February 8, 2023

The effectiveness of dual-AI ITNs distributed at scale

Evidence from the New Nets Project pilots

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PATH

The New Nets Project

New Nets Project partners

Unitaid Innovation in Global Health · The Global Fund To Fight AIDS, Tuberculosis and Malaria · USAID FROM THE AMERICAN PEOPLE · Bill & Melinda Gates foundation · MedAccess

IVCC

- Lead and coordinator
- Liaison with industry partners
- Link to vector control product development pipeline

psi Healthy lives. Measurable results.

- Compilation of cross-country lessons learned from pilot studies, funding for process evaluations

The Alliance for Malaria Prevention

- Technical assistance

Imperial College London

- Modelling of trials design and implementation impact

PATH · CNRFP · rbc Rwanda Biomedical Center, A Healthy People. A Wealthy Nation · University of Rwanda · PNCM · Instituto Nacional de Saúde Moçambique · Tropical Health · Nigerian Institute of Medical Research NIMR · Ibolda Health International Ltd.

- Cost-effectiveness determination from pilot implementations

LSTM Liverpool School of Tropical Medicine

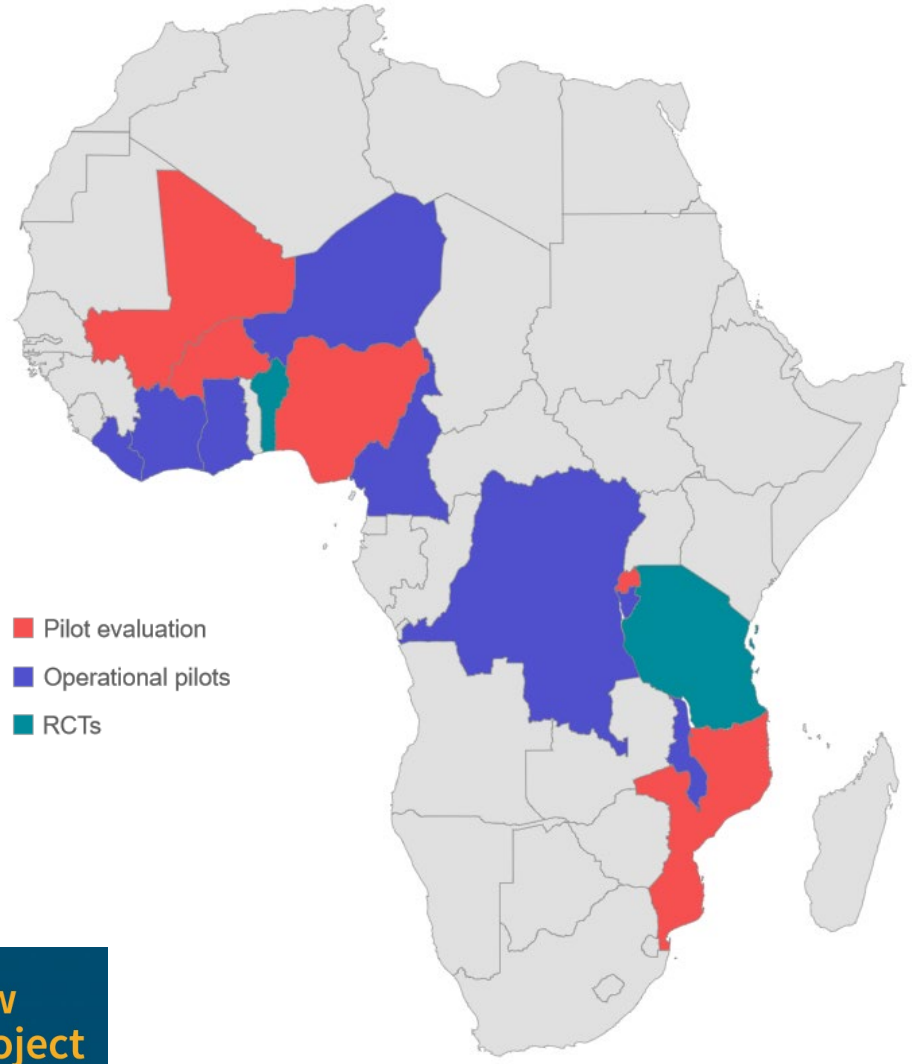
- Entomological correlates of epidemiological impact

