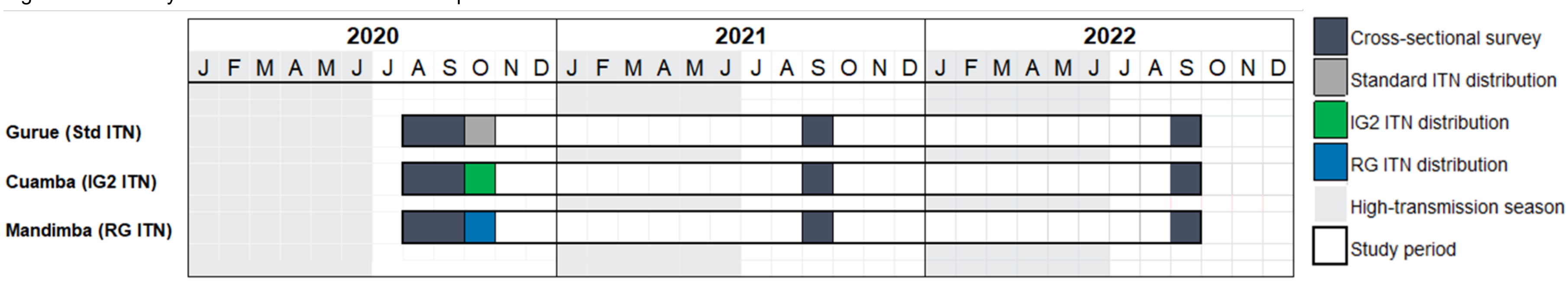
The NMCP prioritized Niassa Province for receipt of dual-AI ITNs based on a high prevalence of malaria in the under-5-year-old population estimated during the 2018 Malaria Indicator Survey, as well as suspected pyrethroid resistance in the dominant vector populations. In neighboring Zambezia Province, standard ITNs were distributed. The entire province of Niassa was initially targeted to receive IG2 ITNs; however, an opportunity to also distribute a limited number of RG ITNs was identified later in the planning cycle. Mandimba District was selected to receive RG ITNs based on having a population size that could accommodate the limited number of RG ITNs available. The three study districts were chosen for inclusion in the pilot study based on their proximity to one another as well as similar health facility case incidence rates in the District Health Information Software 2 (DHIS2) and ITN use patterns reported in the 2018 Malaria Indicator Survey.

Figure MN1. Map of the study districts in northern Mozambique.



a) ITN distribution across Mozambique; b) the three study districts.
Abbreviations: IG2, Interceptor G2; IRS, indoor residual spraying; ITN, insecticide-treated net; PBO, piperonyl butoxide.

Figure MN2. Study timeline in northern Mozambique.



Abbreviations: IG2, Interceptor G2; ITN, insecticide-treated net; RG, Royal Guard; Std, standard.

Epidemiology

Cross-sectional survey

This section has not been updated since the previous report (published in December 2021). The next round of data collection will take place in August 2022.

The baseline cross-sectional survey was conducted from August 2020 to September 2020, in advance of the ITN distribution campaigns and prior to the onset of the high-transmission season in January. The Year 1 (midline) survey was completed in September 2021, roughly 11 months after the ITN distribution campaigns. For each survey, 420 households from each district were targeted for inclusion (15 households from 28 communities within each district). In each household, one child within the ages of 6 to 59 months was selected for the prevalence survey and the head of household or primary caregiver responded to the survey.

Preliminary analysis of Year 1 data indicated that malaria infection prevalence in the under-5-year-old population was lower compared with baseline in each district regardless of the ITN type distributed, though some important differences were noted. Tables MN1, MN2, and MN3 show household and survey participant characteristics for the northern region districts from baseline through Year 1. Complete Year 1 datasets are in the final stages of cleaning, and full analyses of the Year 1 cross-sectional results will be included in the next update.

Table MN1. Survey participant/household demographic characteristics, baseline (2020) and Year 1 (2021).

	Gurue (standard ITNs)		Cuamba (IG2 ITNs)		Mandimba (RG ITNs)	
	2020	2021	2020	2021	2020	2021
Households enrolled (clusters)	425 (28)	419 (28)	411 (28)	438 (28)	427 (28)	420 (28)
Average number of household members (95% CI)	5.59 (5.37–5.80)	5.08 (4.82–5.32)	6.03 (5.74–6.31)	4.88 (4.64–5.11)	5.39 (5.17–5.62)	4.76 (4.57–4.96)
Age, % of total (n)						
≥5 years old	75.3 (1,789)	74.4 (1,583)	76.2 (1,891)	73.6 (1,572)	76.5 (1,759)	74.0 (1,480)
<5 years old	24.7 (587)	25.6 (544)	23.8 (588)	26.4 (564)	23.5 (542)	26.0 (521)
Gender, % of total (n)						
Male	48.9 (1,161)	48.5 (1,032)	50.1 (1,243)	48.9 (1,049)	50.4 (1,160)	51.5 (1,044)
Female	51.1 (1,215)	51.5 (1,097)	49.9 (1,236)	51.1 (1,098)	49.6 (1,141)	48.5 (985)
Education status of head of household, % of total (n)						
None	41.9 (178)	57.4 (236)	20.4 (84)	22.0 (96)	58.9 (252)	65.0 (273)
Primary	39.6 (168)	27.7 (114)	51.6 (212)	49.2 (215)	30.4 (130)	18.8 (79)
Secondary	14.0 (59)	12.2 (50)	23.4 (96)	24.5 (107)	9.3 (40)	15.2 (64)
Postsecondary	4.4 (19)	2.7 (11)	4.6 (19)	4.3 (19)	1.4 (6)	1.0 (4)

Abbreviations: CI, confidence interval; IG2, Interceptor G2; ITN, insecticide-treated net; RG, Royal Guard.

Household characteristics across the study districts were highly similar and exhibited good baseline comparability. While not statistically significant, survey results did suggest that there were slightly more educated households in Cuamba (IG2 district) than Gurue (standard district) and Mandimba (RG district). Subsequent results and further examination of socioeconomic indicators will provide helpful context for interpretation of the final impact assessments.

Table MN2. ITN coverage, access, and use, baseline (2020) and Year 1 (2021).

	Gurue (standard ITNs)		Cuamba (IG2 ITNs)		Mandimba (RG ITNs)	
	2020	**2021**	**2020**	**2021**	**2020**	**2021**
Average number of ITNs per house (95% CI)	0.66 (0.56–0.76)	2.43 (2.27–2.59)	0.62 (0.51–0.73)	1.79 (1.46–2.11)	0.42 (0.35–0.50)	2.06 (1.85–2.27)
Households with at least one ITN, % (95% CI)	37.4 (32.9–42.1)	96.4 (94.7–98.2)	33.3 (28.9–38.0)	74.8 (63.6–85.8)	30.2 (26.0–34.7)	90.0 (84.9–95.0)
Population that slept under a net last night, % (95% CI)	23.0 (21.3–24.7)	87.4 (82.8–90.8)	19.4 (17.9–21.0)	67.9 (57.0–77.1)	17.0 (15.5–18.6)	81.6 (74.7–87.0)
Population ITN access, % (95% CI)	23.1 (21.8–24.4)	85.7 (82.5–88.8)	21.0 (19.7–22.3)	64.8 (54.8–74.8)	16.4 (15.3–17.6)	75.5 (69.0–82.3)
Use given access*	0.99	1.02	0.92	1.05	1.03	1.08

Abbreviations: CI, confidence interval; IG2, Interceptor G2; ITN, insecticide-treated net; RG, Royal Guard.
*Use given access is calculated by dividing use (population that slept under a net last night) by access. Values over 1 are possible given that the calculation is a ratio.

While use given access was consistently high, indicating that those who had access to an ITN tended to use them, overall baseline ITN ownership and use in northern Mozambique were very low, though highly similar, across the study districts. By the time of the Year 1 survey, 11 months after the ITN distribution campaigns, net ownership, access, and use had improved dramatically in all three study districts. Indeed, the proportion of residents reported to have slept under a net the previous night increased to more than 80% in Gurue and Mandimba and to almost 70% in Cuamba.

Table MN3. Malaria prevalence by study district, baseline (2020) and Year 1 (2021).

	Gurue (standard ITNs)		Cuamba (IG2 ITNs)		Mandimba (RG ITNs)	
	2020	**2021**	**2020**	**2021**	**2020**	**2021**
Total tested	417	419	403	436	420	420
Malaria prevalence (RDT+) for under-5-year-olds, % (95% CI)	64.9 (54.8–75.0)	52.5 (42.9–61.9)	47.5 (38.1–57.0)	29.4 (20.9–39.5)	66.0 (57.5–74.4)	46.2 (38.2–54.4)
Percent prevalence reduction	**7% (−15% to 29%)**		**42% (27% to 57%)**		**29% (19% to 39%)**	

Abbreviations: CI, confidence interval; IG2, Interceptor G2; ITN, insecticide-treated net; RDT+, rapid diagnostic test positive; RG, Royal Guard.

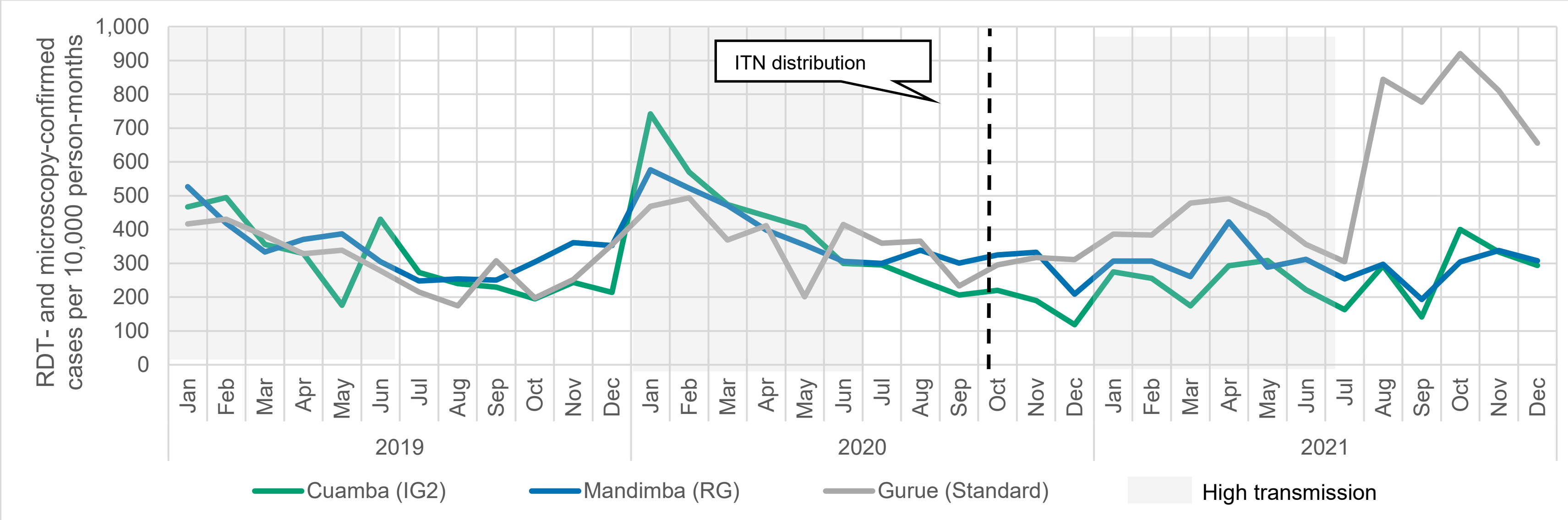
Baseline malaria prevalence in the under-5-year-old population was high in general, especially considering that this survey was conducted outside peak transmission months. Baseline malaria prevalence was similar across the study districts in the north, with values ranging from 47.5% to 66.0%. By the time of the September 2021 Year 1 survey, malaria prevalence had decreased slightly but not significantly in the standard ITN district of Gurue (7% reduction, 95% confidence interval [CI; −15% to 29%]) and decreased substantially in both the IG2 district of Cuamba (42% reduction, 95% CI [27% to 57%]) and the RG district of Mandimba (29% reduction, 95% CI [19% to 39%]). Interestingly, during the Year 1 survey, the standard ITN district of Gurue reported the highest estimated net use but noted the smallest change in malaria prevalence.

Routine health system data

These analyses have been updated to include the months of August through December 2021. Corresponding incidence and difference-in-differences calculations have been updated.

Disease incidence was calculated using passive case data from each of the study districts. Population estimates from 2017 were used as the basis for projected case incidence estimates. Malaria case data presented here were extracted in August 2021 and again in March 2022, representing DHIS2 data from January 2019 through December 2021 and reflecting trends across two high-transmission seasons prior to ITN distribution and one high-transmission season after distribution (Figure MN3 and Tables MN4 and 5).

Figure MN3. Passive incidence rates (RDT-confirmed malaria cases per 10,000 person-months at risk) in study districts in the northern evaluation, 2019–2021.



Abbreviations: IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide; RDT, rapid diagnostic test; RG, Royal Guard.

Table MN4. Malaria case incidence rates (all ages) and incidence rate ratios by study district, baseline and Year 1.

		Incidence rate (per 10,000 person-months)			Incidence rate ratio (95% CI)	
Period	**Months**	**Gurue (standard ITNs)**	**Cuamba (IG2 ITNs)**	**Mandimba (RG ITNs)**	**Cuamba (IG2 ITNs) vs. Gurue (standard ITNs)**	**Mandimba (RG ITNs) vs. Gurue (standard ITNs)**
Baseline	Nov 2019–Oct 2020	352.6	363.5	383.9	1.03 (0.77–1.39)	1.09 (0.90–1.31)
Year 1	Nov 2020–Oct 2021	493.8	236.1	290.7	0.48 (0.35–0.66)	0.59 (0.45–0.78)
Difference in incident cases	Baseline to Year 1	+141.2	−127.4	−93.3		
Percent change	Baseline to Year 1	+40.1	−35.1	−24.3		

Abbreviations: CI, confidence interval; IG2, Interceptor G2; ITN, insecticide-treated net; RG, Royal Guard.

Table MN5. Difference-in-difference comparison of next-generation ITNs to standard pyrethroid ITNs, Year 1.

	Year 1 (November–October) change from baseline (95% CI)	DiD relative to standard ITNs (95% CI)
Gurue (standard ITNs)	+40.1% (18.6% to 56.1%)	
Cuamba (IG2 ITNs)	−35.1% (−38.5% to −29.1%)	75.1% (47.6% to 94.6%)
Mandimba (RG ITNs)	−24.3% (−25.7% to −22.5%)	64.4% (41.1% to 81.8%)

Abbreviations: CI, confidence interval; DiD, difference-in-difference; IG2, Interceptor G2; ITN, insecticide-treated net; RG, Royal Guard.

The passive case surveillance data showed similar trends as those seen in the cross-sectional survey prevalence results, with good baseline comparability in the north (compared with the standard ITN district, neither the IG2 district nor the RG district had an incidence rate ratio significantly different from 1.0 before ITN distributions). Trends in all-age case incidence rates indicated that during the 12 months after the ITN distribution campaigns, the number of cases in the standard ITN district of Gurue increased by 40% compared with the previous year (494 versus 352 positive RDT test results reported per 10,000 person-months at risk). In contrast, in both Cuamba (IG2 ITNs) and Mandimba (RG ITNs), there were reductions in RDT-positive case incidence rates—a 35% reduction in Cuamba (from 364 to 236 cases per 10,000 person-months at risk) and a 24% reduction in Mandimba (from 384 to 291 cases per 10,000 person-months at risk). In Cuamba, this represented a significant 75% greater reduction in passive malaria case incidence relative to Gurue, and in Mandimba this was a significant 64% larger reduction.

Entomology

This section has been updated with entomological findings from data collected between collected between November 2020 and November 2021 (Year 1).

In northern Mozambique, entomological surveillance included paired indoor-outdoor HLCs, which were performed at three sentinel houses in three sentinel villages per study district for two consecutive nights every other month (totaling 27 paired collections per district per collection month). Mosquito larval sampling was performed annually in each district to support insecticide-resistance monitoring. Entomological surveillance activities began in November 2020. This report summarizes data collected between November 2020 and November 2021 (Year 1), roughly corresponding to the first year after ITN distribution.

Analysis of Year 1 data showed that both *An. Gambiae* s.l. and *An. Funestus* s.l. were present; this remained the case even as their relative abundance fluctuated somewhat as the first year of surveillance progressed (they were roughly equally abundant in Gurue and Mandimba, but *An.*

Funestus was not collected in Cuamba). See Table MN6 for details. Forthcoming sporozoite screening and molecular genotyping will confirm which of these species are the dominant vectors across the range of the northern Mozambique evaluation.

The first round of larval sampling and mosquito rearing and insecticide-resistance testing were completed to establish the insecticide-resistance profiles of the local vector populations. Insecticide susceptibility patterns in local *An. Gambiae* s.l. populations indicated a high level of resistance to pyrethroids across all districts, particularly to alphacypermethrin. There are historical indications that PBO pre-exposure can mitigate the resistance observed in *An. Gambiae*, with mortality increasing to greater than 85%. Based on historical vector surveillance from nearby regions, WHO tube assay mortality rates since 2017 in Zambezia and Tete have been between 60% and 85% in *An. Funestus*. The testing of *An. Gambiae* and *An. Funestus* from Mandimba for susceptibility to pyriproxyfen has been prioritized for 2022.

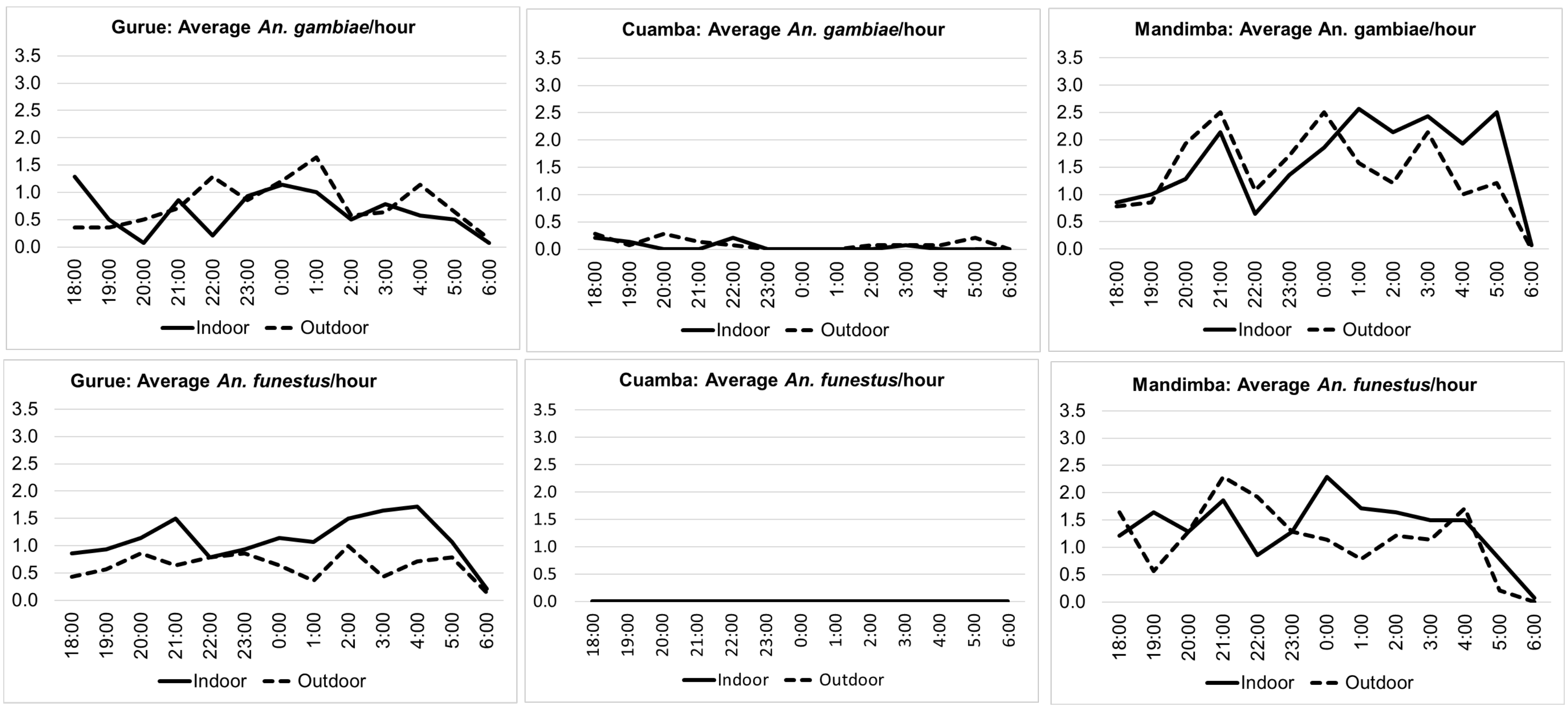
Table MN6. Baseline entomological characteristics of the study districts in northern Mozambique.

	Gurue (standard ITNs)	Cuamba (IG2 ITNs)	Mandimba (RG ITNs)
	Year 1	**Year 1**	**Year 1**
Most abundant vector (% of likely vector species collected)	*An. Funestus* s.l. (54.6%)	*An. Gambiae* s.l. (100%)	*An. Gambiae* s.l. (53.9%)
Second most abundant vector (% of all likely vectors collected)	*An. Gambiae* s.l. (44.5%)	–	*An. Funestus* s.l. (45.1%)
***An. Gambiae* molecular IDs**			
	Pending	Pending	Pending
HLC nightly landing rates (*An. Gambiae* s.l.)			
Indoor:outdoor ratio	0.84	0.5	1.1
HLC nightly landing rates (*An. Funestus* s.l.)			
Indoor:outdoor ratio	1.8	–	1.2
Pyrethroid-resistance profile	**MODERATE to HIGH: Mitigated by PBO**		
WHO tube test mortality (*An. Gambiae)*	15%–89%	54%–83%	54%–83%
WHO tube test mortality (*An. Funestus)*	60%–100% (*An. Funestus*)*		

Abbreviations: HLC, human landing collection; ID, identification; IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide; RG, Royal Guard; WHO, World Health Organization.
*Historical data, 2018 and 2019.

Figure MN4 shows Year 1 nightly biting patterns for *An. Gambiae* and *An. Funestus*. Year 1 *An. Gambiae* s.l. biting patterns showed that both indoor and outdoor biting were common, though there may have been a slight preference for indoor biting in Mandimba District. In the northern zone, *An. Gambiae* s.l. biting patterns were not that distinct, beginning before 19:00 and without an obvious peak in activity either indoors or outdoors. *An. Gambiae* s.l. biting rates were significantly higher in Mandimba; how this might affect entomological inoculation rates relative to the other districts will be clarified by forthcoming molecular analysis. *An. Funestus* s.l. biting patterns in Gurue and Mandimba showed a preference for indoor biting, though this preference was strongest in Gurue. The biting patterns of *An. Funestus* s.l. remained relatively constant throughout the evening, night, and early morning, decreasing rapidly at 6:00 in both districts. Further refining these mosquitoes feeding characteristics and aligning results with human behavior patterns will provide valuable context for interpreting the final results on the impact of the ITN distributions on malaria transmission—in particular, what may be a tendency toward early evening biting.

Figure MN4. Nightly biting patterns for *An. Gambiae* s.l. and *An. Funestus s.l.* across the northern region to date, estimated from human landing collections from November 2020 through November 2021.