Tulane University

- Cost effectiveness study design and data collection

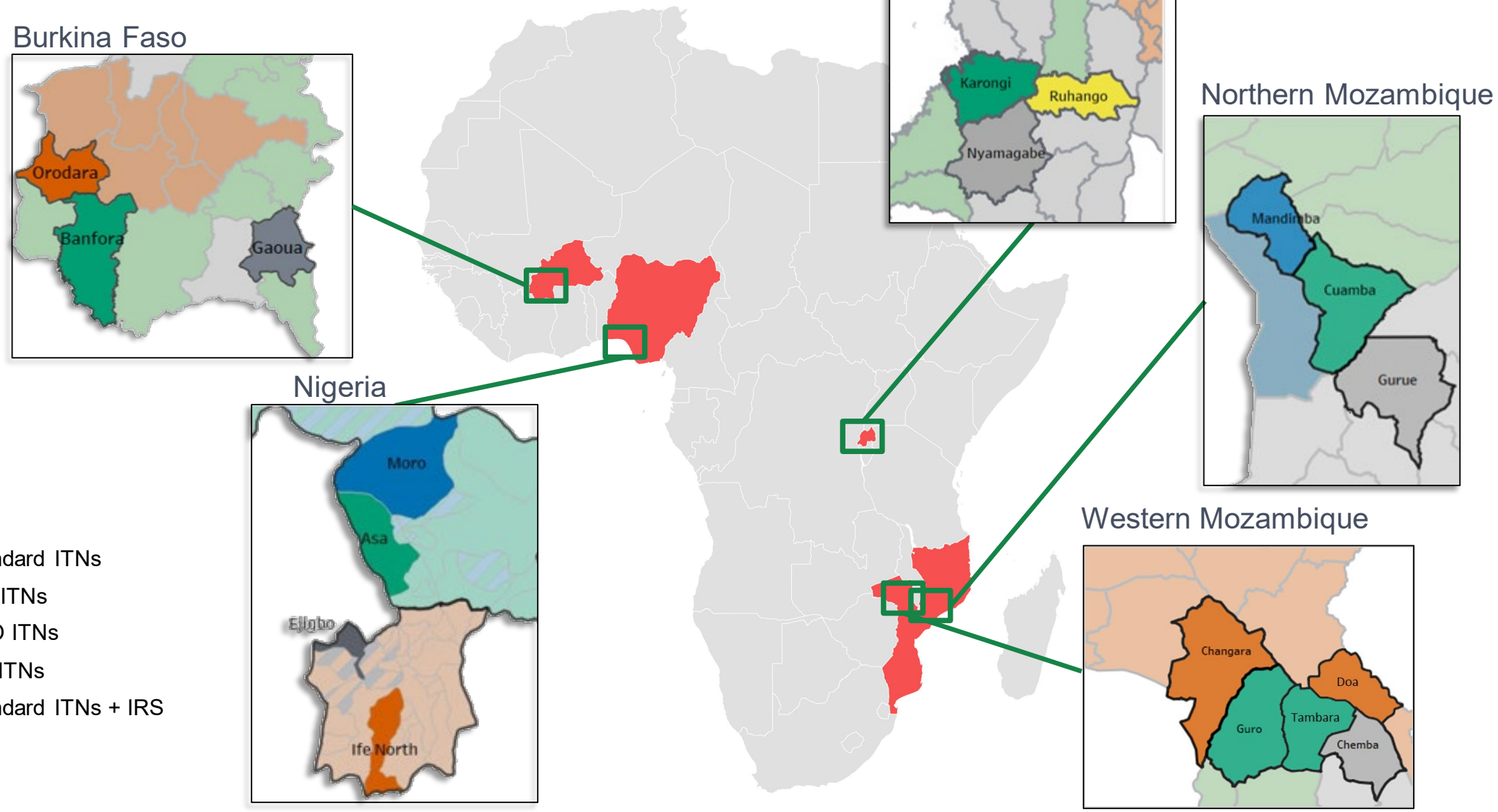
London School of Hygiene & Tropical Medicine