Human behavior

This section has been updated with a brief description of activities to date. Analysis will be updated in the final report, which will be published in early 2023.

Nighttime observations of peridomestic activities and net use began in October 2021 in Cuamba and Mandimba. Observations occurred in eight households in each district. Observations accompanying HLCs also began in September 2021 and are ongoing. Analysis of observations is currently underway. Fourteen FGDs were conducted with eight participants each. In one village, miscommunication resulted in one FGD with 16 participants rather than two groups of 8 (Table MN7). Coding of the FGD transcripts is complete and analysis is in progress.

Table MN7. Number of households and participants by human behavior data collection activity, 2021.

	Number of households or participants
Structured observations (households)	16
HLC-based observations (households)	54
Focus group discussions (participants)	128

Abbreviation: HLC, human landing collection.

Durability monitoring

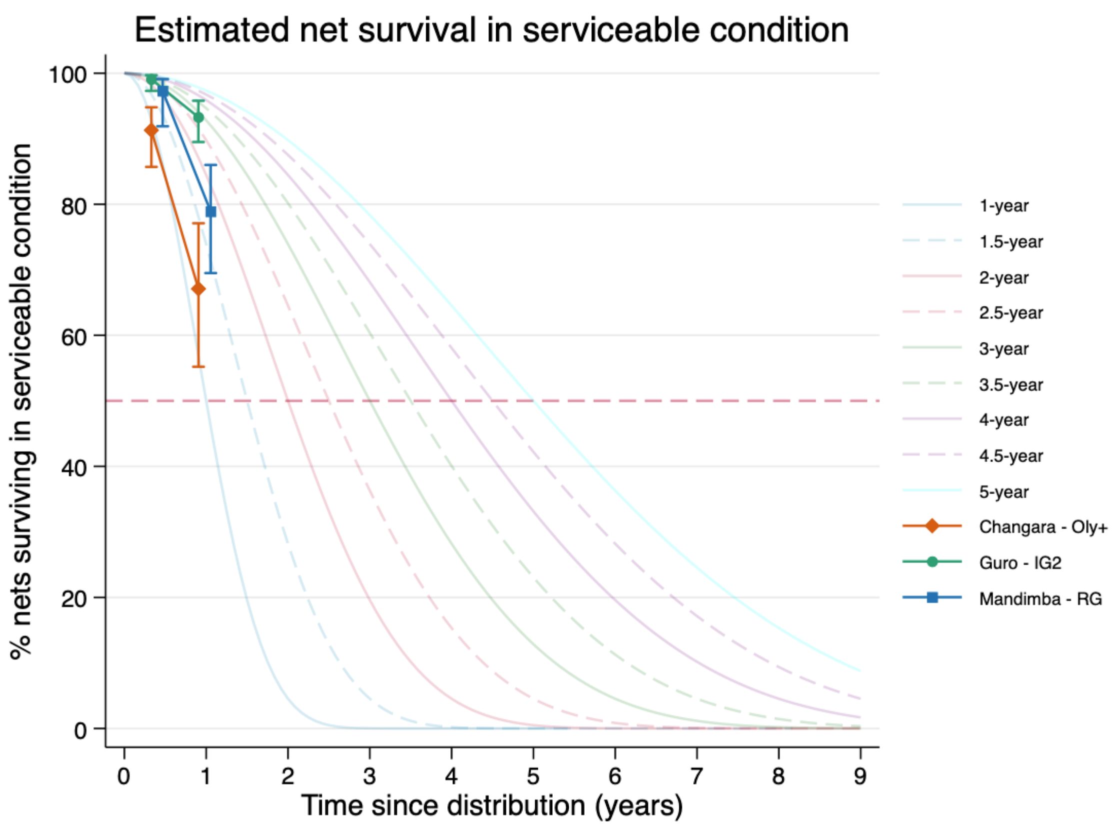
This section has been updated to include summary findings from the October 2021 12-month data collection in Northern and Western Mozambique.

Field activities for the baseline durability monitoring were completed in March 2021, and the 12-month assessment took place in October 2021. Bioassay net collection occurred in Gurue in November 2021. In all, 1,035 campaign nets from 450 households across three districts were identified for the durability monitoring cohort.

The proportion of nets that were reportedly used the previous night was 76% in Guro, 66% in Mandimba, and 42% in Changara. A total of 12.0% of ITNs were still in their packages at 12 months, down from 20.8% at baseline. Hanging rates were high in Guro (75%) and Mandimba (72%), but in Changara only 44% of ITNs were hanging. Most used nets were used consistently throughout the week, and 95% of households reported using their ITNs in both rainy and dry seasons. Nets from other sources continued to be limited at 12 months. The most common other sources were previous campaigns of ANC visits.

At the 12-month assessment, 62% of nets in Mandimba, 78% in Guro, and 53% in Changara were determined to be "in good condition" based on the proportionate Hole Index. About a third of nets in Changara, 7% in Guro, and 21% in Mandimba were too torn to be useful. Combining these results with the attrition rate resulted in estimates for the survival of campaign nets in serviceable condition after 12 months of 67% in Changara, 93% in Guro, and 79% in Mandimba (Figure MN5).

Figure MN5. Estimated net survival in serviceable condition with 95% error bars plotted against hypothetical survival curves with defined median survival.



Full durability monitoring reports are available upon request for the baseline and 12-month assessments. Baseline and 12-month bioassay testing of nets was completed in collaboration with the Centre de Recherches Entomologiques de Cotonou in Benin, West Africa. These results will be available in future reports.

Summary

Results of this interim analysis indicated that the ITN distribution campaign of 2020 successfully and dramatically increased net ownership and use across all study districts. Results also suggested that after 11 months, districts that distributed one of the new net types—either IG2 or RG—saw significantly larger decreases in malaria transmission relative to the control district that distributed standard pyrethroid-only ITNs (75% greater reduction in the IG2 district; 64% greater reduction in the RG district). Also of note, the largest reductions in prevalence (42%) and incidence (75%) to date were observed in the IG2 district of Cuamba, which also reported the lowest rates of ITN ownership and use (75% and 68%, respectively), suggesting an important community effect for IG2 relative to standard nets. Data collection for costing should be completed by the second quarter of 2022, and preliminary work on the cost-effectiveness analyses will begin shortly thereafter.

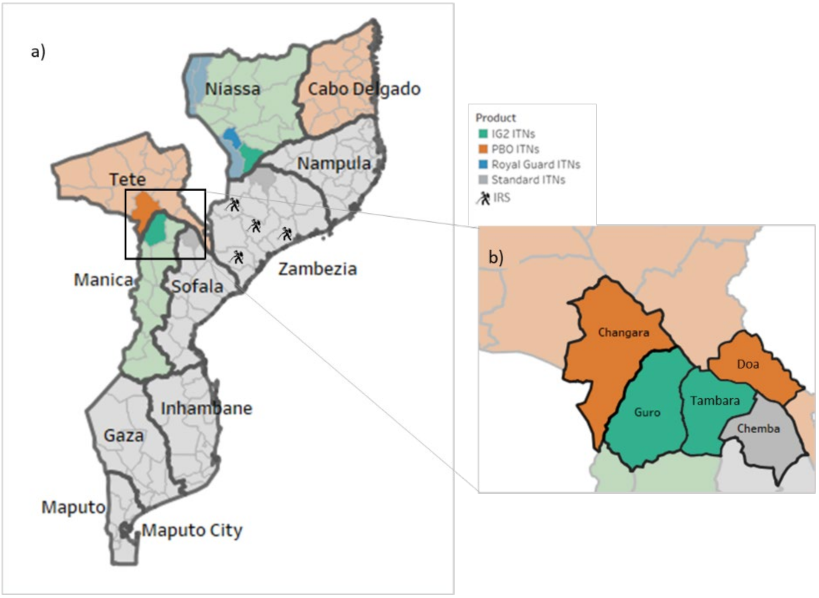
Western Mozambique

The western Mozambique evaluation began in September 2020. It has been conducted in Chemba District (standard ITNs) in Sofala Province, Guro District (IG2 ITNs) in Manica Province, and Changara District (PBO ITNs) in Tete Province (Figure MW1). The high-transmission season occurs in western Mozambique from January through June. Baseline activities were scheduled to begin in March 2020; however, the NMCP suspended activities and study preparations in March 2020 due to COVID-19. Pandemic mitigation policies and procedures were in place by June 2020, and all critical activities resumed in July 2020. ITN distribution in western evaluation districts was completed in November 2020 (Figure MW2). Final reports on the distribution campaign results are expected from project partners in late 2021.

After the baseline cross-sectional survey results indicated less than expected comparability among the study districts in terms of underlying malaria prevalence, the decision was made to include two auxiliary districts in the passive case surveillance component of the pilot study in western Mozambique—Doa (a district in Tete Province that received PBO ITNs) and Tambara (a district in Manica Province that received IG2 ITNs).

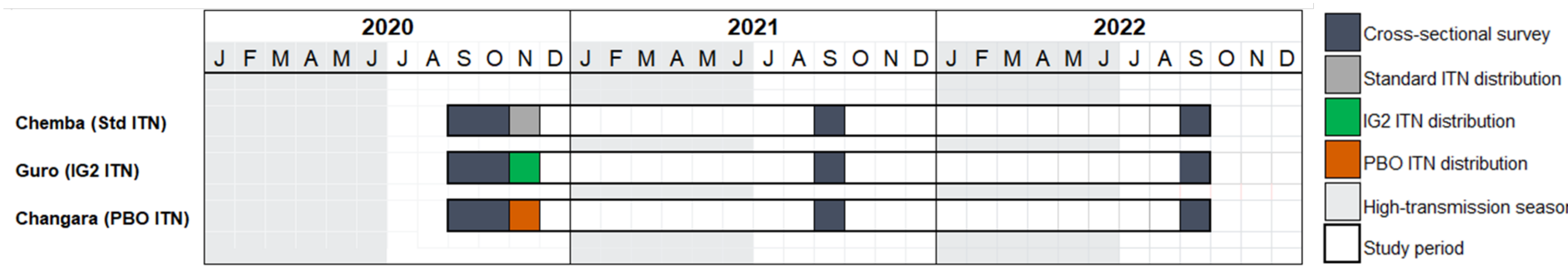
The NMCP prioritized Manica Province for receipt of IG2 ITNs based on a high prevalence of malaria in the under-5-year-old population that was estimated during the 2018 Malaria Indicator Survey, as well as suspected pyrethroid resistance in the dominant vector populations. Neighboring Sofala Province was targeted for standard ITN distribution. The opportunity to also distribute some PBO ITNs was identified, and NMCP leadership prioritized their distribution in Tete Province. The three study districts were chosen for inclusion in the pilot study based on their proximity to one another as well as similar health facility case incidence rates in the DHIS2 and ITN use patterns reported in the 2018 Malaria Indicator Survey; these conditions were also met by the newly added passive surveillance districts of Doa and Tambara.

Figure MW1. Map of the study districts in western Mozambique.



a) ITN distribution across Mozambique; b) the three study districts and the two auxiliary districts in the passive case surveillance component (Doa and Tambara). Abbreviations: IG2, Interceptor G2; IRS, indoor residual spraying; ITN, insecticide-treated net; PBO, piperonyl butoxide.

Figure MW2. Study timeline in western Mozambique.



Abbreviations: IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide; Std, standard.

Epidemiology

Cross-sectional survey

This section has not been updated since the previous report (published in December 2021). The next round of data collection will take place in September 2022.

The baseline cross-sectional survey was conducted from September to October 2020, in advance of the ITN distribution campaigns and prior to the onset of the high-transmission season in January. The Year 1 (midline) survey was completed in September 2021, roughly ten months after the ITN distribution campaigns. For each survey, 420 households in each district were targeted for inclusion (15 households from 28 communities within each district). In each household, one child within the ages of 6 to 59 months was selected for the prevalence survey and the head of household or primary caregiver responded to the survey.

Preliminary analysis of Year 1 data indicated that malaria infection prevalence in the under-5-year-old population was lower compared with baseline in each district regardless of the ITN type distributed, though some important differences were noted. Tables MW1, MW2, and MW3 show household and survey participant characteristics for the western Mozambique districts from baseline through Year 1.

Table MW1. Survey participant/household demographic characteristics, baseline (2020) and Year 1 (2021).

	Chemba (standard ITNs)		Guro (IG2 ITNs)		Changara (PBO ITNs)	
	2020	**2021**	**2020**	**2021**	**2020**	**2021**
Households enrolled (clusters)	418 (28)	421 (28)	420 (28)	420 (28)	417 (28)	420 (28)
Average number of household members (95% CI)	5.61 (5.44–5.78)	6.05 (5.60–6.51)	5.26 (5.02–5.50)	5.12 (4.82–5.41)	5.30 (5.06–5.54)	4.94 (4.75–5.12)
Age, % of total (n)						
<5 years old	75.4 (1,768)	76.0 (1,938)	76.8 (1,697)	75.4 (1,621)	76.4 (1,689)	74.9 (1,552)
≥5 years old	24.6 (577)	24.0 (611)	23.2 (512)	24.6 (529)	23.6 (521)	25.1 (521)
Gender, % of total (n)						
Male	50.4 (1,182)	47.4 (1,218)	50.9 (1,124)	49.4 (1,075)	49.2 (1,087)	48.6 (1,018)
Female	49.6 (1,163)	52.6 (1,353)	49.1 (1,085)	50.6 (1,103)	50.8 (1,123)	51.4 (1,078)
Education status of head of household, % of total (n)						
None	46.4 (194)	44.6 (187)	34.3 (144)	44.3 (186)	26.4 (110)	21.4 (78)
Primary	33.5 (140)	41.3 (173)	47.1 (198)	43.1 (181)	47.6 (198)	61.6 (217)
Secondary	17.9 (75)	12.4 (52)	17.6 (74)	12.1 (51)	21.6 (90)	17.0 (62)
Postsecondary	2.2 (9)	1.7 (7)	1.0 (4)	0.5 (2)	4.3 (18)	2.2 (8)

Abbreviations: CI, confidence interval; IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide.

Household characteristics across the study districts were highly similar and exhibited good baseline comparability. Subsequent results and further examination of socioeconomic indicators will provide helpful context for interpretation of the final impact assessments.

Table MW2. ITN coverage, access, and use, baseline (2020) and Year 1 (2021).

	Chemba (standard ITNs)		Guro (IG2 ITNs)		Changara (PBO ITNs)	
	2020	**2021**	**2020**	**2021**	**2020**	**2021**
Average number of ITNs per house (95% CI)	0.86 (0.78–0.94)	3.08 (2.77–3.39)	0.49 (0.40–0.57)	2.51 (2.35–2.67)	0.71 (0.62–0.79)	2.32 (2.18–2.46)
Households with at least one ITN, % (95% CI)	63.2 (58.4–67.7)	98.8 (97.4–100.0)	30.7 (26.5–35.3)	97.9 (96.2–99.5)	48.2 (43.4–53.0)	96.1 (93.4–99.0)
Population that slept under a net last night, % (95% CI)	33.3 (32.1–34.7)	90.1 (87.1–92.4)	18.5 (17.2–19.8)	92.8 (90.4–94.7)	23.0 (21.8–24.2)	84.6 (80.5–88.0)
Population ITN access, % (95% CI)	30.4 (29.3–31.6)	86.0 (82.0–90.1)	18.8 (17.5–20.1)	88.9 (86.8–91.1)	26.3 (24.9–27.6)	84.2 (81.1–87.3)
Use given access*	1.10	1.05	0.98	1.04	0.88	1.00

Abbreviations: CI, confidence interval; IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide.
*Use given access is calculated by dividing use (population that slept under a net last night) by access. Values over 1 are possible given that the calculation is a ratio.

Despite high use given access, differences were noted in baseline net ownership and use across study districts in western Mozambique, with the standard ITN district of Chemba reporting greater household ownership and use of ITNs. This trend was not consistent in the Year 1 survey, however, as net ownership, access, and use improved dramatically in all three study districts after the 2020 distribution campaign. Indeed, the proportion of residents reported to have slept under a net the previous night increased to more than 80% in all districts.

Table MW3. Malaria prevalence by study district, baseline (2020) and Year 1 (2021).

	Chemba (standard ITNs)		Guro (IG2 ITNs)		Changara (PBO ITNs)	
	2020	**2021**	**2020**	**2021**	**2020**	**2021**
Total tested	415	421	420	420	414	420
Malaria prevalence (RDT+) for under-5-year-olds, % (95% CI)	44.3 (36.5–52.1)	39.0 (31.3–47.2)	17.1 (11.6–22.7)	3.8 (2.2–6.7)	5.7 (2.3–9.1)	2.1 (0.8–5.4)
Percent prevalence reduction	**12% (−6 to 29%)**		**66% (40 to 92%)**		**67% (43 to 90%)**	

Abbreviations: CI, confidence interval; IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide; RDT+, rapid diagnostic test positive.

Underlying malaria prevalence in the under-5-year-old population was significantly different across study districts. Interestingly, at baseline, the standard ITN district of Chemba reported the highest levels of ITN ownership and use but had the highest malaria prevalence in the region. During the Year 1 survey in September 2021, malaria prevalence decreased slightly, but not significantly, in Chemba (12% reduction, 95% CI [−6% to 29%]). However, malaria prevalence decreased substantially in both the IG2 district of Guro (66% reduction, 95% CI [−40% to 92%]) and the PBO district of Changara (7% reduction, 95% CI [43% to 90%]) despite significant differences in their baseline prevalence measurements.

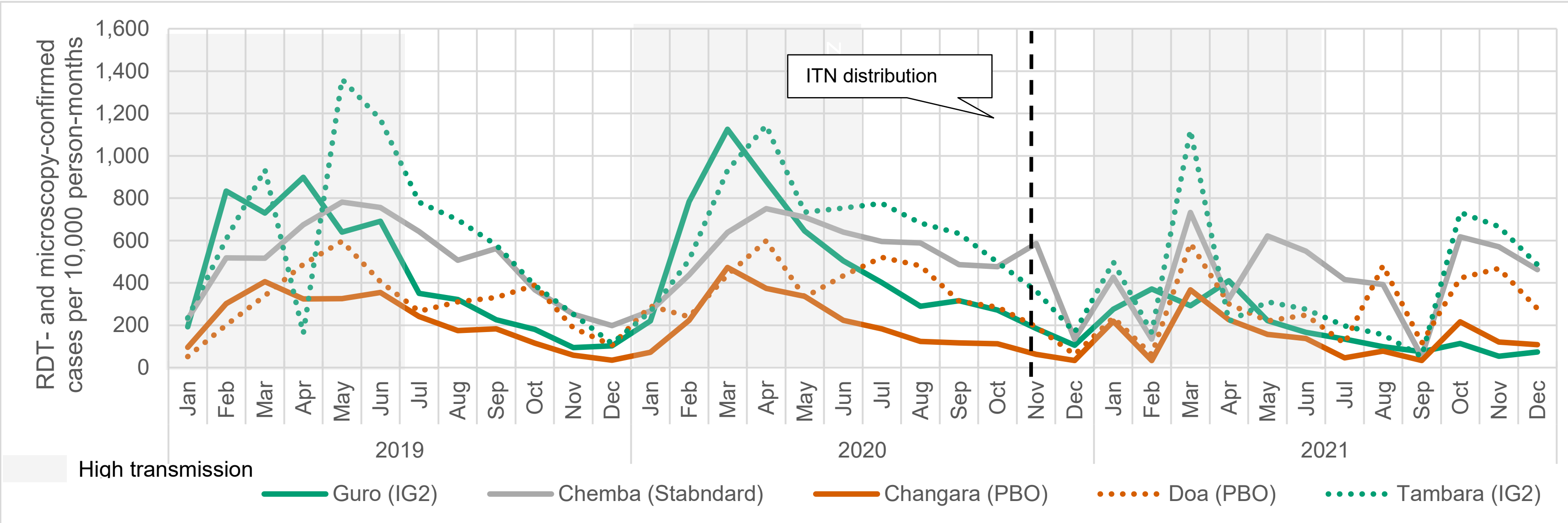
As previously described, there were concerns after the baseline surveys that the western Mozambique evaluation may have been underpowered to detect the expected levels of impact due to higher than expected variability in underlying malaria burdens across study districts and lower than expected malaria prevalence in the IG2 and PBO districts. This interim report considers only the initial analysis of Year 1 data; however, the magnitude of changes in malaria prevalence following the IG2 and PBO distribution campaigns is such that significant differences relative to the standard ITN are apparent. The additional passive surveillance ongoing in Doa and Tambara is expected to strengthen these comparisons. These analyses will be updated through 2022 and detailed in the final report.

Routine health system data

This section has been updated to include monthly incidence through December 2021. Corresponding incidence and difference-in-differences calculations have been updated.

Disease incidence was calculated using passive case data from each of the study districts. Population estimates from the 2017 national census conducted by the National Institute of Statistics were used as the basis for projected case incidence estimates. Malaria case data presented here were extracted in September 2021 and March 2022, representing DHIS2 data from January 2019 through December 2021, which encompass one low-transmission and two high-transmission seasons after ITN distribution (Figure MW3, Table MW4).

Figure MW3. Passive incidence rates (RDT-confirmed malaria cases per 10,000 person-months at risk) in study districts in western Mozambique, 2019–2021.



Abbreviations: IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide; RDT, rapid diagnostic test; RG, Royal Guard.

Table MW4. Malaria case incidence rates (all ages) and incidence rate ratios by study district, baseline and Year 1.

		Incidence rate (per 10,000 person-months)							**Incidence rate ratio (95% CI)**	
Period	Months	**Chemba (standard ITNs)**	**Guro (IG2 ITNs)**	**Tambara (IG2 ITNs)**	**Overall IG2**	**Changara (PBO ITNS)**	**Doa (PBO ITNs)**	**Overall (PBO ITNs)**	**Overall IG2 vs. standard**	**Overall PBO vs. standard**
Baseline	Dec 2019–Nov 2020	531.2	477.0	616.6	**546.8**	194.8	352.6	**273.7**	1.03 (0.78–1.36)	0.51 (0.39–0.69)
Year 1	Dec 2020–Nov 2021	414.4	193.3	379..9	**286.6**	139.3	276.2	**207.8**	0.69 (0.44–1.09)	0.50 (0.33–0.76)
Difference in incident cases	Baseline–Year 1	−116.8	−283.7	−236.76	**−260.2**	−55.5	−76.4	**−66.0**		
Percent change	Baseline–Year 1	−22.0%	−59.5%	−38.4%	**−47.6%**	−28.5%	−21.7%	**−24.1%**		

Abbreviations: CI, confidence interval; IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide.

Passive case surveillance data showed similar trends as those seen in the baseline cross-sectional survey prevalence results, with disproportionately low incidence rates reported in Changara (note the incidence rate ratio significantly less than 1.0 in Table MW4). This provided further incentive to expand passive surveillance data quality assessment activities into Doa District in Tete Province, which received PBO ITNs, and Tambara District in Manica Province, which received IG2 ITNs. The addition of these districts did improve the baseline comparability. Trends in all-age case incidence rates indicated that during the 12 months after the ITN distribution campaigns, the number of cases in the standard ITN district of Chemba decreased by 22% compared with the previous year (414 versus 531 positive RDT test results reported per 10,000 person-months at risk). Rates decreased by a similar magnitude (24%) in the PBO districts of Changara and Doa, from 274 to 208 positive RDT test results reported per 10,000 person-months at risk. In the IG2 districts of Guro and Tambara, however, malaria case rates showed a significant 26% larger reduction—from 547 to 287 cases per 10,000 person-months at risk (Table MW5).

Table MW5. Difference-in-difference comparison of next-generation ITNs with standard pyrethroid ITNs, Year 1.

	Year 1 (January–June) change from baseline (95% CI)	DiD relative to standard ITNs (95% CI)
Chemba (standard ITNs)	−22.0% (−34.1% to −13.7%)	
Guro (IG2 ITNs)	−59.5% (−60.3% to −57.6%)	25.6% (22.5% to 28.2%)
Tambara (IG2 ITNs)	−38.4% (−57.0% to −27.9%)	
Changara (PBO ITNS)	−28.5% (−31.4% to −27.3%	2.1% (2.6% to 5.8%)
Doa (PBO ITNs)	−21.7% (−36.3% to −12.8%)	

Abbreviations: CI, confidence interval; DiD, difference-in-difference; IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide.

Entomology

This section has been updated with entomological findings from data collected between collected between November 2020 and November 2021 (Year 1).

In western Mozambique, entomological surveillance included paired indoor-outdoor HLCs, which were performed at three sentinel houses in three sentinel villages per study district for two consecutive nights every other month (totaling 27 paired collections per district per collection month). Mosquito larval sampling was performed annually in each district by the NMCP to support insecticide-resistance monitoring. Entomological surveillance activities began in November 2020. These results summarize data collected between November 2020 and November 2021 (Year 1), roughly corresponding to the first year after ITN distribution.

Analysis of Year 1 data showed that *An. gambiae* s.l. was present across all study districts in western Mozambique and was the only species collected in Guro and Changara. *An. funestus* s.l. was also present in the standard ITN district of Chemba and accounted for the majority of collected species there. See Table MW6 for details. It was expected that *An. funestus* s.l. would be the primary vector species in both zones, but forthcoming sporozoite screening and molecular genotyping will confirm if this is consistent across each of the study districts.

The first round of larval sampling and mosquito rearing and insecticide-resistance testing were completed to establish insecticide-resistance profiles of the local vector populations. Insecticide susceptibility patterns in local *An. gambiae* s.l. populations indicated some level of resistance to pyrethroids across all districts, though resistance was much stronger in Sofala near Chemba District, where WHO tube assay mortality ranged from 17% to 53%. There are historical indications that PBO pre-exposure can mitigate the resistance observed in *An. gambiae*, with mortality increasing to greater than 85%. Based on historical vector surveillance from nearby regions, WHO tube assay mortality rates for *An. funestus* have been between 60% and 85% in Zambezia and Tete since 2017.

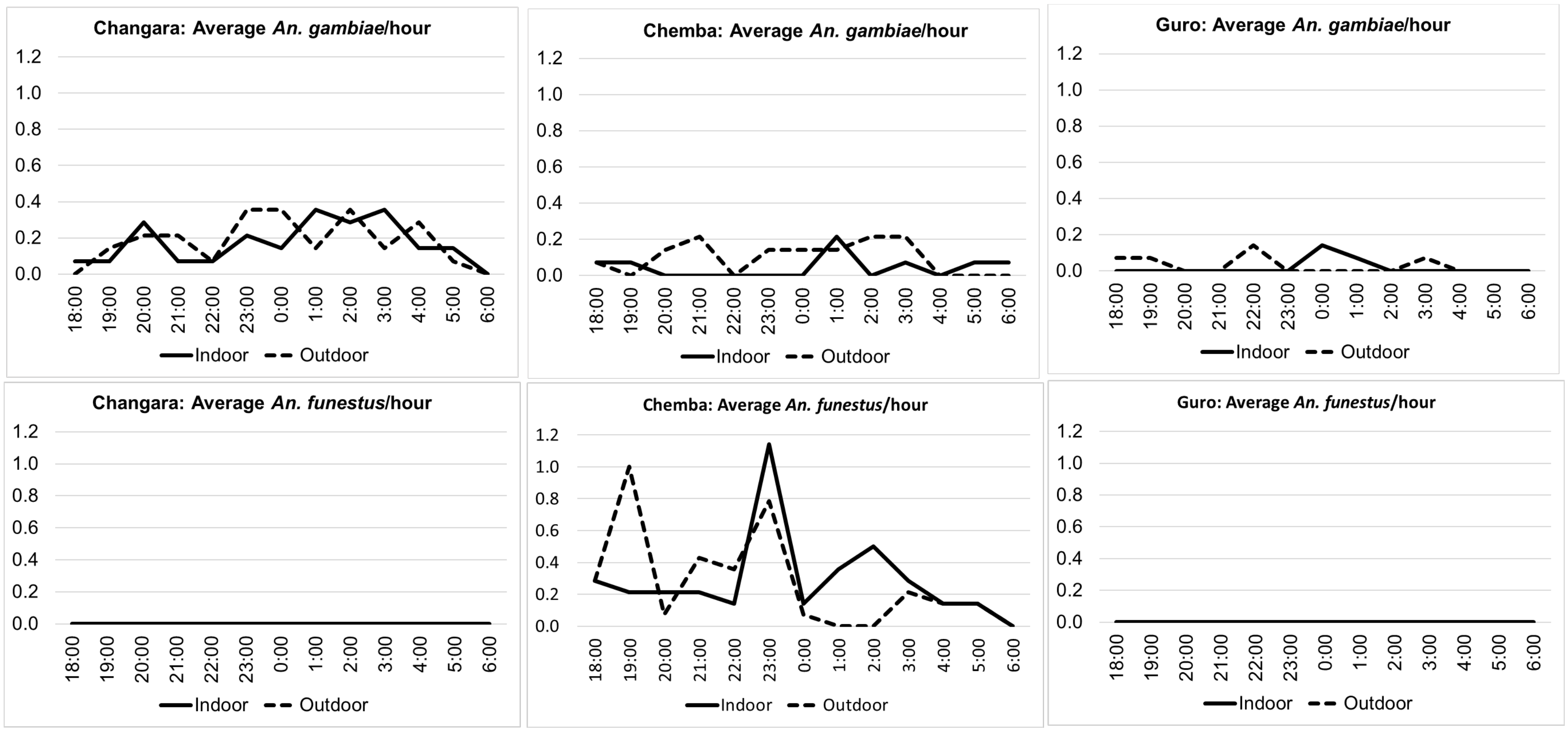
Table MW6. Baseline entomological characteristics of the study regions in western Mozambique.

	Chemba (standard ITNs)	Guro (IG2 ITNs)	Changara (PBO ITNs)
	Year 1	**Year 1**	**Year 1**
Most abundant vector (% of all likely vectors collected)	*An. funestus* s.l. (79.7%)	*An. gambiae* s.l. (100.0%)	*An. gambiae* s.l. (100.0%)
Second most abundant vector (% of all likely vectors collected)	*An. gambiae* s.l. (20.31%)	–	–
***An. gambiae* molecular IDs**			
Pending	Pending	Pending	Pending
HLC nightly landing rates (*An. gambiae* s.l.)			
Indoor:outdoor ratio	0.4	0.6	0.94
HLC nightly landing rates (*An. funestus* s.l.)			
Indoor:outdoor ratio	1.1	–	–
Pyrethroid-resistance profile	**MODERATE to HIGH: Mitigated by PBO**		
WHO tube test mortality (*An. gambiae)*	17%–53%	88%	92%
WHO tube test mortality (*An. funestus)*	60%–100% (*An. funestus*)*		

Abbreviations: HLC, human landing collection; ID, identification; IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide; WHO, World Health Organization.
*Historical data, 2018 and 2019.

Figure MW4 shows nightly biting patterns for *An. gambiae* and *An. funestus*. Year 1 data on indoor and outdoor biting patterns of *An. gambiae* s.l. showed a preference for outdoor biting in all three study districts, though this was strongest in Chemba. *An. gambiae* biting rates were relatively low, always less than 0.4 per hour across all districts, but they were sustained throughout the collection period. Additionally, *An. gambiae* s.l. biting rates were highest in Changara compared with either Guro or Chemba. In Chemba, the only district where *An. funestus* s.l. was found, indoor and outdoor biting rates were relatively similar, with a pronounced peak occurring at 23:00 both indoors and outdoors. How this might affect entomological inoculation rates relative to the other districts will be clarified by forthcoming molecular analysis. Further refining these mosquito feeding characteristics and aligning results with human behavior patterns will provide valuable context for interpreting the final results on the impact of the ITN distributions on malaria transmission.

Figure MW4. Nightly biting patterns for *An. gambiae* s.l. across western Mozambique to date, estimated from human landing collections from November 2020 through November 2021.



Human behavior

This section has been updated with a brief description of activities to date. Analysis will be updated in the final report, which will be published in early 2023.

Nighttime observations of peridomestic activities and net use began in October 2021 in Guro and Changara. Observations occurred in four households in each district. Observations accompanying HLCs also began in October 2021 and are ongoing. Analysis of observations is currently underway. Fourteen FGDs were conducted with eight participants each. In one village, miscommunication resulted in one FGD with 16 participants rather than two discussions with 8 participants each (Table MW7). Coding of the FGDs is complete and analysis is in progress.

Table MW7. Number of households and participants by human behavior data collection activity, 2021.

	2021
Structured observations (households)	8
HLC-based observations (households)	27
Focus group discussions (participants)	128

Abbreviation: HLC, human landing collection.

Durability monitoring

Results from the 12-month durability monitoring can be found in the Northern Mozambique section.

Summary

Results of this interim analysis indicated that the ITN distribution campaign of 2020 successfully and dramatically increased net ownership and use across all study districts, and that malaria prevalence also declined in each study district—though the reductions were greatest in Guro (IG2 district) and Changara (PBO district). Results also showed that, after ten months, districts that distributed IG2 nets saw larger decreases in malaria transmission relative to the control district that distributed standard pyrethroid-only ITNs (a 26% greater reduction); reductions in transmission were similar in the standard ITN and PBO districts. Data collection for costing should be completed by the second quarter of 2022, and preliminary work on the cost-effectiveness analyses will begin shortly thereafter.

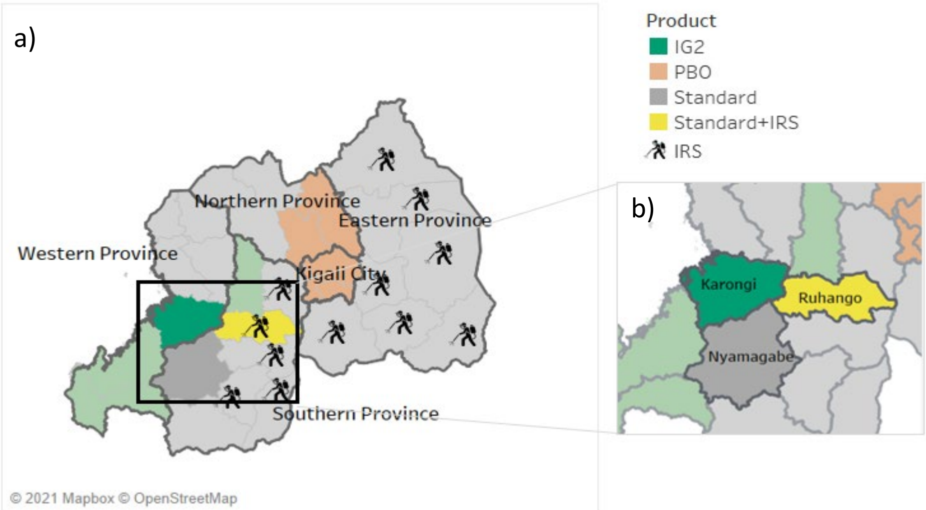
Rwanda

The Rwanda evaluation began in February 2020. It has taken place in three districts: Nyamagabe (standard ITNs), Ruhango (standard ITNs + IRS), and Karongi (IG2 ITNs) (Figure R1). There are two malaria transmission seasons in Rwanda, the smaller one occurring from May to June and the larger one occurring from November to early January.

The 2020 mass ITN distribution campaign dates varied by district: standard ITNs were distributed first in Nyamagabe and Ruhango in February 2020, and IG2 ITNs were distributed in Karongi in June 2020. IRS with Fludora® Fusion was also implemented in Ruhango in October 2019 andNovember 2020, and in October 2021 with Actellic®. Implementation of IRS is planned again for November 2022 (Figure R2). A second ITN distribution campaign took place in Nyamagabe in June 2022, and additional campaigns are planned for Ruhango and Karongi in July.

Rwanda's central health implementation agency, the Rwanda Biomedical Centre, with support from international donors, chose where to distribute various net types. In the higher-burden districts of the south and east, standard pyrethroid nets were distributed along with implementation of IRS. In and around the capital city of Kigali, PBO ITNs were distributed. The remaining districts were allocated either IG2 ITNs or standard ITNs. The pilot evaluation districts were selected based on their geographic proximity to each other. Given that PBO ITNs were distributed in a noncomparable geographic area of the country, it was decided to not incorporate PBO ITN districts in the analysis.

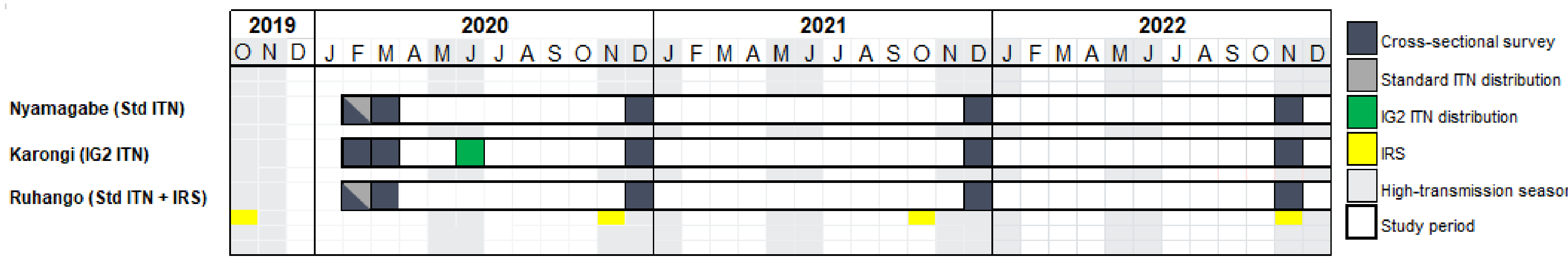
Figure R1. Map of study districts in Rwanda.



a) ITN distribution across five regions of Rwanda; b) the three study districts.

Abbreviations: IG2, Interceptor G2; IRS, indoor residual spraying; ITN, insecticide-treated net; PBO, piperonyl butoxide.

Figure R2. Insecticide-treated net distribution and transmission timeline.



Abbreviations: IG2, Interceptor G2; IRS, indoor residual spraying; ITN, insecticide-treated net; Std, standard.

Epidemiology

Cross-sectional survey

This section has been updated with results from the Year 2 survey conducted in November 2021.

The baseline cross-sectional survey was conducted from February 24 to March 13, 2020, during low malaria transmission to capture a baseline measurement prior to the ITN distribution. The target date of subsequent surveys was shifted to December to align with the high-transmission season. The second cross-sectional survey (referred to as the Year 1 survey) occurred from December 3 to 18, 2020. As a result, the Year 1 parasite prevalence measures were not directly comparable with the initial baseline measures given the likelihood that any changes were more indicative of the temporal change in malaria transmission rather than of the absolute change that could be attributable to the intervention. The Year 2 survey took place from November 4 to 19, 2021, serving as a better comparison for the Year 1 survey. The Year 3 survey will take place in November 2022 and will occur after the next ITN mass distribution campaign – which has been moved forward more than six months because of shifting NMCP strategies. While therefore not serving as a comparator for the Year 1 and 2 surveys, this final survey may provide relevant data to help RBC understand how more frequent mass campaigns might affect ITN coverage and use metrics. For each survey, 150 households were selected in each district, totaling 450 households across all three districts. The head of household was asked to respond to the household survey, and all eligible household members 6 months of age or older were consented and asked to test for malaria by RDT.

Table R1 shows that household demographics were mostly similar across districts and surveys. Household members 15 years of age and older represented most of the population, and there were more female household members than male. Most participants either had no formal education or had primary education.

Table R1. Participant/household demographic characteristics, February 2020, December 2020, and November 2021.

	Nyamagabe (standard ITNs)			Karongi (IG2 ITNs)			Ruhango (standard ITNs + IRS)		
	Feb 2020	**Dec 2020**	**Nov 2021**	**Feb 2020**	**Dec 2020**	**Nov 2021**	**Feb 2020**	**Dec 2020**	**Nov 2021**
Households enrolled (clusters)	150 (10)	150 (10)	150 (10)	150 (10)	150 (10)	150 (10)	150 (10)	150 (10)	150 (10)
Average number of household members (95% CI)	4.18 (3.87–4.49)	4.41 (4.10–4.73)	4.58 (4.24-4.92)	4.28 (3.99–4.57)	4.51 (4.16–4.85)	4.26 (3.96–4.56)	4.54 (4.21–4.87)	4.03 (3.74–4.33)	3.95 (3.67–4.24)
Age, % of total (n)									
≤5 years old	15.00 (94)	15.00 (99)	15.60 (107)	13.10 (84)	16.90 (114)	14.20 (91)	14.70 (100)	14.90 (90)	13.66 (81)
6–14 years old	20.30 (127)	23.40 (155)	22.45 (154)	26.90 (173)	28.90 (195)	22.93 (147)	22.00 (150)	23.80 (144)	22.26 (132)
≥15 years old	64.80 (406)	61.30 (406)	61.95 (425)	60.00 (385)	54.10 (366)	62.87 (403)	63.10 (430)	60.70 (367)	64.08 (380)
Gender, % of total (n)									
Male	48.50 (304)	44.00 (291)	46.72 (321)	45.30 (291)	45.30 (306)	47.58 (305)	46.70 (318)	47.40 (287)	46.04 (273)
Female	51.50 (323)	56.00 (371)	53.28 (366)	54.70 (351)	54.70 (370)	52.42 (336)	53.30 (363)	52.60 (318)	53.96 (320)
Education status of head of household, % of total (n)									
None	47.30 (71)	41.30 (62)	41.33 (62)	44.00 (66)	47.30 (71)	50.00 (75)	38.00 (57)	36.70 (55)	27.33 (41)
Primary/IGA	42.70 (64)	49.30 (74)	49.33 (74)	52.00 (78)	50.00 (75)	44.66 (67)	56.00 (84)	60.00 (90)	64.67 (97)
Junior/senior secondary/technical	8.00 (12)	8.70 (13)	7.33 (11)	4.00 (6)	2.70 (4)	4.67 (7)	6.00 (9)	3.33 (5)	8.00 (12)
Postsecondary	2.00 (3)	0.67 (1)	2.00 (3)	0.00 (0)	0.00 (0)	0.67 (1)	0.00 (0)	0.00 (0)	0.00 (0)

Abbreviations: CI, confidence interval; IGA, Ikigo Gihugura Abaturage/center for villagers' training; IG2, Interceptor G2; IRS, indoor residual spraying; ITN, insecticide-treated net.

Nyamagabe and Ruhango (standard ITN districts) received their mass distribution of ITNs in February 2020, the same month as the baseline survey. Karongi (IG2 district) received its campaign nets later in June 2020. A postcampaign distribution report drafted by the Rwanda Biomedical

Centre showed household coverage to be 103.8% in Nyamagabe, 95.5% in Karongi, and 104.4% in Ruhango. Karongi had not received its campaign nets at the time of the baseline survey; therefore, its results reflected the number of ITNs per household prior to distribution. In contrast, Nyamagabe and Ruhango had already received their campaign nets at the time of the survey. Household ownership was lowest in Karongi during the baseline survey at 89%, though this increased to 95% for the Year 1 survey and was down to 90% for the Year 2 survey. During the Year 1 survey, population ITN access was above 80% in all three districts, as was ITN use given access. During the Year 2 survey, population ITN access decreased across all districts, ranging from 65.50% in Nyamagabe to 78.32% in Karongi. See Table R2 for details.

Table R2. ITN coverage, access, and use, February 2020, December 2020, and November 2021.

	Nyamagabe (standard ITNs)			Karongi (IG2 ITNs)			Ruhango (standard ITNs + IRS)		
	Feb 2020	**Dec 2020**	**Nov 2021**	**Feb 2020**	**Dec 2020**	**Nov 2021**	**Feb 2020**	**Dec 2020**	**Nov 2021**
Average number of ITNs per house (95% CI)	2.45 (2.21–2.70)	2.27 (2.03–2.51)	2.02 (1.84–2.20)	2.64 (2.37–2.91)	2.37 (2.17–2.56)	2.20 (2.04–2.35)	2.87 (2.62–3.12)	2.35 (2.18–2.53)	1.94 (1.79–2.10)
Households with at least one ITN, % (95% CI)	93.30 (88.10–96.80)	96.00 (91.50–98.50)	83.33 (76.39–88.91)	89.30 (83.30–93.80)	95.30 (90.60–98.10)	90.00 (84.04–94.29)	94.70 (89.80–97.70)	98.00 (94.30–99.60)	94.00 (88.92–97.22)
Population that slept under a net last night, % (95% CI)	70.50 (66.80–74.00)	68.70 (65.00–72.20)	56.90 (53.11–60.65)	68.20 (64.50–71.80)	70.90 (67.30–74.30)	70.00 (66.33–73.57)	73.30 (69.80–76.60)	78.80 (75.40–82.00)	55.10 (51.04–59.20)
Population ITN access, % (95% CI)	81.80 (79.50–84.10)	80.70 (78.60–82.70)	65.50 (63.00–68.00)	82.20 (79.80–84.70)	86.10 (84.30–87.90)	78.32 (76.00–80.60)	88.10 (86.50–89.80)	88.60 (87.20–90.00)	76.39 (74.10–78.70)
Use given access*	0.86	0.85	0.87	0.83	0.82	0.89	0.83	0.89	0.72

Abbreviations: CI, confidence interval; IG2, Interceptor G2; IRS, indoor residual spraying; ITN, insecticide-treated net.

*Use given access is calculated by dividing use (population that slept under a net last night) by access. Values over 1 are possible given the calculation is a ratio.

Malaria prevalence was low across all three districts during the baseline survey in February 2020 (Table R3). February was outside of peak transmission, which generally occurs in November and December, but start-up delays prevented an earlier survey. Prevalence was also relatively low during the Year 1 and Year 2 surveys, however, which took place during the high-transmission season in December 2020 and November 2021, respectively. In Ruhango, a historically high-burden district prioritized for IRS, prevalence varied across surveys, ranging from 5.24% during the Year 1 survey to less than 1.00% during the Year 2 survey. In Nyamagabe, prevalence was low and stable during the baseline and Year 1 surveys at less than 3.00%, decreasing to less than 0.50% during the Year 2 survey. In Karongi, prevalence during the baseline and Year 1 surveys was also less than 3.00%, decreasing further to 1.22% during the Year 2 survey. Given that each survey has shown low prevalence across districts, it may not be possible to detect statistically significant differences over time. The sample size could be increased to obtain more precision at these low prevalence numbers; however, this increase would be enormous and costly. Therefore, the modeled impact using all gathered data will be critical, as will the routine data analysis.

Table R3. Malaria prevalence by study district, February 2020, December 2020, and November 2021.