- Cluster-randomized trials of dual active-ingredient ITNs and entomological correlates in trials



The New Nets Project

New Nets Project pilot evaluations



Key findings

- Mass ITN distributions (universal coverage campaigns) are **strongly associated with increases in ITN access and use and decreases in malaria transmission - regardless of ITN type**.

- In areas with moderate to high transmission and pyrethroid-resistant vectors:
    - Distribution of **IG2, PBO, or RG ITNs seem more effective at controlling malaria** than distribution of standard, pyrethroid-only ITNs (through 1 year)
    - This improved control is **more sustained with IG2 (and with PBO in Burkina Faso)**

- Increased impact may be **less pronounced in settings like Rwanda** with overall low malaria burden and low levels of pyrethroid resistance.

- ITN durability likely affecting the duration of effect for RG and PBO (polyethylene) ITNs – at least in Southeastern Africa

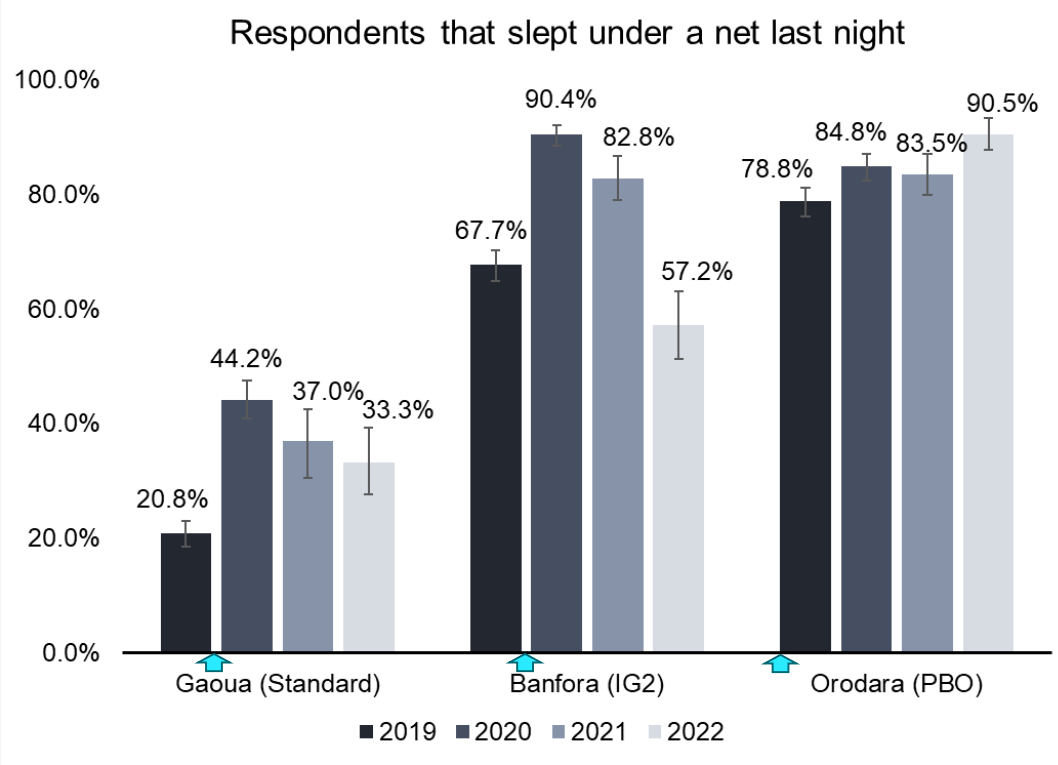
- **These pilot study results align well with results from the cluster randomized trials in Tanzania and Benin**