	Nyamagabe (standard ITNs)			Karongi (IG2 ITNs)			Ruhango (standard ITNs + IRS)		
	Feb 2020	**Dec 2020**	**Nov 2021**	**Feb 2020**	**Dec 2020**	**Nov 2021**	**Feb 2020**	**Dec 2020**	**Nov 2021**
Total tested	423	407	324	445	446	326	451	401	313
Malaria prevalence (RDT+) for all ages, % (95% CI)	2.360 (1.140–4.300)	2.700 (1.360–4.780)	0.308 (0.008–1.708)	2.470 (1.240–4.380)	2.690 (1.400–4.650)	1.227 (0.335–3.112)	1.330 (0.490–2.870)	5.240 (3.270–7.890)	0.958 (0.198–2.775)

Abbreviations: CI, confidence interval; IG2, Interceptor G2; IRS, indoor residual spraying; ITN, insecticide-treated net; RDT+, rapid diagnostic test positive.

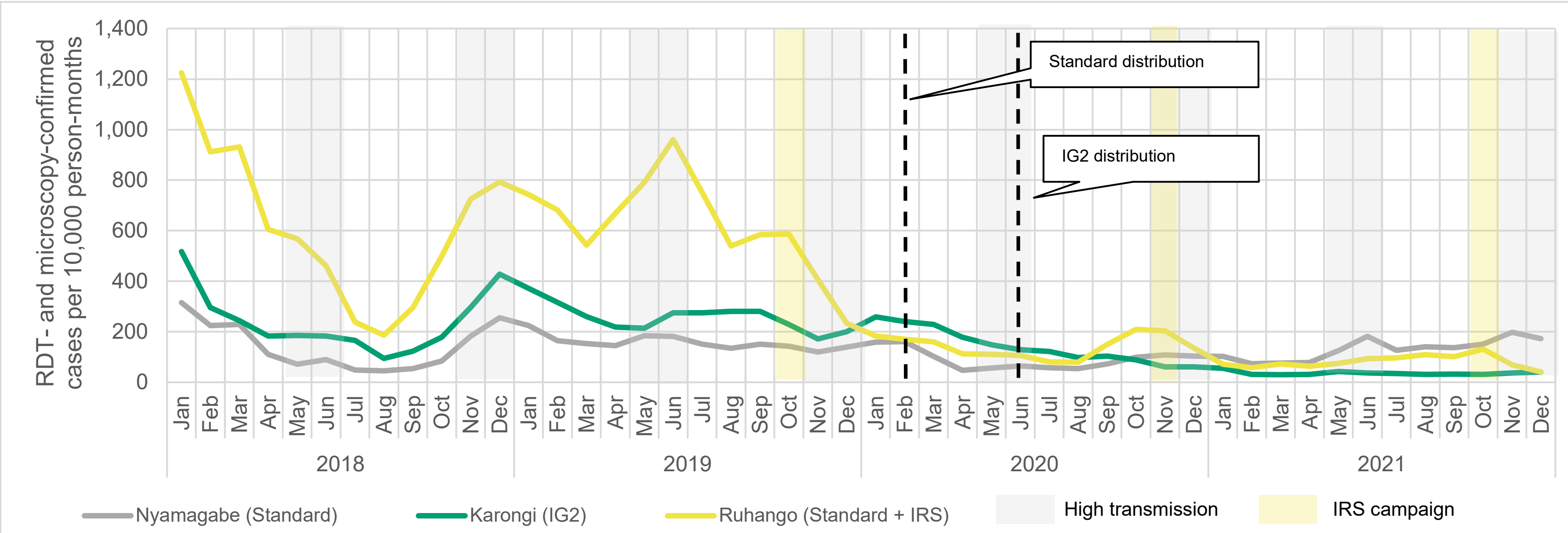
Routine health system data

Figure R3 in this section has been updated with routine data through December 2021.

Disease incidence was calculated using passive case detection data from health facilities and community health workers located in the three study districts—Karongi (IG2), Nyamagabe (standard), and Ruhango (standard + IRS). District population estimates came from the fourth population and housing census conducted in 2012 and were projected for 2018, 2019, 2020, and 2021 by the National Institute of Statistics of Rwanda.

Across all three districts, malaria incidence rates were higher in 2018 and most of 2019 compared with 2020 and 2021. Ruhango had higher incidence compared with Nyamagabe and Karongi in 2018 and 2019, but it rapidly decreased after the first IRS campaign in October 2019. Both standard net districts (Nyamagabe and Ruhango) experienced a decrease in incidence following their net campaigns in February 2020, but this was expected given seasonality trends. Karongi, the IG2 district, also experienced a decrease in incidence following its ITN campaign in June 2020, though this decrease began earlier in the year and also corresponded with seasonality. Although malaria incidence decreased from 2018 to 2021 across all districts, given their different baselines, further analysis and modeling will be conducted to strengthen interpretation of the trends observed. See Figure R3.

Figure R3. Overall malaria incidence per 10,000 person-months, 2018–2021.



Abbreviations: IG2, Interceptor G2; IRS, indoor residual spraying; ITN, insecticide-treated net.

Substantial differences in incidence rates were found between the pilot districts at baseline, particularly between Ruhango (500.9) and Nyamagabe (147.6). See Table R4. Incidence rates evened out and were more similar during Year 1, with the highest in Ruhango (115.5), followed by Karongi (91.9) and Nyamagabe (76.4). Unadjusted incidence rate ratios comparing malaria incidence between the IG2 district and the standard district and between the standard + IRS district and the standard district were calculated for the baseline year (April 2019 to March 2020) and Year 1 (April 2020 to March 2021). At baseline, there were 1.62 times more malaria in Karongi compared with Nyamagabe. One year later, however, after the mass distribution campaign, that was reduced to just 1.20 times more malaria. Ruhango, the standard + IRS district, had over 3.00 times more malaria compared with Nyamagabe at baseline, but by Year 1, this was reduced to just 1.51 times more malaria.

Table R4. Malaria case incidence rates (all ages) and incidence rate ratios by study district, 2019–2021.

		Incidence rate (per 10,000 person-months)			Incidence rate ratio (95% CI)	
Period	Months	**Nyamagabe (standard ITNs)**	**Karongi (IG2 ITNs)**	**Ruhango (standard ITNs + IRS)**	**Karongi (IG2 ITNs) vs. Nyamagabe (standard ITNs)**	**Ruhango (standard ITNs + IRS) vs. Nyamagabe (standard ITNs)**
Baseline	April 2019–March 2020	147.6	239.5	500.9	1.62 (1.61–1.64)	3.39 (3.37–3.42)
Year 1	April 2020–March 2021	76.4	91.9	115.5	1.20 (1.19–1.22)	1.51 (1.49–1.53)
Difference in incident cases		71.2	147.6	385.4		
Percent change		**−48.24**	**−61.63**	**−76.94**		

Abbreviations: CI, confidence interval; IG2, Interceptor G2; IRS, indoor residual spraying; ITN, insecticide-treated net.

Difference-in-difference comparisons of standard ITNs with IG2s and standard ITNs with standard ITNs + IRS were made to determine if any additional protection was provided either by IG2s or standard ITNs + IRS compared with standard ITNs only. When comparing the baseline year with Year 1, IG2s were found to confer an additional 13.39% reduction in overall malaria incidence compared with standard ITNs. When comparing standard ITNs with standard ITNs + IRS, standard ITNs + IRS were found to confer an additional 28.70% reduction in overall malaria incidence compared with standard ITNs only. See Table R5 for details. These analyses are still preliminary and will be adjusted as more data become available.

Table R5. Difference-in-difference comparison of next-generation ITNs with standard pyrethroid ITNs and standard pyrethroid ITNs + IRS, Year 1.

	Year 1 (April–March) change from baseline (95% CI)	DiD relative to standard ITNs (95% CI)
Nyamagabe (standard ITNs)	−48.24% (−44.7% to −52.7%)	
Karongi (IG2 ITNs)	−61.63% (−53.9% to −70.6%)	13.39% (9.2% to 17.9%)
Ruhango (standard + IRS)	−76.94% (−74.9% to −78.1%)	28.7% (22.2% to 33.3%)

Abbreviations: CI, confidence interval; DiD, difference-in-difference; IG2, Interceptor G2; IRS, indoor residual spraying; ITN, insecticide-treated net.

Entomology

This section has been updated with entomological results from data collected between March 2020 and March 2021 (Year 1).

In Rwanda, entomological surveillance included indoor CDCLT collections, which were performed for two consecutive nights twice a month at five sentinel houses in each study district (totaling 60 collection nights per district per month), as well as paired indoor-outdoor HLCs, which were performed at three houses per study district concurrently with the CDCLT collections but at different houses (totaling 36 collections per district per month). Mosquito larval sampling was performed annually in each district to support insecticide-resistance monitoring.

Baseline entomological surveillance began in March 2020, just prior to the suspension of study activities because of the COVID-19 pandemic. Activities began again in July 2020, though further disruptions in data collection occurred in January, February, and July of 2021. This report summarizes data collected between March 2020 through March 2021 (Year 1), roughly corresponding to the first year after ITN distribution.

The most abundant vector species group varied across the study districts, with *An. gambiae* s.l. dominating in Karongi and Ruhango and *An. funestus* s.l. dominating in Nyamagabe. Within the *An. gambiae* group, both *An. gambiae* s.s. and *An. arabiensis* were present, though *An. gambiae* s.s. was dominant in each district. While the overall sporozoite rate was low (6 positive mosquitoes out of 1,429 total tested), specimens from both of these key vector species groups tested positive for sporozoites (five *An. gambiae* s.s. and one *An. funestus* s.l.), confirming that members of both species groups play a role in malaria transmission in Rwanda. See Table R6 for details.

Table R6. Baseline entomological characteristics of the study districts in Rwanda.

	Nyamagabe (standard ITNs)	Karongi (IG2 ITNs)	Ruhango (standard ITNs + IRS)
	Year 1	**Year 1**	**Year 1**
Most abundant vector (% of likely vector species collected)	*An. funestus* s.l. (78.30%)	*An. gambiae* s.l. (89.50%)	*An. gambiae* s.l. (69.54%)
Second most abundant vector (% of likely vector species collected)	*An. gambiae* s.l. (21.28%)	*An. funestus* s.l. (7.31%)	*An. funestus* s.l. (30.46%)
Third most abundant vector (% of likely vector species collected)	*An. coustani* (0.43%)	*An. coustani* (3.19%)	–
***An. gambiae* molecular IDs**			
An. gambiae s.s.	91.3%	81.6%	80.0%
An. arabiensis	8.7%	18.4%	20.0%
HLC nightly landing rates			
Indoor:outdoor ratio (*An. gambiae* s.l.)	0.48	1.10	0.58
Indoor:outdoor ratio (*An. funestus* s.l.)	0.27	1.05	1.09
Pyrethroid-resistance profile	**LOW to MODERATE: Mitigated by PBO**		
WHO tube test mortality	97%–100%	86%–99%	93%–95%

Abbreviations: HLC, human landing collection; ID, identification; IG2, Interceptor G2; IRS, indoor residual spraying; ITN, insecticide-treated net; PBO, piperonyl butoxide; WHO, World Health Organization.

Insecticide susceptibility patterns in local *An. gambiae* s.l. populations indicated emerging resistance to pyrethroids, which was mitigated by pre-exposure to PBO, in each district (Table R7).

Table R7. Insecticide-resistance tests conducted in three sites with WHO tubes or CDC bottles, 2020.

		Nyamagabe (standard ITNs)		Karongi (IG2 ITNs)		Ruhango (standard ITNs + IRS)	
Insecticide	**Method**	**Tested**	**Mortality**	**Tested**	**Mortality**	**Tested**	**Mortality**
Deltamethrin 0.05%	WHO tubes	100	97	100	99	100	93
Permethrin 0.75%	WHO tubes	100	99	100	86	100	95
Lambda cyhalothrin 0.05%	WHO tubes					100	94
Alphacypermethrin 0.05%	WHO tubes	100	100	100	93		
Bendiocarb 0.1%	WHO tubes	100	86	100	98	100	95
Pirimiphos-methyl 0.25%	WHO tubes	100	100	100	100	100	100
Fenitrothion 1%	WHO tubes	100	100	100	100	100	100
DDT 4%	WHO tubes	100	98	100	93	100	96
Permethrin 0.75% + PBO	WHO tubes			100	100		
Permethrin 3.75%	WHO tubes			100	100		
Permethrin 7.5%	WHO tubes			100	100		
Chlorfenapyr 100 µg (60 min)	CDC bottles			100	33		
Chlorfenapyr 100 µg (24 h)	CDC bottles			100	100		
Chlorfenapyr 200 µg (60 min)	CDC bottles			100	46		
Chlorfenapyr 200 µg (24 h)	CDC bottles			100	100		

Note: Mortality scores highlighted in green indicate susceptibility to the insecticide tested; yellow indicates possible or moderate resistance; red indicates confirmed resistance.

Abbreviations: CDC, US Centers for Disease Control and Prevention; IG2, Interceptor G2; IRS, indoor residual spraying; ITN, insecticide-treated net; PBO, piperonyl butoxide; WHO, World Health Organization.

Data on nightly biting patterns of *An. gambiae* s.l. (Figure R4) showed that biting occurred both indoors and outdoors, with slight preferences for outdoor biting in Ruhango and Nyamagabe. Peak biting times differed by district, with biting occurring throughout the night in Karongi, earlier in the evening in Nyamagabe (19:00 to 21:00), and later at night in Ruhango (1:00 to 4:00). Nightly biting patterns of *An. funestus* (Figure R5) showed that biting occurred both indoors and outdoors, though indoor biting was higher in Karongi and Ruhango. While *An. funestus* biting patterns were generally low across districts, Nyamagabe had a distinct outdoor peak between 19:00 and 22:00. Further refining these mosquitos feeding characteristics and aligning results with human behavior patterns will provide valuable context for interpreting final results on the impact of the ITN distributions on malaria transmission.

Figure R4. Nightly biting patterns for *An. gambiae* s.l. in each study site, estimated from human landing collections, March 2020 through March 2021.

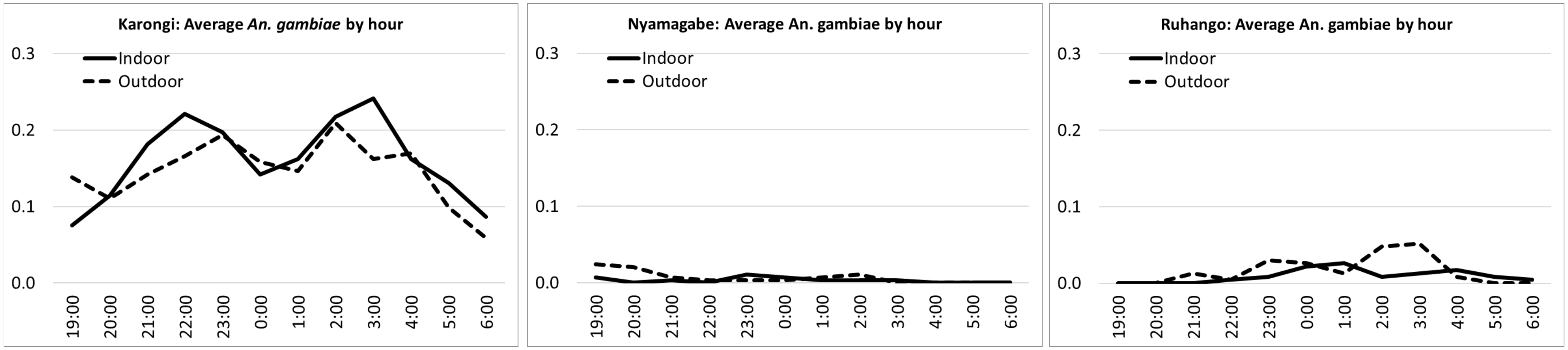
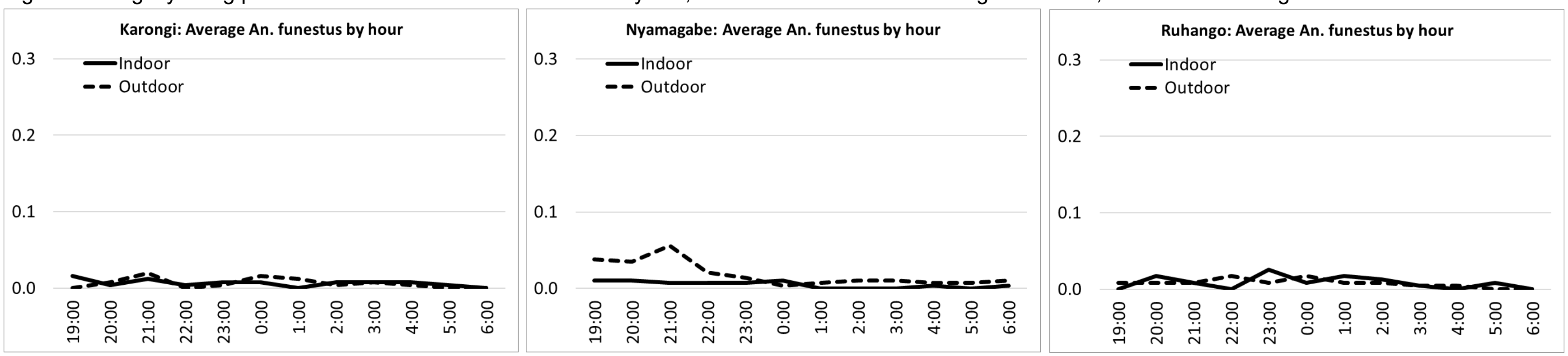


Figure R5. Nightly biting patterns for *An. funestus* s.l. in each study site, estimated from human landing collections, March 2020 through March 2021.



Human behavior

This section has not been updated since the previous report (published in December 2021). This section will be updated in the final report, which is expected to be published in early 2023.

Four rounds of human behavior data collection occurred in 2020 and 2021 (Table R8). Indirect monitoring began in 2021. Research participants were recruited from nine villages in three districts. A cohort of 182 participants were enrolled in indirect monitoring. A total of 107 participants were enrolled for IDIs and 455 for FGDs, resulting in a total of 744 participants enrolled. Round 1 enrollment was lower than expected due to delays resulting from COVID-19 lockdowns. Coding and analysis of Rounds 1 through 4 were completed. Data collection for Round 5 was completed in April 2022. Data entry and cleaning are currently in progress.

Table R8. Number of participants by human behavior data collection activity, 2020 and 2021.

	Number of participants				
	Round 1 (2020 low-transmission season)	**Round 2 (2020 high-transmission season)**	**Round 3 (2021 high-transmission season)**	**Round 4 (2021 low-transmission season)**	**Total**
Indirect monitoring		182	182	182	182
In-depth interviews	18	30	47	12	107
Focus group discussions	28	205	108	114	455

ITN use

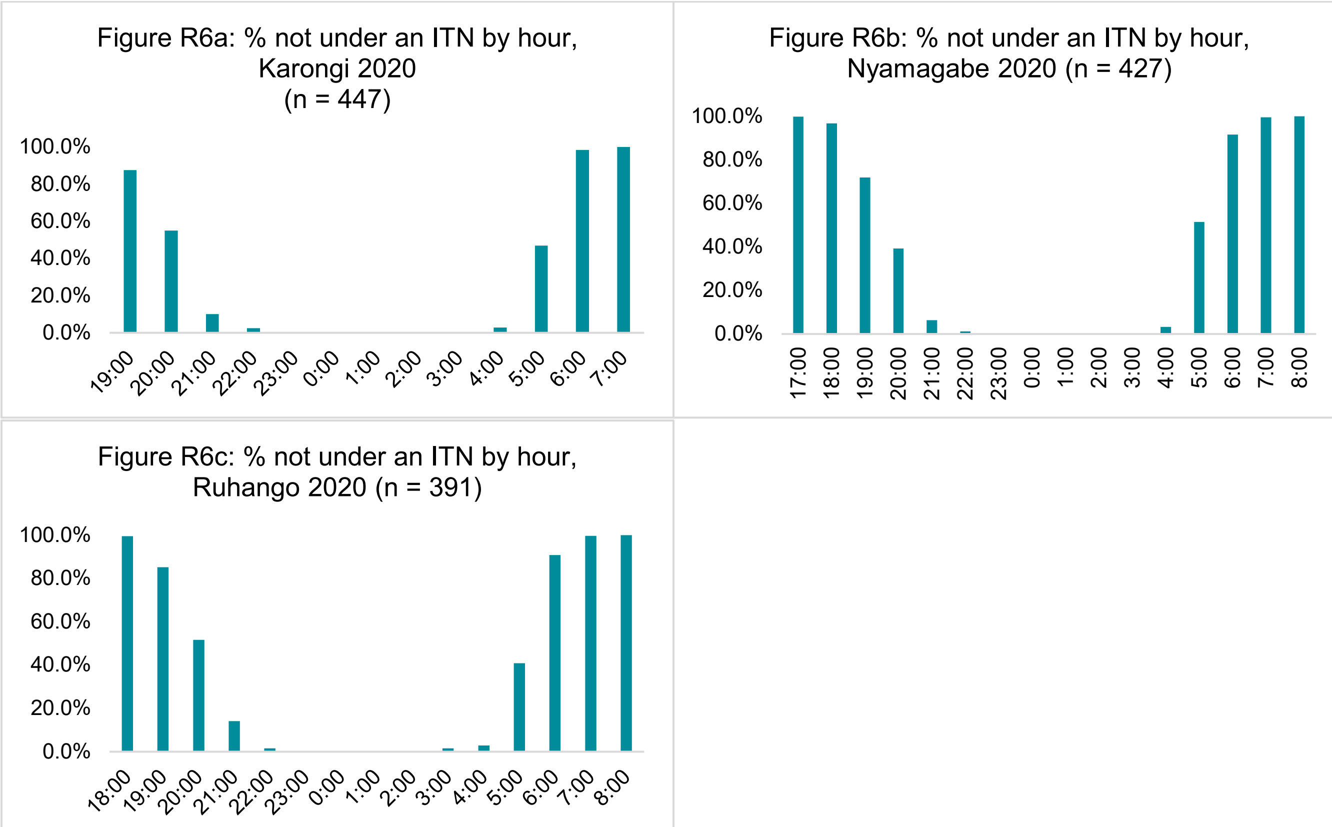
Data from Round 1 indirect monitoring showed that participants, on average, went to bed around 21:00 and got out of bed around 6:00 (Table R9). The average bedtime was similar across the three districts, but there were variations within districts. For example, in Nyamagabe, the earliest bedtime was at 17:55 and the latest bedtime was at 0:11, a more than six-hour difference. Figure R6 illustrates the percentage of observations when participants were not under the net. Most participants in Karongi and Nyamagabe never got out of bed once they got into bed during the night (82% and 63%, respectively); in Ruhango, only 26% stayed in bed. Across all three districts, the most common reason for getting out of bed at night was to use the toilet (89%). Other less common reasons included caring for children (6%) and attending to livestock (2%).

Table R9. Indirect monitoring participant characteristics, November–December 2020.

	Nyamagabe (standard ITNs)	**Karongi (IG2 ITNs)**	**Ruhango (standard ITNs + IRS)**
Households enrolled	18	18	18
Participants enrolled	61	64	57
Average bedtime (minimum–maximum)	20:37 (17:55–0:11)	21:02 (19:03–23:14)	21:02 (18:12–0:55)
Average wake time (minimum–maximum)	6:01 (3:36–8:02)	5:56 (4:17–7:59)	6:07 (3:20–8:03)
Average # times out of bed (minimum–maximum)	0.4 (0.0–3.0)	0.2 (0.0–2.0)	0.9 (0.0–3.0)

Abbreviations: IG2, Interceptor G2; IRS, indoor residual spraying; ITN, insecticide-treated net.

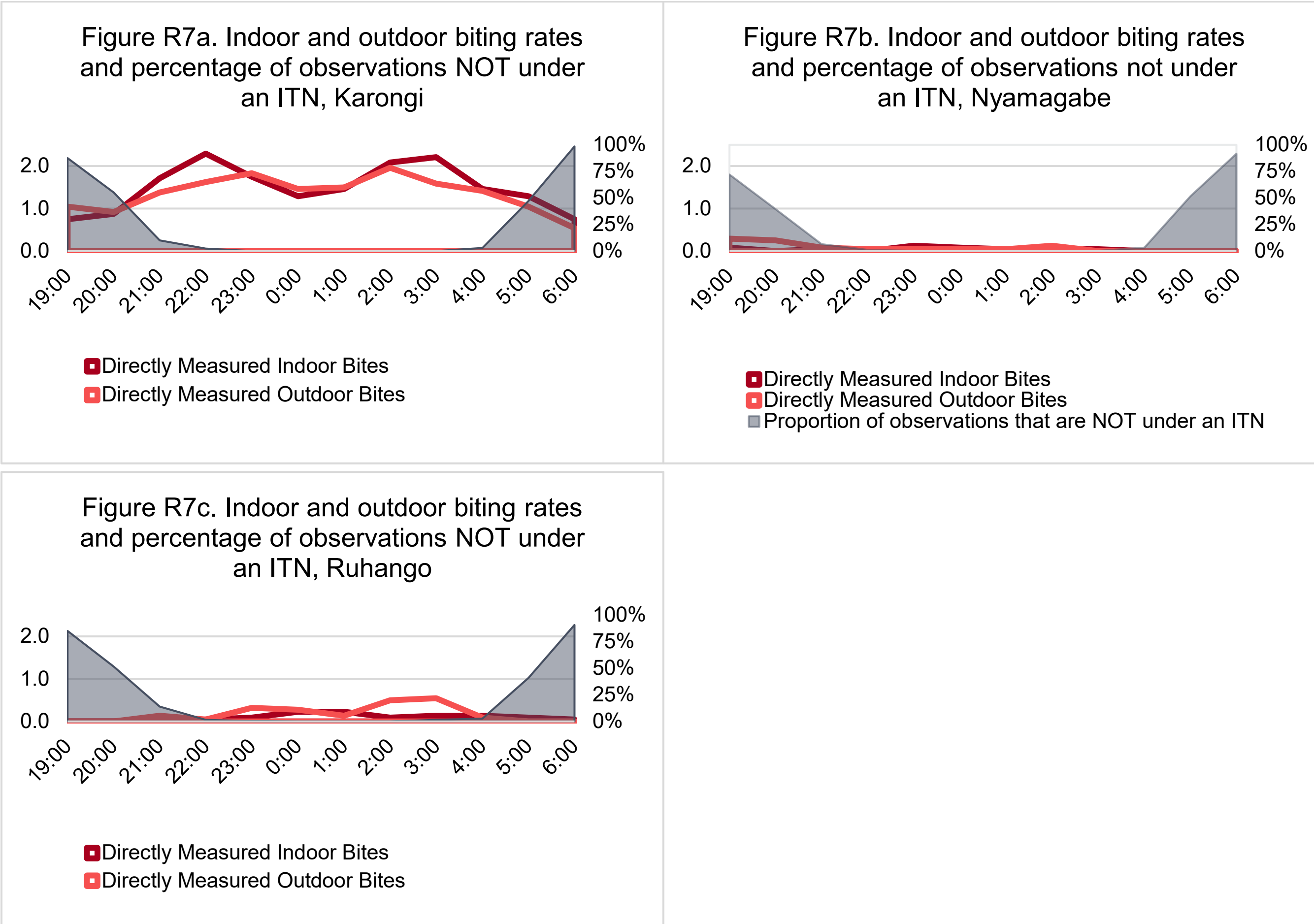
Figure R6. Proportion of indirect monitoring observations not under an ITN, by hour and by district.



Abbreviation: ITN, insecticide-treated net.

Figures R7a to R7c compare average indoor and outdoor biting rates with the proportion of observations not under an ITN from 19:00 to 6:00. Biting rates were calculated using data collected from March to December 2020, and the percentage of observations not under a net was calculated using data collected from November to December 2020.

Figure R7. Indoor and outdoor biting rates and percentage of observations not under an ITN, by district.



Abbreviation: ITN, insecticide-treated net.

In Karongi and Ruhango, the majority of observations were under ITNs (90% and 86%, respectively) prior to peak biting rates, which occurred between 21:00 and 4:00. Higher biting rates in Karongi overall meant that participants there were exposed to increased biting risk relative to the other districts despite reporting a similar bedtime. While biting rates in Nyamagabe were low throughout the night, outdoor biting was highest between 19:00 and 20:00, when at least 39% of observations were not yet under ITNs. Additional rounds of indirect monitoring data will be included in upcoming reports.

Drivers of ITN use and non-use

Exposure risks due to work and domestic responsibilities. Across all three districts, participants described how early morning and nighttime work and domestic responsibilities put them at risk for malaria, even if they slept under ITNs at night.

> *"Malaria, in villages like this one, commonly affect people who wake up early going to work because they pass in dews and bushes along the roads. Hence, they can easily be bitten by mosquitoes, which will later cause malaria to them."*
>
> *—Interviewee, Nyamagabe*
>
> *"We delay outside to finish housework and cook food for dinner. We often enter the house around 9 p.m., and I think that mosquitoes can bite us when we are delayed outside."*
>
> *—Interviewee, Karongi*
>
> *"I may go to look for grasses to feed the cow and then return late. After that, I have to prepare food for supper and do other domestic activities. All that may lead me to delay going to bed."*
>
> *—Interviewee, Ruhango*

Domestic responsibilities during mosquito biting times included housework, such as cooking and fetching water. Work responsibilities during mosquito biting times included working as a security guard. Farming responsibilities included collecting grass, checking on livestock, and fishing.

Participant reports of risk of malaria exposure due to work and domestic responsibilities were common across all three districts in Round 2 data collection. During Round 1 data collection, many explained that they were not engaging in nighttime outdoor activities, such as shopping and socializing, due to COVID-19 precautions.

Non-net prevention activities. The most mentioned malaria-prevention methods, other than net use, across all three districts were closing windows and doors and removing mosquito breeding areas around the house by reducing trash, removing stagnant water, and cutting down bushes. In Karongi, a few participants mentioned the use of mosquito repellents.

> *"We try our best to prevent mosquitoes in our home by clearing bushes around our home and also removing all stagnant water places or anything in the compound where rainwater can collect, such as old jerry cans, buckets, pots, tins, basins, cups, plates, and so forth. Because if water collect[s] in these utensils and stay there for long, they serve as breeding sites for mosquitoes."*
>
> *—Interviewee, Nyamagabe*

Ruhango was the only study district that received annual IRS campaigns. Many participants noted that IRS was an important tool in the prevention of malaria, though some doubted its effectiveness.

> *"The indoor spray helped a lot. Because nowadays we no longer see any insects moving around."*
>
> *—Interviewee, Ruhango*
>
> *"The first time the government sprayed the insecticide in the house, the mosquitoes couldn't stand it, but the last time they did, it didn't work.... I think the insecticide they last used was fake."*
>
> *—Interviewee, Ruhango*

Access. Lack of access to ITNs was a major driver for non-ITN use across all three districts. IDI and FGD participants during Round 1 and Round 2 data collection repeatedly described being dependent on government distribution campaigns to acquire ITNs. This meant that if an ITN were no longer usable or if there were issues with the distribution campaign, participants could not easily supplement or replace their ITNs and would need to sleep without an ITN. Participants did describe issues with the most recent distribution campaign, including an insufficient supply of nets and households not receiving the appropriate number of ITNs for their household size.

> *"When they supplied bednets recently, they told us that the bednets that were brought [were] few, so they gave me only one, yet I have two beds in my home."*
>
> *—Interviewee, Ruhango*
>
> *"Most of the time, you find bednets are few. For instance, in my home, we have five beds, but we were given only three bednets. They told me there were few; hence, they had to share them among all citizens sparingly so that at least all people may get some bednets. Hence, you will find some of my family members who don't sleep under bednets."*
>
> *—FGD participant, Karongi*

Additionally, although a few participants noted that the distribution campaigns happened regularly enough to replace old nets in time, many described their current nets to be "very old" such that "they can't be used any longer." For example, one IDI participant in Karongi explained that they had received a bednet more than three years ago and had not received any additional nets since. They described the only net they owned to be "really old—it has changed color and is even torn with many holes."

In some locations, participants explained that government distribution campaigns were the only way people could acquire bednets and that they were unaware of any locations where they could buy bednets. Others expressed the intention of investigating if pharmacies sold bednets.

> *"There is no other way I can get [bednets]. When bednets are old before the government distributes other bednets to us, we have nothing else to do; we just stay without bednets."*
>
> *—FGD participant, Nyamagabe*

The consequence of not having a means to replace unusable ITNs is that people then do not use bednets. As one IDI participant summarized:

> *"We don't sleep under bednets. And the reason is because we don't have it. If we had bednets, we would be sleeping in it."*
>
> *—Interviewee, Karongi*

Participants proposed solutions to this access issue, which varied from increasing the frequency of distribution, changing who distributes the bednets, and making nets more widely available to purchase.

> *"I feel they should find a way of supplying bednets after every three months so that even those who missed the previous supply may get them in the next supply."*
>
> *—FGD participant, Nyamagabe*
>
> *"I feel [bednets] should be given to the community health workers so that they may supply them to us. Simply because they know us well, they know those who got them and those who [were] missed. And they should be given surplus to keep and then supply them."*
>
> *—FGD participant, Nyamagabe*

Use. When nets were available, participants reported using nets every day and throughout the year in both the dry and rainy seasons. Parents reported needing to ensure their children used their nets properly:

> *"For instance, children may forget to spread their bednet over the bed, or they may spread it but not tuck the edges well under their beddings. Hence, it's important for you as a parent to check and tuck the bednet properly under the beddings of the children before you go to sleep."*
>
> *—FGD participant, Ruhango*

Participants explained that nets were considered old and no longer usable when mosquitoes could land on the net, indicating that the insecticide was no longer effective, or when the net was "torn beyond repair."

> *"Something that will show you that your bednet is old is that when the mosquito comes and rests on it and it remains normal. That means that the chemical in the bednet has expired, and hence we say that bednet is old."*
>
> *—FGD participant, Ruhango*

Maintenance. Most people used similar procedures to wash their nets, though there was wide variability in the washing frequency. Most reported washing nets whenever the net appeared dirty, which ranged in intervals of a few weeks to a few months. Some reported washing their nets once or twice a week. Participants explained that washing frequency depended on factors such as exposure to dirt or smoke.

> *"If you live in a house which is not plastered or [has an] uncemented floor, it gets dirty quickly, at least within three months.... When you live in a house that has cemented floors and plastered walls, it takes long to get dirty."*

—FGD participant, Nyamagabe

"We make fire in our house while we are cooking. The mosquito nets catch the smoke, and we are obliged to wash the nets many times, and they lose their quality and effectiveness."

—FGD participant, Ruhango

There was also variability in people's ability to repair holes. Participants reported nets being torn or damaged from catching on bed nails or the wood of the bed. Some reported mice as the cause of net damage. When nets were torn or damaged, some people repaired their nets using needle and thread. Some were motivated to mend their nets due to the lack of availability and/or affordability of nets.

"If my mosquito net is torn, I should mend it as I cannot afford a new net myself."

—FGD participant, Karongi

There were also participants who did not know how, or did not think it was possible, to mend a net.

"There is no way you can repair it. You have to wait until they give us another one to replace the old one."

—FGD participant, Nyamagabe

Preferences. Most participants strongly preferred conical nets because they were easier to hang than the rectangular nets, which required more space and work to hang. One participant explained that, instead of building four posts on a bed to hang the rectangular net, many people hung it like a conical net, which put users at risk for mosquito bites.

"The rectangular type is tiresome and difficult to use.... You are required to get four pieces of wood and nail them on the four corners of the bed ... but many people don't use it that way. Instead, they pierce in the middle of the net and try to tie a rope, which is hanged under the roof of the house, just as how they hang the conical type. And yet, this can't be possible. Because when you use it like that, it can't reach the base of the bed. It will remain hanging vaguely in the space over the bed. Hence, you can't find way of tucking the edges under the mattress."

—Interviewee, Karongi

Relatedly, participants explained that for those without a ceiling or those with large bedrooms, the large size of the rectangular net was beneficial. For those with small bedrooms or multipurpose rooms (e.g., with "a bed, a table where I take my meal, or sometimes with a cupboard"), it was difficult to find space to hang the rectangular net; this served as a "reason for not using a bednet."

Additionally, one participant in Nyamagabe said that they had heard that the previously distributed conical nets were more effective than the recently distributed rectangular nets.

“Basing on the report I get from the citizens in my village who have been using the bednet given to us recently, they say that the previous conical type was more effective than recent square type of bednets”

—FGD participant, Nyamagabe

A few participants expressed a preference for the brightness of white bednets, whereas others expressed a preference for blue nets as they hid dirt better than white nets.

Benefits. Round 1 and 2 participants enjoyed other benefits to using bednets in addition to malaria prevention. While participants noted malaria prevention as an important benefit to using ITNs, they also described feeling more comfortable under a bednet because they were protected from mosquitoes and other insects. Participants also commented that ITNs kept the users warm while they slept under it.

“We all sleep under bednets; otherwise, we cannot sleep. When you sleep under a bednet, you are protected from any bites of mosquitoes and any other insects. Without a bednet, you cannot sleep well.”

—Interviewee, Ruhango

Challenges. Participants reported other drivers of non-ITN use: A few reported knowing others who did not use ITNs because the bednet caused “skin irritation” and “pruritic wheals.” Participants also reported knowing others, especially children, who did not use ITNs because they were “affected by the smell” and so “fail[ed] to breathe.” A few other participants also mentioned inconsistent use of ITNs due to issues with setting up ITNs; the issues were due to lack of space for ITNs when the room was used for purposes other than just sleeping and the participants sleeping on mats on the floor and thus not being able to tuck the nets in place.

Durability monitoring

The Rwanda Biomedical Centre, with support from PMI, is conducting durability monitoring in Rwanda separately from this pilot evaluation. An interim report is being drafted. This section will be updated to include those findings once the report becomes available.

Summary

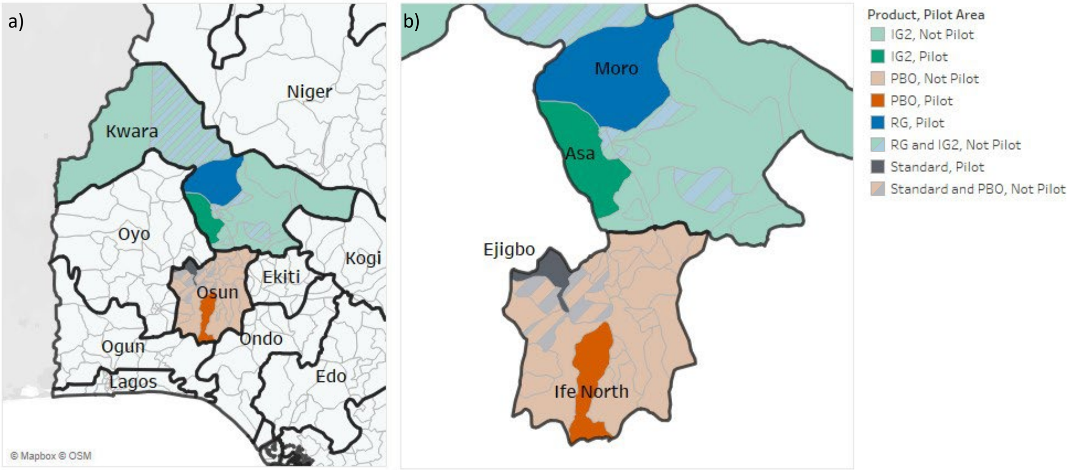
This report incorporates monthly routine HMIS data through December 2021. Unadjusted incidence rate ratios showed that, at baseline, there were 1.62 times more malaria in the IG2 district compared with the standard ITN district. Additional data from Year 1, however, showed that the gap is closing, as there are now only 1.20 times more malaria in the IG2 district. Difference-in-differences analyses also showed that IG2s conferred an additional 13.39% reduction in overall malaria incidence compared with standard ITNs, and standard ITNs + IRS conferred an additional 28.70% reduction in overall malaria incidence compared with standard ITNs only. Additional human behavior data, including quantitative indirect monitoring data, helped explain challenges to ITN use and defined the risk of indoor and outdoor biting when not under the protection of an ITN. Analysis of human behavior data showed that when ITNs were available, participants reported using nets every day during both the dry and rainy seasons. Lack of access to ITNs was a major driver of non-ITN use across all three districts. Early morning and nighttime work and domestic responsibilities were frequently cited as exposure risks.

Nigeria

The evaluation in Nigeria has taken place in two LGAs in Kwara State, Asa (IG2 ITNs) and Moro (RG ITNs), and two LGAs in Osun State, Ejigbo (standard ITNs) and Ife North (PBO ITNS) (Figure N1). The four study LGAs were chosen due to similar malaria transmission dynamics—including malaria prevalence, incidence, vector species composition, insecticide-resistance status, and general climate and geographic similarities—and consistencies in other planned malaria control interventions. While Kwara and Osun experience year-round transmission, the high-transmission season occurs from July to November.

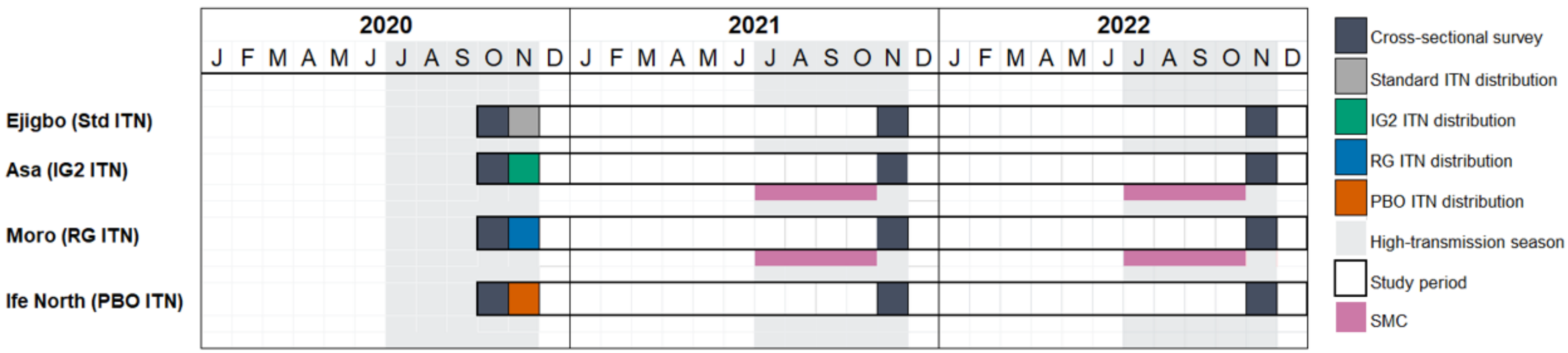
The evaluation in Nigeria began in October 2020. The ITN distribution occurred in November 2020 (Figure N2). The previous ITN campaign in Kwara and Osun was held in 2017. SMC for children under 5 years old was introduced in Kwara in 2021 and was conducted with four rounds between July and October. Since SMC was not conducted during the baseline period (or in Osun), prevalence estimates in children under 5 years old would likely overestimate the impact of IG2 and RG ITNs. To mitigate this, the cross-sectional survey was expanded for 2021 and 2022 to include children within the ages of 5 to 15 years in addition to children under 5 years old. Estimates for malaria prevalence in the absence of SMC for children under 5 will be modeled for 2021 and 2022. The cross-sectional survey was also shifted roughly one month later, so that it would be conducted one month after the last dose of SMC but still within the high-transmission season.

Figure N1. Map of study LGAs in Nigeria.



a) States included in the study; b) ITN distribution in Kwara and Osun States, with pilot LGAs highlighted.
Abbreviations: IG2, Interceptor G2; LGAs, local government area; PBO, piperonyl butoxide; RG, Royal Guard.

Figure N2. Insecticide-treated net distribution and transmission timeline.



Abbreviations: IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide; RG, Royal Guard; SMC, seasonal malaria chemoprevention; Std, standard.

Epidemiology

Cross-sectional survey

This section has been updated with results from the Year 1 cross-sectional survey, which was conducted from November to December 2021.

The baseline cross-sectional survey was conducted from October 5 to 10, 2020, in Ejigbo and Ife North LGAs and from October 26 to 31, 2020, in Asa and Moro LGAs. The survey occurred prior to ITN distribution campaigns and during the high-transmission season in each LGA. In each LGA, 420 households were targeted for inclusion in the survey (15 households from 28 communities within each LGA). For each household, one child within the ages of 6 to 59 months was selected for the prevalence survey and the head of household or primary caregiver responded to the survey.

The Year 1 cross-sectional survey was conducted from November 22 to December 10, 2021, across all LGAs. Due to the introduction of SMC in Kwara, the target sample for each LGA was expanded to 420 children under 5 years old and 420 children from ages 5 to 15 years across 28 communities (15 children in each age group per cluster).

Household demographic characteristics (Table N1) were similar across the four LGAs within the same year. However, the average number of household members increased across Ejigbo, Asa, and Moro, with the most substantial increases in Ejigbo and Moro. This was likely due to the inclusion of children withing the ages 5 to 15 years, as households with older children tend to be larger. The education status of heads of households surveyed was similar across LGAs within the same year, although Ife North had relatively more heads of households with a secondary education or higher compared with other LGAs in 2020. The 2021 survey indicated higher levels of education than in 2020, except for Ife North, which had relatively little difference in educational status between years. Education status across LGAs was similar in 2021. After the baseline survey identified large proportions of heads of households with no or unknown education, more prompting was done during the 2021 survey. As a result, a shift to higher education levels was observed compared with the 2020 survey.

Table N1. Participant/household demographic characteristics at baseline, 2020–2021.