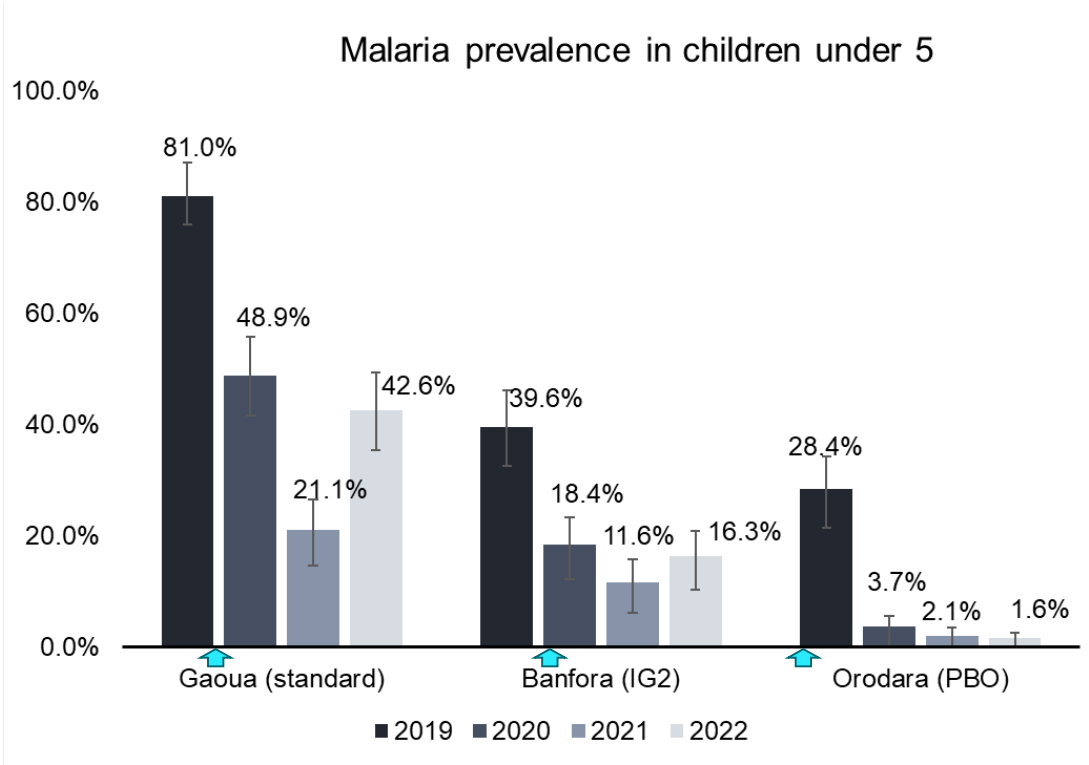
- No indications of major changes required to distribution systems to accommodate new net types
- Costs of distribution remain driven by costs of net products
- New products can be price competitive with Standard LLIN with copayment
    - Dual-AI nets are currently price-competitive without a copayment
- CE of new nets will depend on ***sustained price reductions*** and ***deployment in places with enhanced effect***

Burkina Faso

Malaria prevalence and ITN use

Cross-sectional surveys 2019–2022



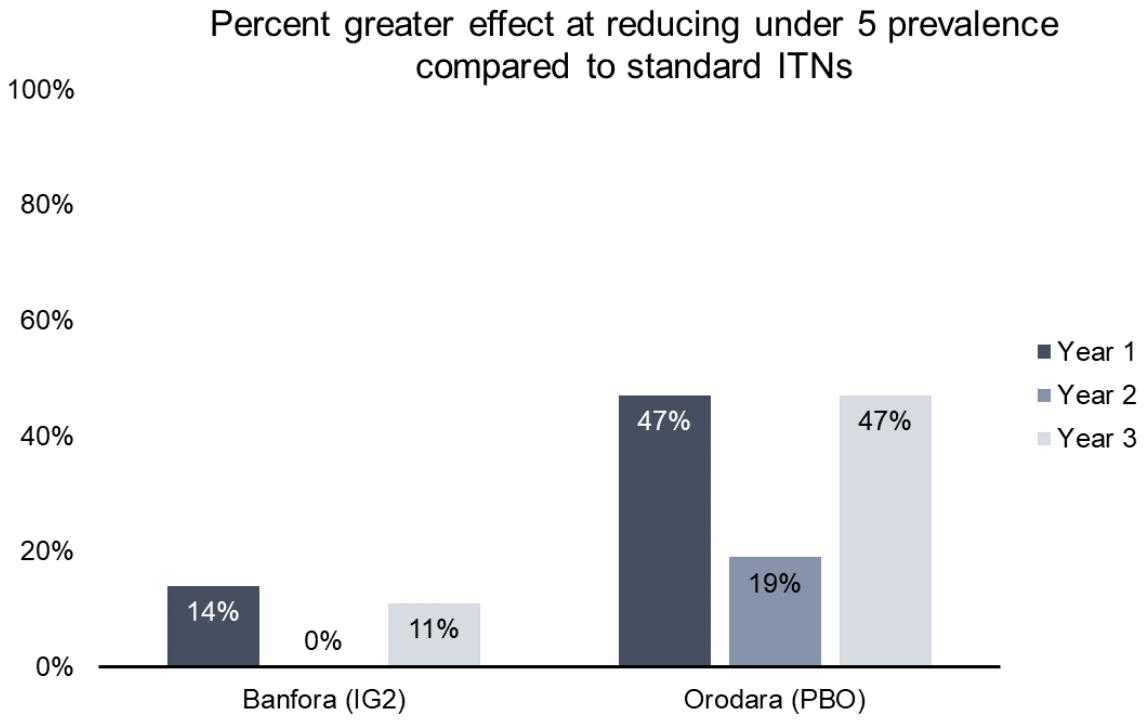


2019 Net distribution

* 2021 and 2022 results include expanded SMC

Comparative changes in malaria prevalence

Preliminary results of the logistic differences in differences model



Year 2 and Year 3 results include expanded SMC

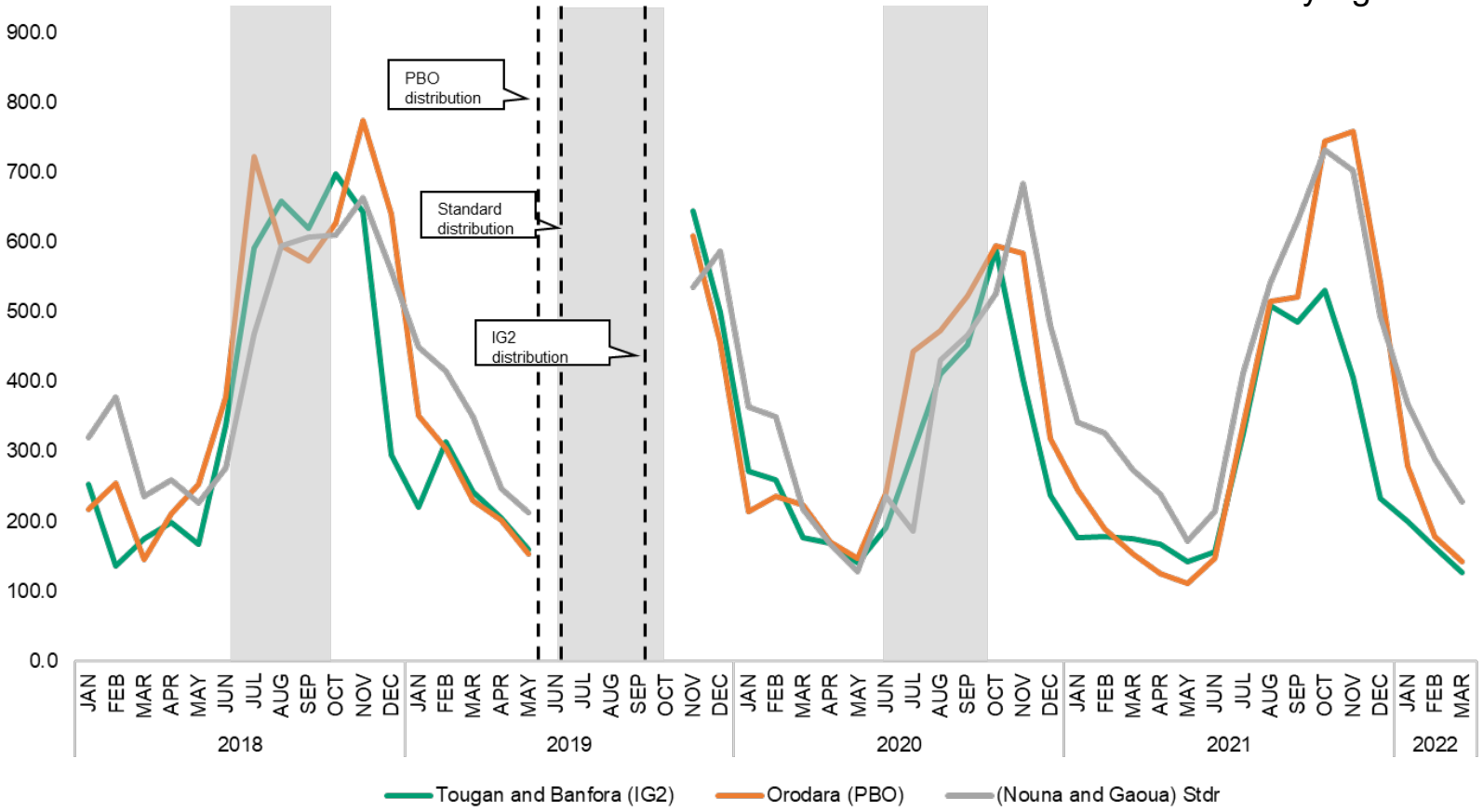
These are the preliminary, unadjusted differences in differences results, which suggest that **there were greater reductions in u5 prevalence in the IG2 and the PBO districts.**

The formal model will adjust for ITN use, socioeconomic status (Malaria Indicator Survey Wealth Index), the presence of an extra SMC round, other relevant covariables

Malaria case incidence

through March 2022

After controlling for rainfall, clustering, and other covariables, the formal difference in differences analysis suggests that **there were greater reductions in all ages malaria incidence reported in the routine health system in the IG2 and PBO districts** compared to the standard ITN district (though only the year 2 IG2 reduction was statistically significant at p=0.05).