	Ejigbo (standard ITNs)		Asa (IG2 ITNs)		Moro (RG ITNs)		Ife North (PBO ITNs)	
	2020	2021	2020	2021	2020	2021	2020	2021
Households enrolled (clusters)	425 (28)	433 (28)	427 (28)	425 (28)	421 (28)	428 (28)	422 (28)	425 (28)
Average number of household members (95% CI)	3.91 (3.81–4.01)	4.47 (4.39–4.54)	3.91 (3.83–4.00)	4.04 (3.98–4.11)	3.67 (3.57–3.76)	4.41 (4.29–4.53)	4.14 (4.01–4.27)	3.91 (3.85–3.97)
Age, % of total (n)								
<5 years old	29.3 (487)	25.4 (486)	30.9 (517)	25.0 (423)	31.6 (488)	25.6 (453)	29.1 (509)	26.6 (432)
≥5 years old	70.7 (1,175)	74.6 (1,426)	69.1 (1,154)	75.0 (1,272)	68.4 (1,056)	74.5 (1,320)	70.9 (1,239)	73.4 (1,194)
Gender, % of total (n)								
Male	49.5 (822)	52.0 (995)	51.2 (855)	48.7 (825)	50.3 (777)	48.9 (867)	49.1 (858)	51.5 (838)
Female	50.5 (840)	48.0 (917)	48.8 (816)	51.3 (870)	49.7 (767)	51.1 (906)	50.9 (890)	48.5 (788)
Education status of head of household, % of total (n)								
None/don't know	38.1 (162)	32.1 (139)	48.7 (208)	10.8 (46)	27.1 (114)	16.5 (70)	14.2 (60)	14.6 (62)
Literate	22.1 (94)	5.1 (22)	3.8 (16)	14.6 (62)	12.4 (52)	6.6 (28)	13.7 (58)	14.4 (61)
Primary	11.1 (47)	15.0 (65)	15.7 (67)	12.8 (53)	16.4 (69)	22.4 (95)	10.7 (45)	14.8 (63)
Secondary	23.8 (101)	37.0 (160)	27.4 (117)	49.2 (209)	40.9 (172)	36.0 (153)	49.8 (210)	44.7 (190)
Postsecondary	4.9 (21)	10.9 (47)	4.5 (19)	12.9 (55)	3.3 (14)	18.6 (79)	11.6 (49)	11.5 (49)

Abbreviations: CI, confidence interval; IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide; RG, Royal Guard.

Following the ITN distribution in November 2020, all LGAs recorded an increase in the average number of ITNs per house and in the proportion of households with at least one ITN in Year 1 compared with baseline (Table N2). Ejigbo and Ife North LGAs continued to report higher average numbers of ITNs per house than Asa LGA or Moro LGA in Year 1. Households in Asa and Moro, on average, reported fewer than one ITN per house. The proportion of the population that slept under a net the previous night increased from 19% to 48% in Ejigbo, increased from 3% to 44% in Asa, remained about the same at 19% in Moro, and increased from 24% to 34% in Ife North. Overall population ITN access increased significantly across all LGAs. Use given access increased in Ejigbo and Asa but decreased substantially in Moro and Ife North, suggesting that lack of access to an ITN might not have been a primary driver of net non-use in Nigeria.

Table N2. ITN coverage, access, and use, 2020–2021.

	Ejigbo (standard ITNs)		Asa (IG2 ITNs)		Moro (RG ITNs)		Ife North (PBO ITNs)	
	2020	**2021**	**2020**	**2021**	**2020**	**2021**	**2020**	**2021**
Average number of ITNs per house (95% CI)	0.57 (0.50–0.64)	1.39 (1.29–1.48)	0.09 (0.06–0.12)	0.91 (0.83–0.98)	0.36 (0.30–0.43)	0.72 (0.64–0.80)	0.60 (0.51–0.69)	1.24 (1.13–1.35)
Households with at least one ITN, % (95% CI)	43.1 (41.1–45.1)	75.8 (74.0–77.5)	8.0 (6.9–9.1)	66.6 (64.7–68.5)	26.6 (24.8–28.4)	50.7 (48.7–52.7)	37.9 (35.9–39.9)	67.5 (65.6–69.4)
Population that slept under a net last night, % (95% CI)	19.7 (18.9–20.5)	46.8 (45.9–47.8)	3.0 (2.6–3.3)	43.6 (42.6–44.6)	18.1 (17.3–18.9)	19.4 (18.6–20.2)	24.2 (23.3–25.1)	34.3 (33.3–35.3)
Population ITN access, % (95% CI)	28.1 (26.4–29.8)	58.0 (56.3–59.7)	4.4 (3.7–5.2)	43.4 (41.7–45.1)	17.7 (16.1–19.2)	31.2 (29.6–32.8)	25.4 (23.8–27.0)	51.8 (49.8–53.8)
Use given access*	0.70	0.81	0.68	1.00	1.02	0.62	0.95	0.66

Abbreviations: CI, confidence interval; IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide; RG, Royal Guard.

*Use given access is calculated by dividing use (population that slept under a net last night) by access. Values over 1 are possible given the calculation is a ratio.

Malaria prevalence among children under 5 years old (Table N3) varied across LGAs, but decreases were noted from baseline to Year 1 across all LGAs. The largest decreases were observed in Asa and Moro; **these LGAs also received four rounds of SMC prior to the Year 1 survey**. To account for the addition of SMC, the survey was expanded to include children 5 to 15 years old (who had not received SMC) to help model the expected prevalence among children under 5 years old without SMC. This modeling is forthcoming. A series of systematic reviews was conducted for the modeling to collate data on key parameters (e.g., human immunity, heterogeneity in biting, drug treatment impact, seasonal patterns in transmission, and mosquito bionomics) that inform malaria parasite transmission between people and mosquitoes in the presence of vector control. Together with the data recorded during the pilot study in Nigeria, these parameters were used to inform and calibrate the model simulation to the baseline situation.

Of the two LGAs that did not receive SMC, Ejigbo reported a percent prevalence reduction of more than 30% and Ife North reported more than 15%. Preliminary modeled estimates also indicated a substantial prevalence decrease in Asa due to IG2 ITNs in the theoretical absence of SMC.

Table N3. Malaria prevalence among children <5 years old by study local government area, 2020–2021.

	Ejigbo (standard ITNs)		Asa (IG2 ITNs)		Moro (RG ITNs)		Ife North (PBO ITNs)	
	2020	**2021**	**2020**	**2021**	**2020**	**2021**	**2020**	**2021**
Total tested	424	433	425	425	421	426	422	425
Malaria prevalence (RDT+), % (95% CI)	38.4 (36.5–40.4)	25.6* (23.9–27.4)	63.1 (61.1–65.0)	15.8* (14.3–17.2)	49.9 (47.8–51.9)	21.1* (19.5–22.8)	48.3 (46.3–50.4)	40.9* (38.9–42.9)
Percent prevalence reduction from baseline to year 1, %	33.3		75.0		57.7		15.3	

Abbreviations: CI, confidence interval; IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide; RDT+, rapid diagnostic test positive; RG, Royal Guard.

*Prevalence among children <5 years old in 2021 was measured approximately one month after a four-dose series of seasonal malaria chemoprevention.

Routine data

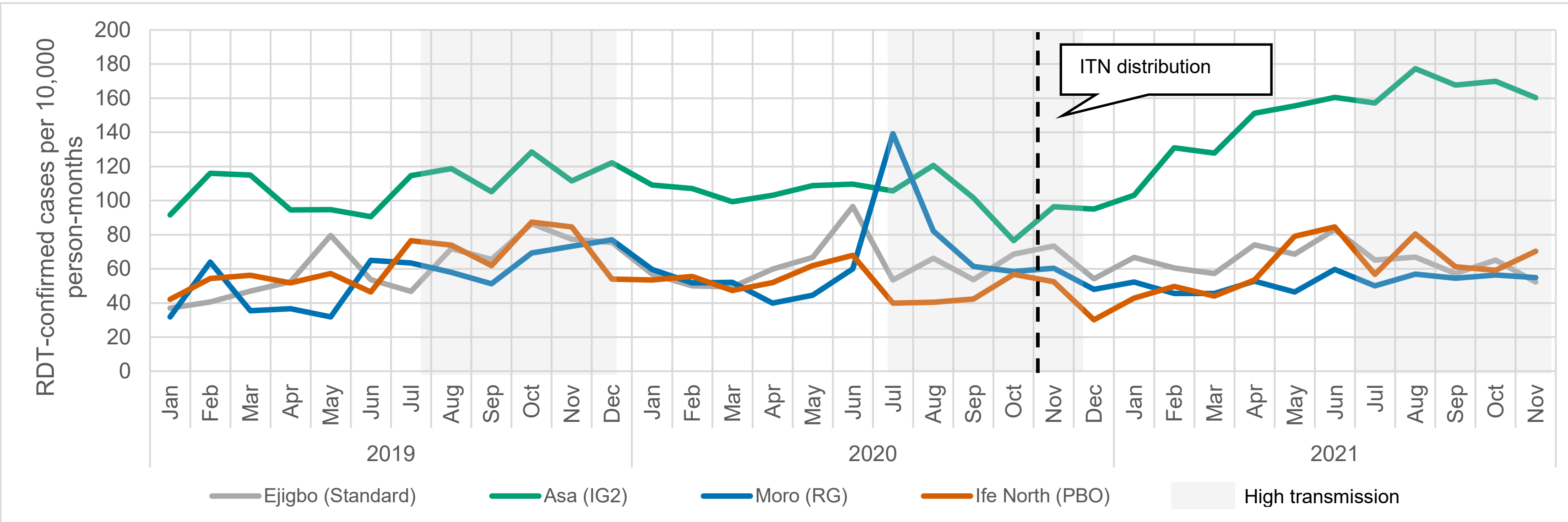
Additional months of data have been added to this section (February 2021 to November 2021).

Disease incidence was calculated using passive case data from all facilities that reported to the HMIS in the four LGAs. Population estimates were from microplanning exercises that had been conducted for the 2020 ITN campaign. The estimated population was designated as the midyear population in 2020, and monthly population estimates were produced using annual growth rates. Malaria case data presented here were extracted in March 2022.

A total of 157 health facilities in the four LGAs were identified for inclusion in the routine data analysis; 134 facilities (or 85% of all facilities) reported any data between January 2019 to November 2021. Of the 134 facilities with any data during the study period, 35% of facilities reported for all months of the study period, 59% of facilities reported between 75% and 99% of the months, and 7% reported for less than 75% of the months. Private-sector facilities, based on the ownership classification in Nigeria's Health Facility Registry, and facilities that were listed as closed in the DHIS2 were excluded from this analysis. Seven facilities whose facility ownership was unknown were included in the final list of facilities, four of which reported data to DHIS2. Additional follow-up will be conducted to determine if any of these facilities are private-sector facilities that need to be removed.

Malaria transmission (as measured by the incidence rate) appeared relatively consistent in Ife North and Ejigbo LGAs. Moro LGA showed a significant spike in cases in July 2020, and Asa LGA showed a significant and steady increase from October 2020 to November 2021 (Figure N3). Increases were observed in most wards within Asa LGA. However, the wards with the highest increases in malaria case incidence between the baseline year (November 2019 to October 2020) and the first year post-campaign (November 2020 to December 2021) were all clustered between the shared border with Oyo State and Ilorin, the capital of Kwara State; facilities with the highest rates were situated along the Oyo State border. This could signal that an increase in incidence may be the result of population migration. These increases in Asa LGA and the spike in Moro LGA in July 2020 will be investigated further. See the "Antenatal care–based surveillance" section below for a different view of longitudinal burden.

Figure N3. Average monthly incidence rate (per 10,000 person-months at risk) by LGA, 2019–2021.



Abbreviations: IG2, Interceptor G2; ITN, insecticide-treated net; LGA, local government area; PBO, piperonyl butoxide; RDT, rapid diagnostic test; RG, Royal Guard.

The incidence rate ratios were calculated to compare the incidences in Asa, Moro, and Ife North with the incidence in Ejigbo (the LGA that received standard ITNs) in the baseline year (November 2019 to October 2020) and the first year postcampaign (November 2020 to October 2021) (Table N4). Asa had significantly higher rates than Ejigbo during both years. Moro had a significantly higher rate than Ejigbo in the baseline year but a lower rate in the first year postcampaign. Ife North had a lower incidence rate than Ejigbo during both years. Further planned analysis of difference will quantify any impact the different nets had on the malaria case incidence in the respective LGAs two years postcampaign. A difference-in-difference comparison (Table N5) between each net type and standard ITNs showed a relatively greater increase in incidence in Asa (IG2 ITNs) than in Ejigbo (standard ITNs), a relative decrease in incidence in Moro (RG ITNs) compared with Ejigbo, and a slightly larger increase in Ife North (PBO ITNs) compared with Ejigbo.

Table N4. Malaria case incidence rates (all ages) and incidence rate ratios by study LGA and year, 2019–2021.

		Incidence rate (per 10,000 person-months)				Incidence rate ratio (95% CI)		
Period	**Months**	**Ejigbo (standard ITNs)**	**Asa (IG2 ITNs)**	**Moro (RG ITNs)**	**Ife North (PBO ITNs)**	**Asa (IG2 ITNs) vs. Ejigbo (standard ITNs)**	**Moro (RG ITNs) vs. Ejigbo (standard ITNs)**	**Ife North (PBO ITNs) vs. Ejigbo (standard ITNs)**
Baseline	November 2019–October 2020	64.5	106.3	66.6	54.7	1.65 (1.62–1.68)	1.03 (1.0–1.06)	0.85 (0.83–0.87)
Year 1	November 2020–October 2021	66.0	141.1	52.4	57.8	2.14 (2.10–2.18)	0.79 (0.78–1.06)	0.88 (0.86–0.90)

Abbreviations: CI, confidence interval; IG2, Interceptor G2; ITN, insecticide-treated net; LGA, local government area; PBO, piperonyl butoxide; RG, Royal Guard.

Table N5. Difference-in-difference comparison of next-generation ITNs to standard ITNs, Year 1.

	Year 1 (November–May) change from baseline (95% CI)	**Year 1 DiD relative to standard ITNs**
Ejigbo (standard ITNs)	2.3% (−2.5% to −8.6%)	
Asa (IG2 ITNs)	32.7% (24.2% to 40.2%)	30.4%
Moro (RG ITNs)	−17.9% (−21.3% to −3.5%)	−23.7%
Ife North (PBO ITNs)	5.7% (1.8% to 8.7%)	3.4%

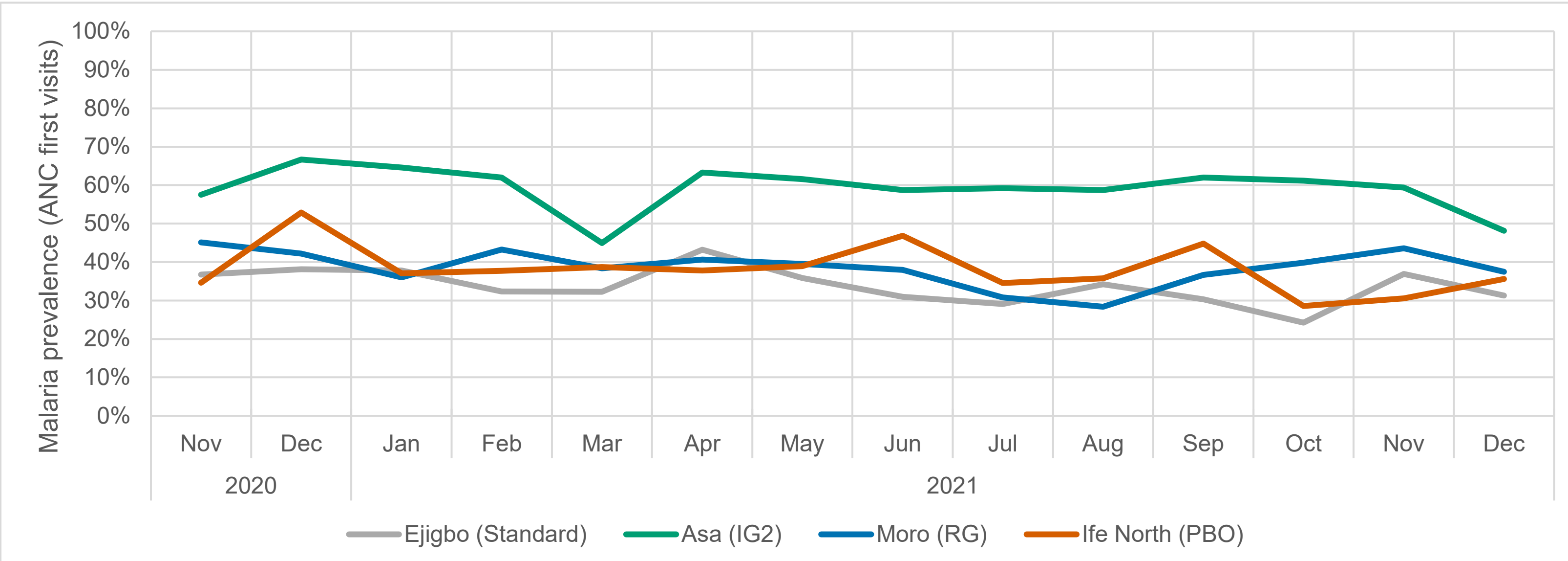
Abbreviations: CI, confidence interval; DiD, difference-in-difference; IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide; RG, Royal Guard.

Antenatal care–based surveillance

Additional months of data have been added to this section (March 2021 to December 2021).

Starting in November 2020, all pregnant women attending their first ANC visit were tested for malaria with an RDT and completed a short questionnaire on net use and care-seeking behavior. Monthly prevalence among ANC attendees was high between November 2020 and December 2021 in each LGA and seemed relatively unaffected by the ITN distribution (Figure N4). The prevalence was highest in Asa.

Figure N4. Prevalence from ANC surveillance by LGA, November 2020–December 2021.



Abbreviations: ANC, antenatal care; IG2, Interceptor G2; ITN, insecticide-treated net; LGA, local government area; PBO, piperonyl butoxide; RG, Royal Guard.

Entomology

This section has not been updated since the last report (published in December 2021). Data from 2021 will be received and analyzed in the coming months.

In Nigeria, paired human-baited CDCLT collections were conducted at four collection points (two indoor and two outdoor) each in three villages in each LGA for three consecutive nights per month (totaling 48 paired collections per LGA per month). In addition, pyrethrum spray collections were performed in 16 houses each in two villages in each LGA three times per month. Mosquito larval sampling was performed annually in each LGA to support insecticide-resistance monitoring.

Baseline mosquito surveillance activities began in November 2020, and surveillance is ongoing. To date, the analytical dataset includes data from November 2020 through April 2021. Additional data are currently being cleaned and validated. These data will be included in the final report.

The most abundant vector species varied by study LGA in Nigeria, with *An. gambiae* s.s. dominant in Ejigbo, Asa, and Moro and *An. funestus* s.l. dominant in Ife North (Table N6). *An. coluzzii* was also present in each LGA, and a few specimens of *An. arabiensis* were identified in Asa and Moro (Table N6). Outdoor biting was common in Ejigbo, where the indoor-to-outdoor ratio of 0.92 indicated that *An. gambiae* s.l. was equally likely to be captured indoors as outdoors. In the other three LGAs, *An. gambiae* s.l. was much more likely to be collected indoors. Ongoing sporozoite screens will help clarify which of these species are the dominant vectors.

Insecticide susceptibility patterns in local *An. gambiae* s.l. populations indicated variable resistance across the study LGAs, with WHO tube test mortalities ranging from 12% to 38% in Asa and 73% to 94% in Ejigbo. In each case, resistance was only partially mitigated by pre-exposure to PBO, indicating that multiple resistance mechanisms were likely present.

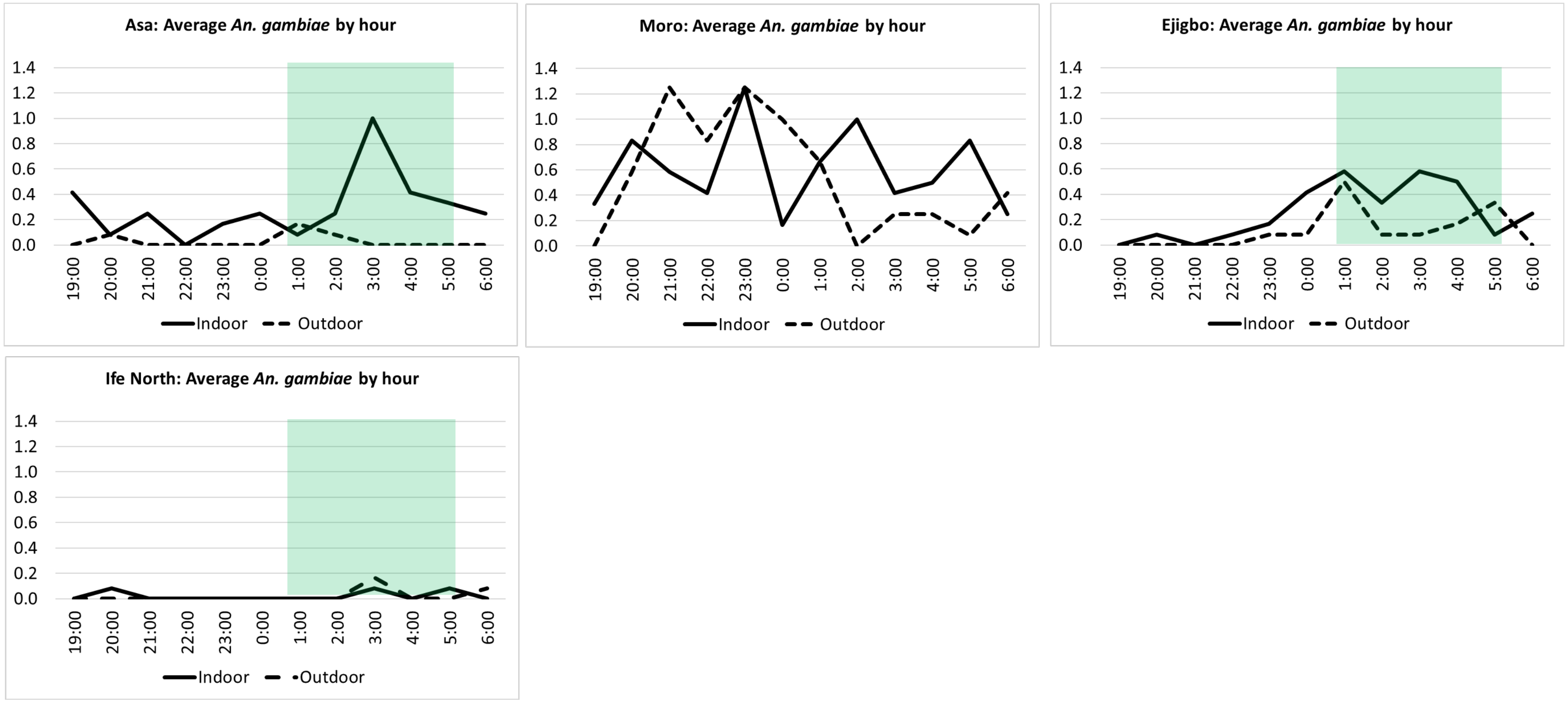
Data on nightly biting patterns of *An. gambiae* s.l. (Figure N5) showed a slight preference for biting indoors. Peak biting activities tended to be between 1:00 and 5:00, except in Moro, where indoor biting activity was consistent throughout the night and outdoor biting peaked earlier in the evening, from 21:00 to 0:00 hours.

Table N6. Baseline entomological characteristics of the study sites in Nigeria.

	Ejigbo (standard ITNs)		Asa (IG2 ITNs)		Moro (RG ITNs)		Ife North (PBO ITNs)	
	Year 1	**Year 2**	**Year 1**	**Year 2**	**Year 1**	**Year 2**	**Year 1**	**Year 2**
Most abundant vector (% of likely vector species collected)	*An. gambiae* s.l. (88%)		*An. gambiae* s.l. (100%)		*An. gambiae* s.l. (100%)		*An. funestus* s.l. (82%)	
Second most abundant vector (% of likely vector species collected)	*An. funestus* s.l. (6%)		n/a		n/a		*An. gambiae* s.l. (14%)	
***An. gambiae* molecular IDs**								
An. gambiae s.s.	73.3%		66.7%		73.4%		66.7%	
An. coluzzii	26.7%		26.7%		21.5%		33.3%	
An. arabiensis	–		2.5%		5.1%		–	
CDCLT nightly landing rates (*An. gambiae* s.l.)								
Indoor:outdoor ratio	0.92		9.75		2.50		10.00	
Pyrethroid-resistance profile	**MODERATE to HIGH: Partially mitigated by PBO**							
WHO tube test mortality	73%–94%		12%–38%		41%–57%		20%–71%	

Abbreviations: CDCLT, US Centers for Disease Control and Prevention light trap; ID, identification; IG2, Interceptor G2; ITN, insecticide-treated net; n/a, not applicable; PBO, piperonyl butoxide; RG, Royal Guard; WHO, World Health Organization.