7.0% greater reduction in the IG2 district

No greater reduction in the PBO district

Through year 1

21.6%* greater reduction in the IG2 district

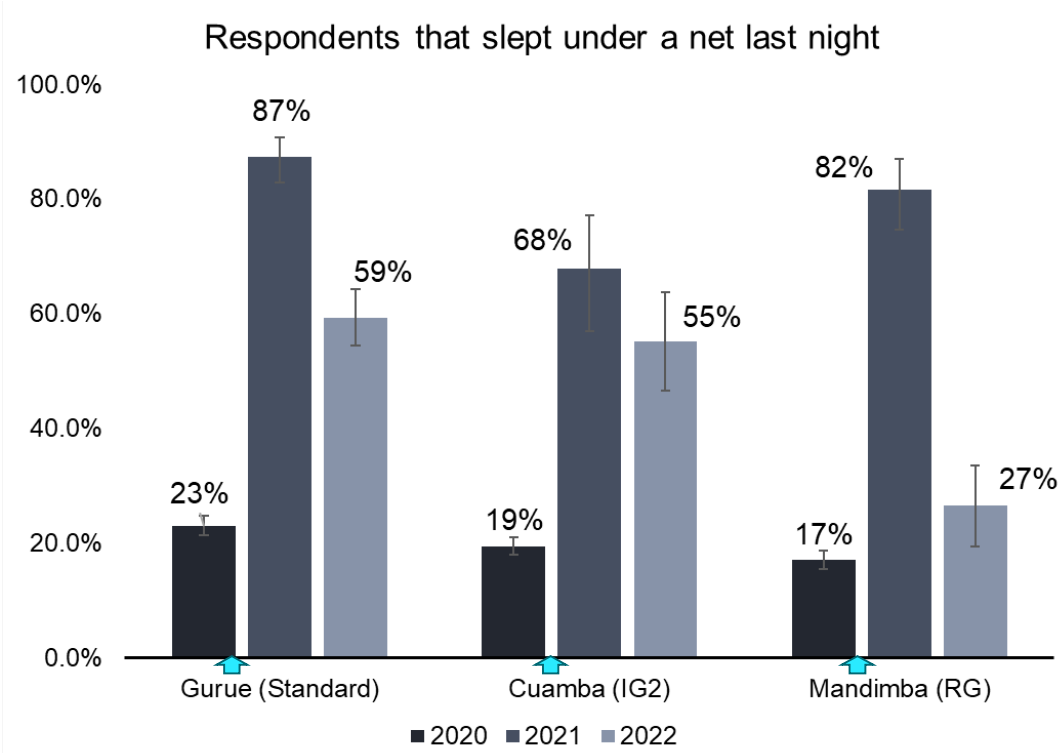
17.5% greater reduction in the PBO district