Figure N5. Nightly biting patterns for *An. gambiae* in each of the study sites, estimated from CDC light trap collections, November 2020–April 2021.



Note: The green shading represents the hours of peak biting.
Abbreviation: CDC, US Centers for Disease Control and Prevention.

Human behavior

This section has not been updated since the previous report (published in December 2021). This section will be updated in the final report, which is expected to be published in early 2023.

Two rounds of human behavior data collection occurred in 2020 and 2021 (Table N7). Indirect monitoring began in 2021. Research participants were recruited from three study sites in each of the four LGAs. A total of 820 participants were enrolled in this study component, comprising 300 participants enrolled in indirect monitoring, 257 enrolled in IDIs, and 263 enrolled in FGDs. After Round 1, it was determined that fewer interviews would be needed to reach saturation and the number of FGDs was increased for future rounds. Coding and analysis of Round 1 and Round 2 were completed. Round 3 data collection is planned for July 2022.

Table N7. Number of participants by human behavior data collection activity, 2020 and 2021.

	Number of participants		
	2020	**2021**	**Total**
Indirect monitoring		300	300
In-depth interview	192	65	257
Focus group discussion	92	171	263

ITN use

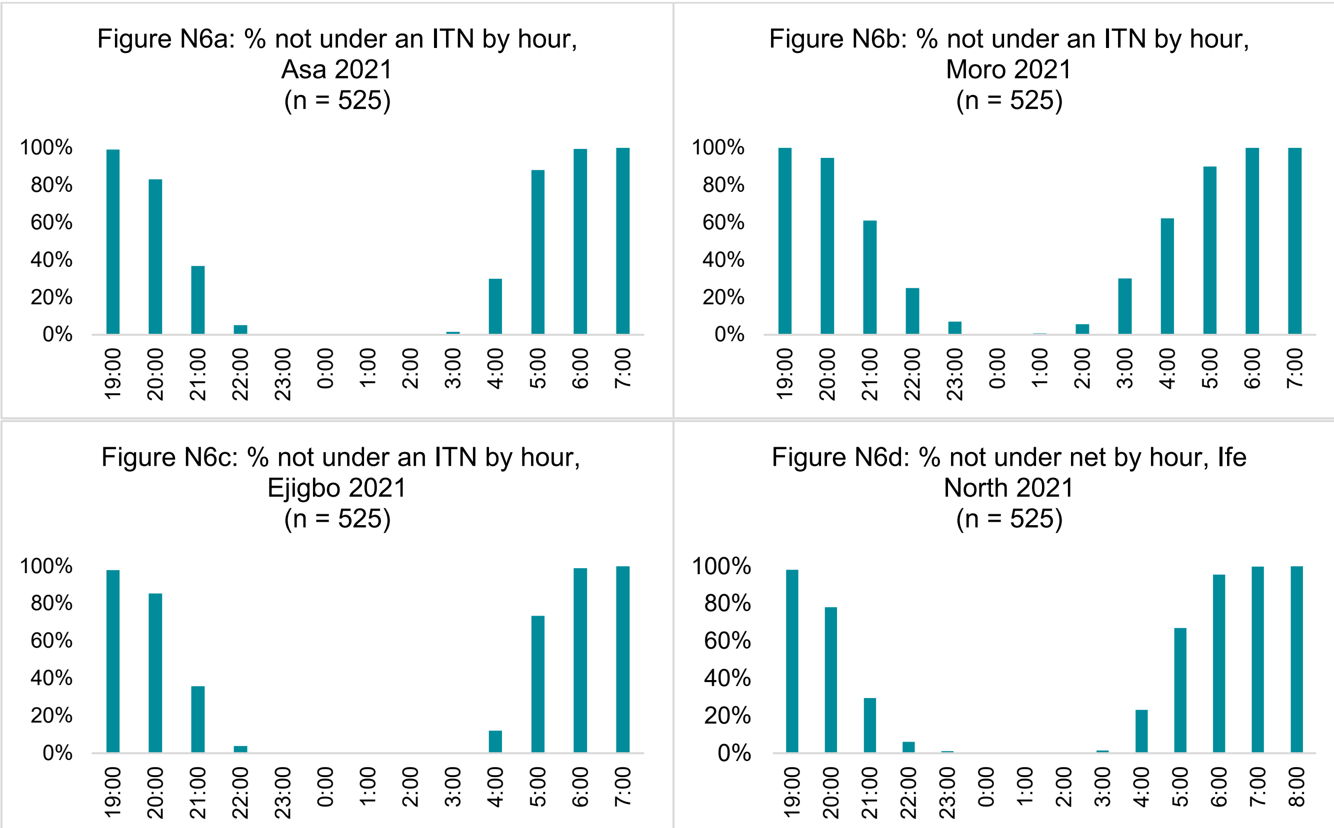
Data from Round 2 indirect monitoring showed that participants in Ejigbo, Asa, and Ife North had very similar average bedtimes of around 21:40 and wake times of about 5:30. Moro had a later average bedtime and earlier wake time (22:20 and 4:28, respectively) compared with the other three LGAs. The number of times participants got out of bed at night also varied across LGAs. For example, in Asa, nearly all participants (95%) got out of bed at least once in the night, whereas in Ife North, only a little over half of the participants (58%) did. Across all four LGAs, the most common reason for getting out of bed at night was to use the toilet. Especially in Asa and Moro, cooking, praying, and eating/drinking were also common.

Table N8. Indirect monitoring participant characteristics, May 2021

	Ejigbo (standard ITNs)	**Asa (IG2 ITNs)**	**Moro (RG ITNs)**	**Ife North (PBO ITNs)**
Households enrolled	15	15	15	15
Participants enrolled	75	75	75	75
Average bedtime (minimum–maximum)	21:43 (19:09–0:05)	21:43 (19:50–0:20)	22:20 (20:03–1:25)	21:39 (19:27–0:51)
Average wake time (minimum–maximum)	5:37 (3:26–7:30)	5:13 (3:15–7:10)	4:28 (1:35–6:55)	5:34 (3:18–8:18)
Average # times out of bed (minimum–maximum)	0.9 (0–3)	1.6 (0–5)	1.6 (0–5)	0.8 (0–5)

Abbreviations: IG2, Interceptor G2; ITN, insecticide-treated net; PBO, piperonyl butoxide; RG, Royal Guard.

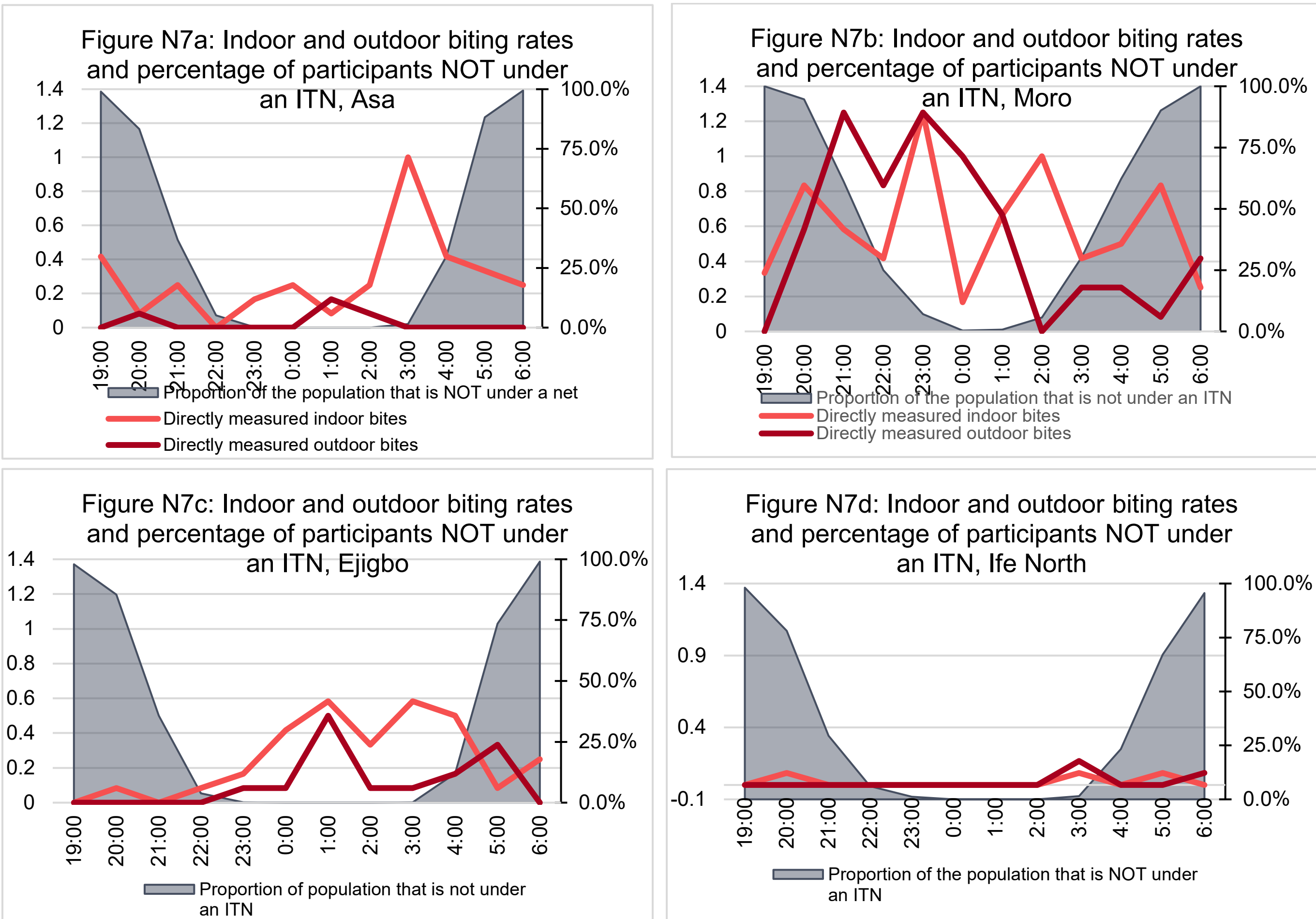
Figure N6. Proportion of indirect monitoring observations not under an ITN by hour and by LGA.



Abbreviations: ITN, insecticide-treated net; LGA, local government area.

Figures N7a to N7d compare the average directly measured indoor and outdoor biting rates with the proportion of indirect monitoring observations not under an ITN from 19:00 to 6:00. Biting rates were calculated using data collected during hourly CDCLT collections from November 2020 to April 2021. Percentages of observations not under a net, by hour, were calculated using data collected from indirect monitoring from March to September 2021.

Figure N7. Indoor and outdoor biting rates and percentage of participants not under an ITN by LGA.



Abbreviations: ITN, insecticide-treated net; LGA, local government area.

In Asa, all observations were under ITNs during peak biting times from 0:00 and 3:00, but the time periods from 19:00 to 21:00 and 4:00 to 6:00 likely exposed at least 30% of observations to indoor biting at some point. Activity during the night (19:00 to 21:00) and early morning (4:00 to 6:00) in Moro exposed at least 60% of observations to increased biting risk. In Ejigbo, all observations were under ITNs during peak biting times between 0:00 and 4:00, but at least 74% of observations were exposed to indoor and outdoor biting at 5:00. In Ife North, there was an overlap between biting times and times participants were not under an ITN in the morning (3:00 to 6:00). However, biting rates were low overall so participants had relatively low exposure to bites. In contrast, overall biting rates were highest in Moro.

Drivers of ITN use and non-use

Malaria-prevention options. Participants named multiple options to prevent malaria. While most participants named ITNs as a malaria-prevention method, they also noted spraying insecticides, using mosquito coils, closing windows, using fans, and reducing mosquito breeding grounds by removing bushes and stagnant water. Many participants described using a combination of methods. Use was based on personal preference and other considerations, such as cost, accessibility, and perceived risks and/or side effects of different interventions. Participants largely noted using insecticides and coils and closing windows and doors as prevention approaches in the absence of an ITN.

Some participants expressed a preference for using drugs or herbs to prevent or treat malaria over using an ITN, as drugs and herbs were cheaper and easier to access than ITNs.

> *"The use of drugs and injection also in order to prevent malaria—you must always protect yourself from mosquito bite, because it [is] the major cause of malaria. We make use of mosquito coil, paper, insecticides, and mosquito net, which [I] am currently using."*
>
> *—Interviewee, Asa*

Weather/seasonal variation. In all LGAs, there was seasonal variation in ITN use. The hot, dry season was associated with less malaria than the colder, wetter months. ITN use and reasons for use also differed in these periods. Many participants said they used ITNs during the wetter months more often than during the dry season. Participants linked this shift to the increased presence of mosquitoes during the rainy months.

> *"Just like my colleague has said: during rainy seasons, there are plant, bushes, and stagnant [water], which breed mosquito there. This will lead to increase in usage of bednet."*
>
> *—FGD participant, Asa*

Heat was also a strong driver for non-ITN use. Participants consistently reported spending time outside until late into the night during the dry season to escape the heat. Similarly, many participants reported not using ITNs during the dry season because it was too hot to use nets and because there were not as many mosquitoes in their homes.

> *"When there is heat, we fold the net since we don't feel comfortable under the net due to the shortage in supply of the national grid during the period. As a result, mosquitoes come in."*
>
> *—Interviewee, Ejigbo*
>
> *"We might hang the net during the summer period. And [when] there is heat ... we will raise the net, but this raising causes the trooping in of mosquitoes."*

—Interviewee, Moro

There were no apparent differences across sites regarding the issue of heat and non-ITN use.

Access. Participants reported getting their nets through government campaigns, as well as ANC and immunization visits. Many participants preferred door-to-door distribution. Others noted challenges in receiving nets because they lived too far away from the distribution sites, were not home at the time of distribution, or were unmarried. Suggestions to address the challenges included having more frequent distributions, distributing nets on weekends to ensure more people will be home, and having nets available at the health facility.

> *"It is different from the previous distribution that you have to fill some document and later take it to where you will collect the net. You have to queue in the sun before you can get the net. One may stay for hours or a day, and yet it won't get to your turn. This method of house to house is the best way of distributing the net."*
>
> *—FGD participant, Ejigbo*
>
> *"The best way is bringing the bednet to our doorstep so that everybody in the neighborhood can easily get enough bednets, but they did not give single ladies the bednet. They said [this] is because we are not yet married."*
>
> *—FGD participant, Ife North*

Use. Some participants used nets every day, and others used ITNs less frequently during the hot, dry months. Many people described spreading out the nets for a few days in order to reduce the potency of the insecticide.

> *"I spread it outside for two days because of the chemical on it. After two days, I took it inside, hanged it, and started using it."*
>
> *—Interviewee, Moro*

Participants also described repurposing nets to cover windows or, when they became old, using them for other domestic purposes, such as to protect livestock or plants, carry materials, or make sponges.

> *"We also use our old bednets to cover our windows. We cut the net into the size of the window and nail it there."*
>
> *—FGD participant, Asa*

Maintenance. Among participants, washing was common, but opinions varied on whether tears could be mended. While some described replacing or not using nets that were torn, others repaired small tears or only repaired tears if they did not have a replacement net available.

> *"When it gets dirty, I wash it; but when it tears, I stop using the bednet."*
>
> *—Interviewee, Asa*

Preferences. Several participants mentioned that protecting against malaria was the most important function of a net and the other factors (shape, color, texture) were less important or did not matter. Participants who did note preferences in color expressed practical and aesthetic reasons. Several participants noted that white nets got dirty easily.

> *"The blue bednet [doesn't] show dirtiness [with] time. Most especially, we that have children, if we use [a] white bednet, within two weeks it will get dirty."*
>
> *—Interviewee, Moro*

Participants liked that rectangular nets were easy to hang and looked nice.

> *"What I like about the rectangular shape is that it is very easy to hang. The bed itself is in rectangular shape so, in view of that, it is very easy to nail the hooks in the four corners of the bed with the provided ropes."*
>
> *—Interviewee, Ife North*

Benefits. In addition to providing protection from mosquitoes and other insects, participants noted that using ITNs kept people healthy and saved money on hospital treatments. Participants also enjoyed the added warmth during cold weather and the peace of mind of using nets.

> *"There are many reasons for using a bednet. People sleep under the bednet with peace of mind knowing that the net will be killing the mosquito for them."*
>
> *—FGD participant, Ife North*

Challenges. Besides seasonal/weather challenges, other drivers of non-ITN use included skin and eye irritation, chemical smells, and concerns about the safety of insecticides, and not having a net available when traveling. Some participants also mentioned not having enough information on how to use nets properly.

> *"Some don't have knowledge on what to do before using the [bednet] in order to reduce the chemical on the bednet. Therefore, they complain of burning sensation whenever they use it."*
>
> *—FGD participant, Ejigbo*

Further analysis will consider differences by age and gender where this information is available.

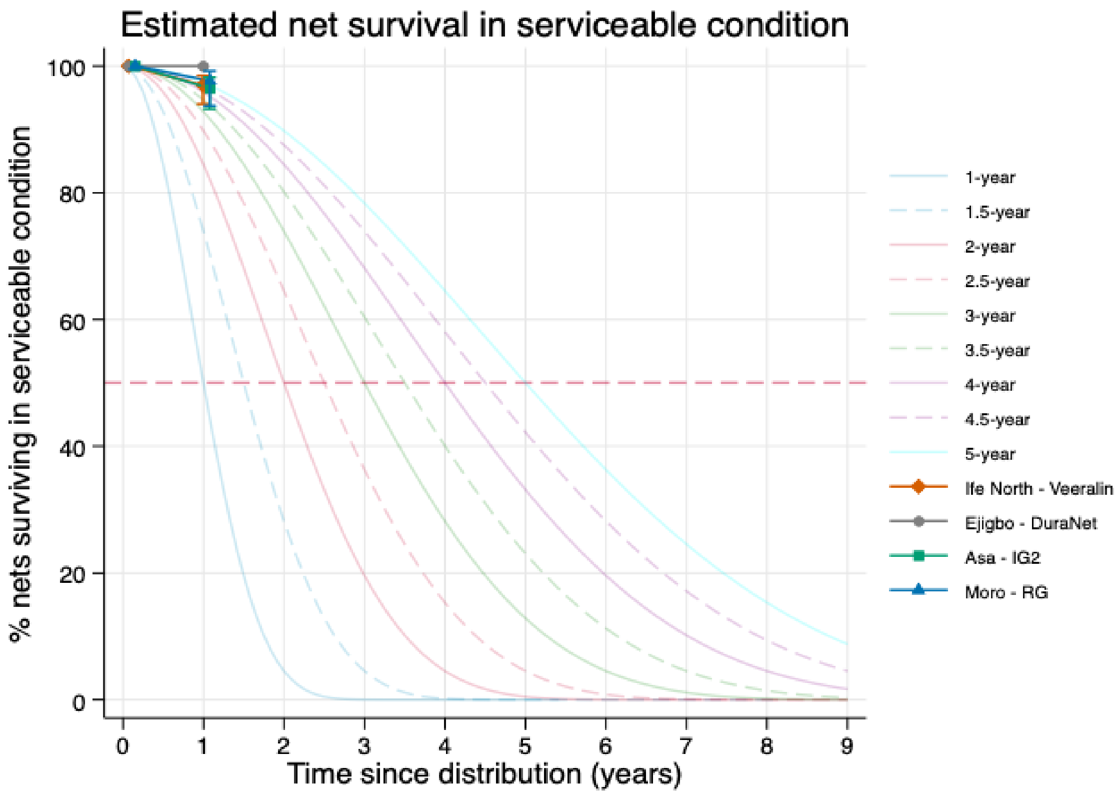
Durability monitoring

This section has been updated with results from the 12-month survey conducted in November 2021.

Participants reported using 77%, 88%, and 80% of nets the previous night in Ejigbo, Asa, and Moro, respectively, compared with only 45% in Ife North. Very few nets (less than 5%) were in their packages at 12 months. Hanging rates tended to mirror use rates in each LGA, with 46% of nets hung in Ife North, 63% in Ejigbo, 71% in Asa, and 87% in Moro. Between 45% and 78% of used nets were used consistently throughout the previous week and 73% of households reported using them during both rainy and dry seasons. Only 10% of households reported using nets only in the dry season or not at all. Nets from other sources continued to be limited at 12 months, with the bulk of them obtained from previous campaigns or ANC visits.

After one year, between 4.7% (Ejigbo) and 27.1% (Asa) of the campaign nets still found in the homes and inspected for damage were found to have any holes. However, the level of damage was limited, such that 94.0% of nets in Ife North, 98.8% in Ejigbo, 89.5% in Asa, and 94.4% in Moro were determined to be “in good condition” based on the proportionate Hole Index. Less than 4% of nets in all LGAs were too torn to be useful. Combining these findings with the attrition rate resulted in estimates for the survival of campaign nets in serviceable condition after 12 months of 97.0% in Ife North, 100.0% in Ejigbo, 96.5% in Asa, and 97.7% in Moro (Figure N8).

Figure N8. Estimated net survival in serviceable condition with 95% error bars plotted against hypothetical survival curves with defined median survival.



Abbreviations: IG2, Interceptor G2; RG, Royal Guard.

Summary

The baseline cross-sectional survey highlighted key differences between LGAs, especially with regard to net ownership and use, with Asa having exceptionally low net ownership and use. After the ITN campaign, the Year 1 survey indicated substantial increases in net ownership across all LGAs. Ejigbo and Asa also reported large increases in the proportion of the population that slept under a net the previous night. Increases in net use in Moro and Ife North were modest even though ownership and access to nets increased. At baseline, Asa had the highest prevalence. At the Year 1 survey, Asa and Moro had the largest decreases in prevalence in children under 5 years old; however, since SMC was also introduced in those LGAs (and not in Ejigbo or Ife North), the amount of prevalence reduction attributable to ITNs is unclear and is the subject of future modeling exercises. Ejigbo and Ife North also reported decreases in prevalence in children under 5 years old since the baseline survey. In contrast to the change in prevalence, Asa continued to show the highest level of all-age incidence and prevalence among pregnant women during ANC-based surveillance, perhaps suggesting that high levels of private-sector healthcare seeking continue to complicate passive malaria surveillance in many parts of Nigeria.

Summary of findings to date

These preliminary results highlight a few things that require further analysis before conclusions can be drawn on the effectiveness of dual-AI and PBO nets. First, there are several important sources of heterogeneity to consider among the drivers of ongoing malaria transmission both within countries and between countries. Second, any discussion of ITN effectiveness must consider the dynamics between vector biology, human behavior, environment, and baseline intensity of malaria transmission.

Having highlighted these caveats, it is clear that mass ITN distribution campaigns are associated with reductions in malaria transmission in all settings, independent of ITN type. What is still less clear is how much of this effect results from the personal protection provided by the barrier effect of an ITN and how much results from the insecticidal effects (lethal and nonlethal) of an ITN on the vector populations. Furthermore, how much the latter is influenced by varying levels of insecticide resistance and the degree to which the next generation of dual-AI ITNs effectively counteract this should become clearer as additional data become available.

Three cross-sectional surveys have been completed in Burkina Faso (2019, 2020, and 2021), three in Rwanda (February and December 2020 and November 2021), and two in Mozambique (2020 and 2021). Two surveys have been completed in Nigeria (2020 and 2021).

In Burkina Faso, results from three surveys provide preliminary year-to-year comparisons (pre-ITN campaign and post-ITN campaign) of prevalence for each ITN type; however, because of the expansion of SMC, these results require further analyses using mathematical modeling and multivariate regression analyses before interpretation. The differences in the ITN distribution campaigns (PBO ITNs in June, standard ITNs in August, and IG2 ITNs in October) and SMC campaigns in children under 5 years old will be adjusted to estimate the “true” impact of IG2 ITNs on malaria compared with other ITN types.

In Rwanda, ITN distribution varied by district: standard ITNs were distributed first in Nyamagabe and Ruhango in February 2020, and IG2 ITNs were distributed in Karongi in June 2020. In addition, Ruhango District (where malaria transmission is historically moderate but higher than in Karongi and Nyamagabe) was selected for annual IRS beginning in October 2019. Rwanda is unique compared with the other three countries in that it includes all ages in prevalence surveys rather than only children under 5 years old. Due to the low February baseline malaria prevalence of about 3% in the three districts, the subsequent prevalence surveys for 2020 through 2022 were shifted to November or December—at the peak of the longer malaria transmission season. Further multivariate regression analyses will adjust for differences in timing of ITN campaigns. Data from the human behavior component and entomology component will be key to further understanding the observed gains and maintaining low malaria transmission.

In Mozambique, the 2020 baseline cross-sectional survey occurred before ITN distribution, which explains the universally low ITN ownership and ITN use and high malaria prevalence observed in five of the six districts. Changara District (PBO) had a significantly lower prevalence than expected at baseline (5%) so it was thought initially that the study may be underpowered to assess the assumed 15% decrease in malaria prevalence after distribution of each net type. However, this interim analysis suggests a larger effect size than assumed initially so it now seems likely that the study is adequately powered. Data presented here show that the distribution campaigns of 2020 successfully and dramatically increased net ownership and use across all study districts. While malaria transmission decreased everywhere after distribution, after 11 months, districts that distributed one of the new net types—IG2 or RG—saw substantially larger decreases in malaria transmission relative to the control district that distributed standard pyrethroid-only ITNs. Data collection for costing is complete, and preliminary work on the cost-effectiveness analyses is underway.

Nigeria conducted the 2020 baseline cross-sectional survey (pre-ITN campaign) in the four LGAs. These areas were selected for their similarities—namely, high malaria transmission, expected dominance of *An. gambiae* s.l. as the primary vector, and known insecticide-resistance patterns. Results from the second survey provide preliminary year-to-year comparison (pre-ITN campaign and post-ITN campaign) of prevalence for standard and PBO ITNs. Due to the introduction of SMC in Asa and Moro (the IG2 and RG LGAs, respectively), these results require further analyses using mathematical modeling and multivariate regression analyses before interpretation.

Interceptor G2 ITNs

IG2 ITNs were distributed across five districts: Banfora in Burkina Faso (2019), Karongi in Rwanda (2020), Cuamba in northern Mozambique (2020), Guro in western Mozambique (2020), and Asa in Nigeria (2020).

Banfora. The IG2 ITNs were distributed in October 2019, three months after the baseline survey (July 2019). There was an increase in ITN ownership, ITN use, and population access to ITNs from 2019 to 2020 followed by a modest decrease in 2021. Malaria prevalence in children under 5 years old decreased from 2019 (40%) to 2020 (18%) and again in 2021 (12%). The 2021 figure is complicated by the expanded SMC campaign, and ITN impacts are still being assessed through mathematical modeling. Baseline entomological surveillance found that highly pyrethroid-resistant *An. gambiae* s.s. and *An. coluzzii* were the primary vectors. Additionally, there was an observed decline in indoor and outdoor biting from 2019 to 2020.

Karongi. There was an observed increase in ITN ownership (89% to 95%) and ITN use (68% to 71%) in the postcampaign survey. Malaria prevalence was low in both the precampaign (2.5%) and postcampaign surveys (2.7% in 2020 and 1.2% in 2021). At baseline, *An. gambiae* s.s. was the dominant vector and showed low levels of pyrethroid resistance. Given the low level of transmission in Karongi, detecting significant differences of malaria prevalence when comparing it with other districts may be difficult.

Cuamba. The cross-sectional survey that was done before IG2 distribution found low ITN ownership (33%), ITN use (19%), and population ITN access (21%). However, substantial increases in ownership (75%), use (68%), and access (65%) were observed in the 2021 survey, almost one year after the campaign. The baseline survey showed that malaria burden was high, with prevalence at 48%, but this declined substantially to 29% in 2021. At baseline, moderately pyrethroid-resistant *An. gambiae* s.l. was the dominant vector species. The Year 2 survey is scheduled for September 2022.

Guro. ITN distribution occurred in November 2020, two months after the baseline survey. Following distribution, ITN ownership, ITN use, and population access to ITNs all substantially increased (from 31%, 19%, and 19%, respectively, in 2020 to 98%, 98%, and 89% in 2021). Correspondingly, malaria prevalence in children under 5 years old declined from 17% in 2020 to 4% in 2021. At baseline, moderately pyrethroid-resistant *An. gambiae* s.l. was the dominant vector species. The Year 2 survey is scheduled for September to October 2022.

Asa. The baseline cross-sectional survey (pre-IG2 distribution) found ITN ownership (8%), ITN use (3%), and use given access (68%) to be low at baseline. Malaria prevalence was 63%. ITN ownership (66.6%), use (43.6%), and prevalence (15.8%) all improved substantially during the Year 1 survey, though the prevalence measure was complicated by a concurrent, expanded SMC campaign. Additionally, ITN impacts are still being assessed through mathematical modeling. At baseline, highly pyrethroid-resistant *An. gambiae* s.s. was the dominant vector.

Royal Guard ITNs

RG ITNs were distributed in two districts: Mandimba in northern Mozambique (2020) and Moro in Nigeria (2020).

Mandimba. At baseline before ITN distribution, ITN ownership (30%) and ITN use (17%) were low, though use given access was high (1.03), indicating that those who had ITNs used them. The Year 1 cross-sectional survey showed a substantial increase in ITN ownership (90%) and use (82%). Malaria prevalence was high (66%) at baseline and decreased to 46% in 2021. Moderately pyrethroid-resistant *An. gambiae* s.l. *and An. funestus* s.l. were the predominant species. Ongoing data analyses are evaluating differences in indoor and outdoor biting patterns. The Year 2 survey is scheduled for September 2022.

Moro. The baseline cross-sectional survey was in October 2020, and distribution of RG ITNs was in November 2020. Prior to RG ITN distribution, household ITN ownership (26%), ITN use (17%), and ITN use given access (18%) were low, and malaria prevalence was 50%. The primary vector species was highly pyrethroid-resistant *An. gambiae* s.s. During the Year 1 survey, ITN ownership (51%) improved but use (19%) remained low. Prevalence (21%) declined substantially, though the prevalence measure was complicated by a concurrent expanded SMC campaign. Additionally, ITN impacts are still being assessed through mathematical modeling.

PBO ITNs

PBO ITNs were distributed in three districts: Orodara in Burkina Faso (2019), Changara in western Mozambique (2020), and Ife North in Nigeria (2020).

Orodara. PBO ITN distribution occurred in June 2019, before the baseline cross-sectional survey in July. This resulted in high proportions of ITN ownership (100%), ITN use (79%), and use given access (94%). The high proportions were maintained at the Year 1 and Year 2 postcampaign surveys: ITN ownership was 100% in 2020 and 99% in 2021, and ITN use was 85% in 2020 and 84% in 2021. Preliminary analyses found a decrease in malaria prevalence from 28% at baseline to 4% at Year 1 and 2% at Year 2. This Year 2 figure is complicated by the expanded SMC campaign; ITN impact independent of this is being assessed through mathematical modeling. Further regression analyses and mathematical modeling will adjust for differences in the timing of PBO ITN distribution relative to the cross-sectional survey. Highly pyrethroid-resistant *An. gambiae* s.s. was the primary vector at baseline, and indoor and outdoor biting rates increased somewhat from 2019 to 2020.

Changara. There was high use given access (0.88) at baseline, though ITN ownership (48%) and ITN use (23%) were low before PBO ITN distribution. Substantial increases in ownership (96%) and use (85%) were observed during the Year 1 survey. At baseline, moderately pyrethroid-resistant *An. gambiae* s.l. was the dominant vector species, but malaria prevalence was substantially lower than expected (5.7%), raising important questions about whether the study may therefore be underpowered to detect the expected impact in this district. Nonetheless, the Year 1 survey did demonstrate a significant decrease in prevalence to 2.1%. The study expanded passive malaria and entomological surveillance to two additional districts—Doa District in Tete Province, which received PBO ITNs, and Tambara District in Manica Province, which received IG2 ITNs.

Ife North. The baseline survey conducted before PBO distribution found low ITN ownership (38%), ITN use (24%), and use given access (24%) since the last net campaign was held in 2017. Malaria prevalence was high at 48%. *An. funestus* s.l. was the most abundant vector species at baseline. ITN ownership (68%), use (34%), and prevalence (40.9%) all improved modestly during the Year 1 survey.

Standard pyrethroid-only ITNs

Standard ITNs were distributed in six districts: Gaoua in Burkina Faso (2019), Nyamagabe and Ruhango in Rwanda (2020), Gurue in northern Mozambique (2020), Chemba in western Mozambique (2020), and Ejigbo in Nigeria (2020).

Gaoua. Overall, there were increases in household ITN ownership (69% to 75%) and ITN use (21% to 44%) from 2019 to 2020; and decreases to 57% for ITN ownership and 37% for ITN use in 2021. The malaria prevalence in Gaoua was 81% (2019) at baseline, which decreased to 49% at the Year 1 2020 survey and to 21% in Year 2. This Year 2 figure is complicated by the expanded SMC campaign; the ITN impact independent of SMC is being assessed through mathematical modeling. Highly pyrethroid-resistant *An. gambiae* s.s. and *An. funestus* s.l. were the most dominant vectors at baseline. Nightly biting rates decreased by 52% from 2019 to 2020.

Nyamagabe. Mass distribution campaigns of standard ITNs occurred in February 2020, the same month as the baseline survey. Malaria prevalence was low in February at 2.4%; it was at 2.7% during the post-ITN campaign survey in December 2020 and 0.3% in November 2021, during the high-transmission seasons. Baseline mosquito collections showed a mix of *An. funestus* s.l. (92%) and *An. gambiae* s.s. (8%) and very little pyrethroid resistance.

Ruhango. Standard ITNs were distributed in February 2020, and IRS was implemented in November 2020 (IRS was initially implemented in October 2019). Standard ITNs were distributed in the same month as the baseline survey (February 2020), which resulted in high and increased ITN ownership (from 94% to 98%), ITN use (from 73% to 79%), and use given access (from 83% to 89%) from February to the postcampaign survey in December. Malaria prevalence was low in February—just 1.3%. This increased to 5.2% in December, most likely due to the survey time shifting to the high-transmission season. By November 2021, prevalence had declined to 1.0%—though again this is a measure of the combined effect of IRS in October 2021 and the standard ITNs. At baseline, the dominant vector species was *An. funestus* s.l., and it showed low levels of pyrethroid resistance.

Gurue. The baseline survey before the ITN distribution found ITN ownership and ITN use were 37% and 24%, respectively. The Year 1 survey found that ITN ownership and ITN use significantly increased to 96% and 87%, respectively. However, the corresponding decrease in malaria burden from baseline (65%) to Year 1 (53%) was not statistically significant. Moderately pyrethroid-resistant *An*. *gambiae* s.l. and *An*. *funestus* s.l. were the predominant vectors; however, there has been low mosquito densities to date.

Chemba. The baseline survey before net distribution found ITN ownership at 63%, ITN use at 33%, and a high ITN use given access of 1.10. ITN ownership and ITN use increased to 99% and 90%, respectively, in the Year 1 survey after the campaign. Malaria burden remained high throughout the first year of the study, with a prevalence of 44% at baseline and 39% at Year 1. Moderately pyrethroid-resistant *An*. *gambiae* s.l. and *An*. *funestus* s.l. were the predominant vectors.

Ejigbo. The precampaign survey found low ITN ownership (43%), ITN use (20%), use given access (27%), and malaria prevalence (38%). The predominant species was *An. gambiae* s.s., which had moderate to high resistance and WHO tube test mortalities from 73% to 94% at baseline. ITN ownership (76%), use (47%), and prevalence (25.6%) all improved during the Year 1 survey.

Discussion

One of the strengths of the New Nets Project pilot evaluations is that they take advantage of natural comparisons that arise as the result of operational decisions made by NMCPs. This allows the impact of various ITN deployment strategies to be evaluated rapidly and in real-world implementation settings; such evaluations can use a combination of programmatic data and targeted surveys to measure public health outcomes that are most useful for national stakeholders, both for monitoring progress toward national goals and for informing future vector control decisions. Using a similar approach, national programs will be able to monitor interventions in the future as new products become available to assess the factors that contribute to ITN impact.

The data from these pilots will be used by NMCPs to guide decisions around which vector control tools to deploy in various settings in their countries. These data will also help to highlight key variables to consider for use in modeling, risk stratification, and assessment of progress. Modeling work will further elucidate how key variables may be associated with impact across districts, taking into account baseline differences in vector species bionomics, prevalence of malaria, case incidence, and human behaviors.

Previous interim analyses from these pilots highlighted the variability and diversity in malaria transmission dynamics among study districts, both across and within countries. For example, population access to ITNs at baseline varied from 4% to 80%. In Burkina Faso, this increased to above 75% in IG2 and PBO districts and remained low at 40% in standard ITN districts two years after ITN distribution campaigns. In northern and western Mozambique, ITN access was above 80% in all districts 11 months after campaigns. This raises questions about drivers of ITN retention as well as the influence of delays between acquisition and first use of a new ITN. Although use given access was generally higher than standard access metrics, it nonetheless ranged from 44% to 100%. This again highlights the importance of further understanding drivers of ITN use, such as population movement, messaging, perceptions on long-term ITN use, and alternative uses of ITNs in some districts for economic activities.

Malaria prevalence at baseline also varied substantially, with estimates ranging from 1.3% to 81.0%. Baseline prevalence is expected to significantly influence the measurement of ITN effectiveness given that low or very high baseline prevalence will influence the percentage changes observable due do the presence of these ITNs. Therefore, further analysis is planned to better describe any differential impacts given widely varying starting points. This is also important for incidence rate calculations and time-series analyses using routine surveillance data.

Since the previous interim report summarized baseline findings, data collection has progressed in each pilot country and preliminary results are beginning to come into focus for several of the evaluations. For example, in both northern and western Mozambique the ITN distribution campaigns resulted in significant increases in ITN ownership (to above 90%) and use at night (to above 80%) in all districts, regardless of the ITN type distributed. However, distribution of standard ITNs was not associated with any significant change in either malaria prevalence or case incidence in either region, whereas distribution of IG2, RG, and PBO nets were all associated with substantially larger decreases in malaria burden than standard ITNs.

Assessing trends in malaria prevalence and incidence in Burkina Faso and Mozambique provides compelling evidence of the impact that ITN distribution campaigns can still have. Two years after mass campaigns in Burkina Faso, ITN ownership (above 90%) and use at night (above 85%) in IG2 and PBO districts remained high, though use at night was under 40% in the standard ITN district. These high rates of ITN ownership and use were associated with decreased malaria prevalence in each study district after two years, though the decrease in prevalence was most substantial in the PBO ITN district of Orodara. Importantly, monthly case incidence data in the study districts over the same time period suggest that these gains were sustained more in the IG2 and PBO net districts than in the standard ITN district, with the greatest sustained impact observed in the IG2 district. Forthcoming analysis will look closely at the duration of effect across each, including data on vectorial resistance

In Rwanda, where ITN ownership and use were highest to begin with (between 68-73%) compared with other countries, the IG2 distribution campaign in Karongi did not increase these overall metrics noticeably. However, analysis from the New Nets Project Net Supplement showed that the type of net most frequently used in Karongi shifted after the 2020 ITN campaign from standard to IG2. Malaria incidence continued to decrease from baseline in 2019 to date in all districts, but the reductions were greater in Karongi (IG2 district) and Ruhango (standard and IRS) compared with Nyamagabe (standard ITN) district. The third post distribution survey in November 2022 will give more insight into how sustained these reductions are in this setting.

In Nigeria, baseline evaluations showed high incidence in all LGAs. Post-campaign evaluations of ANC and passive surveillance data from the DHIS2 system from 2020 to date showed increases in malaria incidence in the IG2 LGA and no changes in malaria incidence in PBO LGAs. Human behavior and entomology results will be very important in the interpretation of the observed trends and will provide feedback on what could be done in communities in the future.

Also in Nigeria, in 2021, SMC was administered to children under 5 years old in two LGAs. Future malaria prevalence will be predicted using mathematical models that take into account vectorial behavior, ITN use, and timing of mass campaigns to predict ITN impact without SMC. Additionally, given the limitations of routine HMIS data for evaluating malaria trends, ANC surveillance has been proposed as an alternative. First-time ANC attendees in the four LGAs were tested for malaria infection from November 2020; prevalence ranged from 30% to 60% across ITN types, though it remained high in all months in the IG2 LGA. This highlights the importance of further understanding the drivers on transmission in this LGA and suggests that high levels of private-sector healthcare seeking may also complicate standard ANC-based malaria surveillance approaches in Nigeria.

Differences in vector species, biting behaviors, and insecticide-resistance status were also major drivers of expected impact for any new ITN type. The data collected thus far showed significant variation in biting rates (from more than 20 to less than 1 per night) and biting times. In some places, these observations suggested significant exposure beyond the traditional nighttime hours in which an ITN is typically able to provide protection. Further refining these mosquito insecticide-resistance profiles and feeding characteristics then aligning results with human behavior data related to net use will provide valuable context and allow interpretation of the final results on the impact of the ITN distributions on malaria transmission.

In addition, while all study participants in the human behavior activities had a strong baseline understanding of malaria transmission factors, there were still differences in preferences that could potentially be important in understanding ITN effectiveness. Examples include the availability of and preference for alternative mosquito control measures (e.g., plants, mosquito coils, spray), as well as how environmental factors (e.g., heat) or practical considerations (e.g., ease of hanging) might affect impact. The effect of preferences on behavior will be explored in subsequent analyses.

The contextual factors that influence the average effect of these ITNs are continually being assessed. The next steps for each country will be to further refine analyses of changes in prevalence and incidence, drivers of ITN use, impacts on vector species, and the intersection between mosquito biting behaviors and human behaviors. As this is an interim report, further analysis using interrupted time-series, difference-in-difference, and negative binomial regression models will be presented in the next report that will include all study data and will allow more substantive conclusions. Routine data incidence rate ratios will compare malaria incidence in standard and PBO districts with incidence in IG2 districts, adjusting for seasonality, lag time in the mass campaigns (Burkina Faso and Rwanda), and other known confounders. The malaria prevalence determined from baseline and Year 1 surveys will be inputted into the logistic regression models—adjusting for ITN use, age group, gender, and household characteristics—to determine the efficacy of IG2 nets. In addition, modeling work is underway using pilot data, which will inform calibration of model parameters to predict distinct impacts in different regions across the pilot countries. This includes using the baseline parameters described in the beginning of this report to model the predicted parasite prevalence in standard and PBO ITN districts so that each district, independent of what ITN they received, will have prediction curves for PBO and standard ITNs to then compare with subsequent prevalence survey results.

Although this is an interim analysis, the remarkable heterogeneity noted above shows a complex set of effects. Understanding these interactions will be critical for NMCP decisions around product choice, deployment, and impact evaluations methods in a setting of constrained resources. Early indications are that universal coverage campaigns using any of the new net types (IG2, PBO, and RG ITNs) are more effective at reducing malaria transmission than universal coverage campaigns using standard pyrethroid-only ITNs. This is particularly evident in Mozambique, where the largest reductions in prevalence (42%) and incidence (75%) to date were observed in the IG2 district of Cuamba, which also happened to report the lowest rates of ITN ownership and use (75% and 68%, respectively). Similar to findings recently reported from cluster randomized control trials in Tanzania and Benin, this is highly suggestive of an important community effect for IG2 relative to standard nets – something that will be investigated further when the complete entomological surveillance datasets are available. However, these differences in effect may be less pronounced in the west African setting of Burkina Faso, where ongoing assessments of the unique and profound vector-resistance profiles will be important to consider. More complete and nuanced analyses that consider access, impact, durability of ITNs after more than one year, as well as sleeping and ITN use patterns, will be presented in the final report.

Impact of COVID-19

The New Nets Project developed and implemented COVID-19 mitigation plans to keep staff and study participants safe. Mitigation measures included providing personnel with personal protective equipment sufficient for field activities and modifying activities, including introducing physical distancing and handwashing practices.

Burkina Faso suspended study activities from March 23 until May 4, 2020. One round of human behavior data collection and one round of entomological data collection were omitted.

Rwanda imposed lockdown measures in January 2021, consequently suspending study activities and resulting in the loss of entomological collections in January and February. Human behavior activities had not been scheduled for that time and were not affected. In July 2021, further restrictions were implemented with the rise in COVID-19 cases, once again pausing entomological collections, as well as human behavior field work. Restrictions were lifted in early August 2021, and study activities resumed shortly thereafter.

In Mozambique, study preparations and NMCP activities in the north and west were suspended from March until June 2020. Pandemic mitigation policies and procedures were in place by June 2020, and all critical activities resumed in July 2020. The cross-sectional surveys were initially planned to begin in April 2020 to capture peak malaria prevalence but were not completed until September (north) and October (west). The ITN distribution campaigns were completed in both evaluation areas by November 2020.

Future results and reports

The New Nets Project is scheduled to produce four interim reports. The final report will be completed in March 2023 (see Supplementary Table 1 for the report schedule).

Supplementary Table 1. Interim reports and final report schedule.

	Key updates *(in addition to latest routine entomological, HMIS, and ANC surveillance data)*	**Date complete**
Interim report 1	**Burkina Faso:** CSS baseline and Year 1, human behavior Round 1 **Mozambique:** CSS baseline **Nigeria:** CSS baseline, human behavior Round 1, DM baseline **Rwanda:** CSS baseline and second/Year 1 survey, human behavior Round 1	June 2021
Interim report 2	**Burkina Faso:** CSS Year 2, human behavior Round 2 **Mozambique:** CSS Year 1, DM baseline **Nigeria:** Human behavior Round 2 **Rwanda:** Human behavior Rounds 2 and 3	December 2021
Interim report 3	**Burkina Faso:** DM Month 12 **Mozambique:** DM Month 12 **Nigeria:** CSS Year 1, DM Month 12 **Rwanda:** CSS Year 2	June 2022
Final report	**Burkina Faso:** CSS Year 3, human behavior Rounds 3 to 5 **Mozambique:** CSS Year 2, DM Month 22 **Nigeria:** CSS Year 2, DM Month 24, human behavior Round 3 **Rwanda:** CSS Year 3, human behavior Rounds 4 to 5	March 2023

Abbreviations: ANC, antenatal care; CSS, cross-sectional survey; DM, durability monitoring; HMIS, health management information system.

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