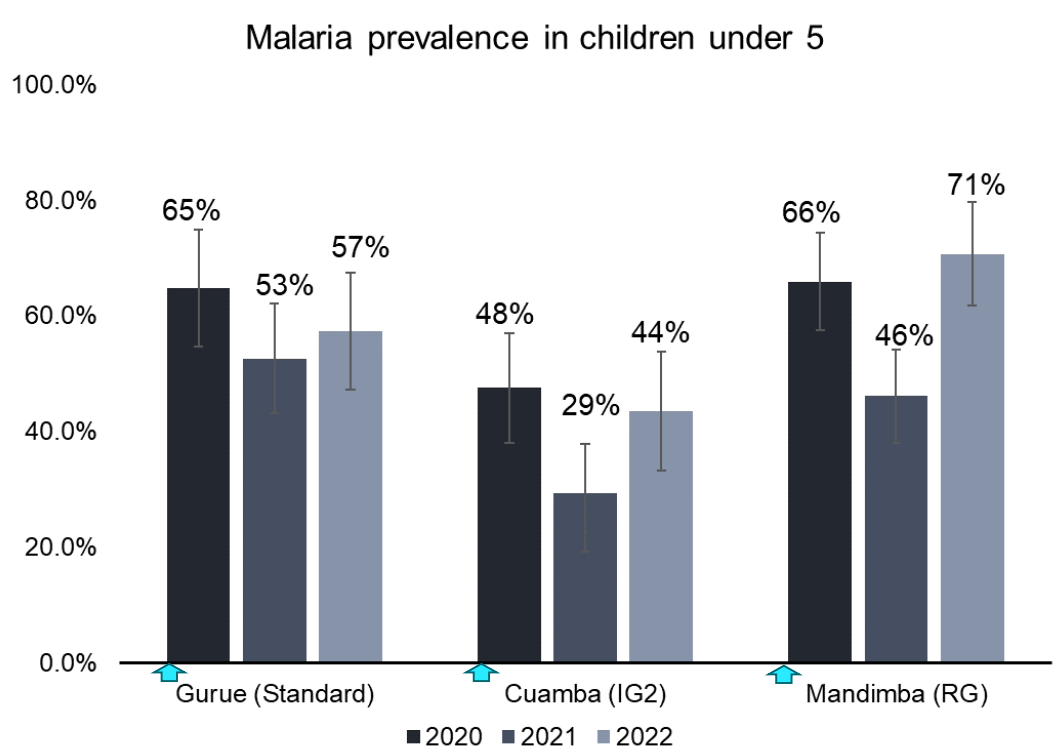
Through year 2

Northern Mozambique

Malaria prevalence and ITN use

Cross-sectional surveys 2020–2022

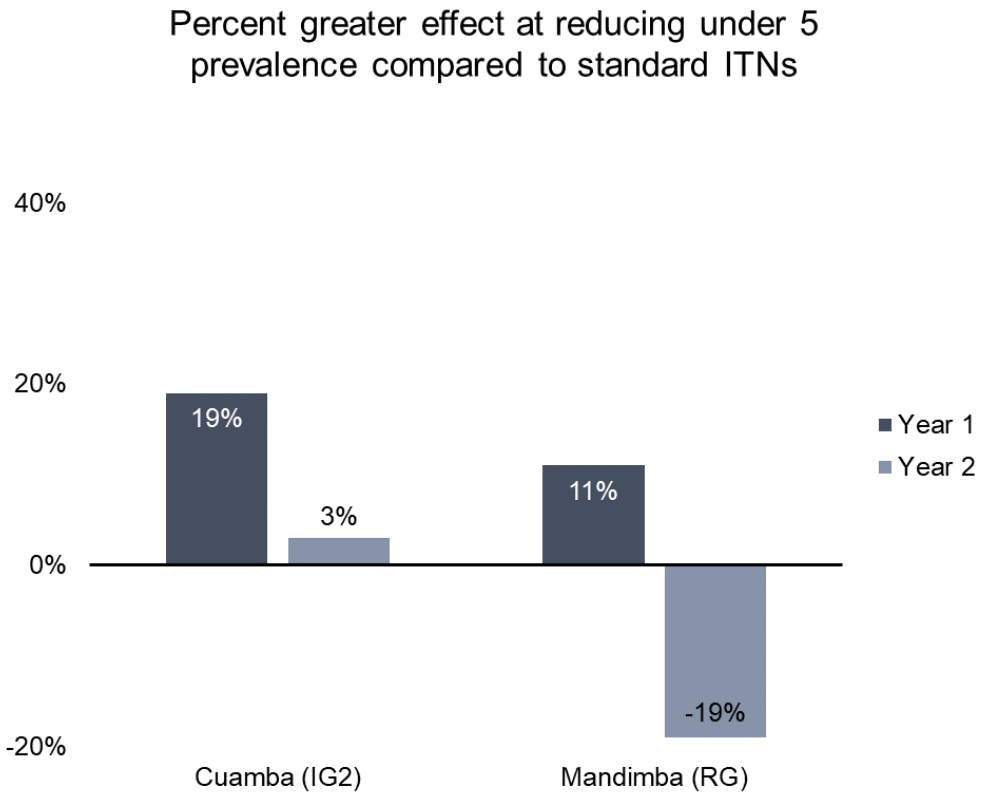




Net distribution

Comparative changes in malaria prevalence

Preliminary results of the logistic differences in differences model



These are the preliminary, unadjusted differences in differences results, which suggest that **there were significantly greater reductions in u5 prevalence in the IG2 and RG districts through one year.**

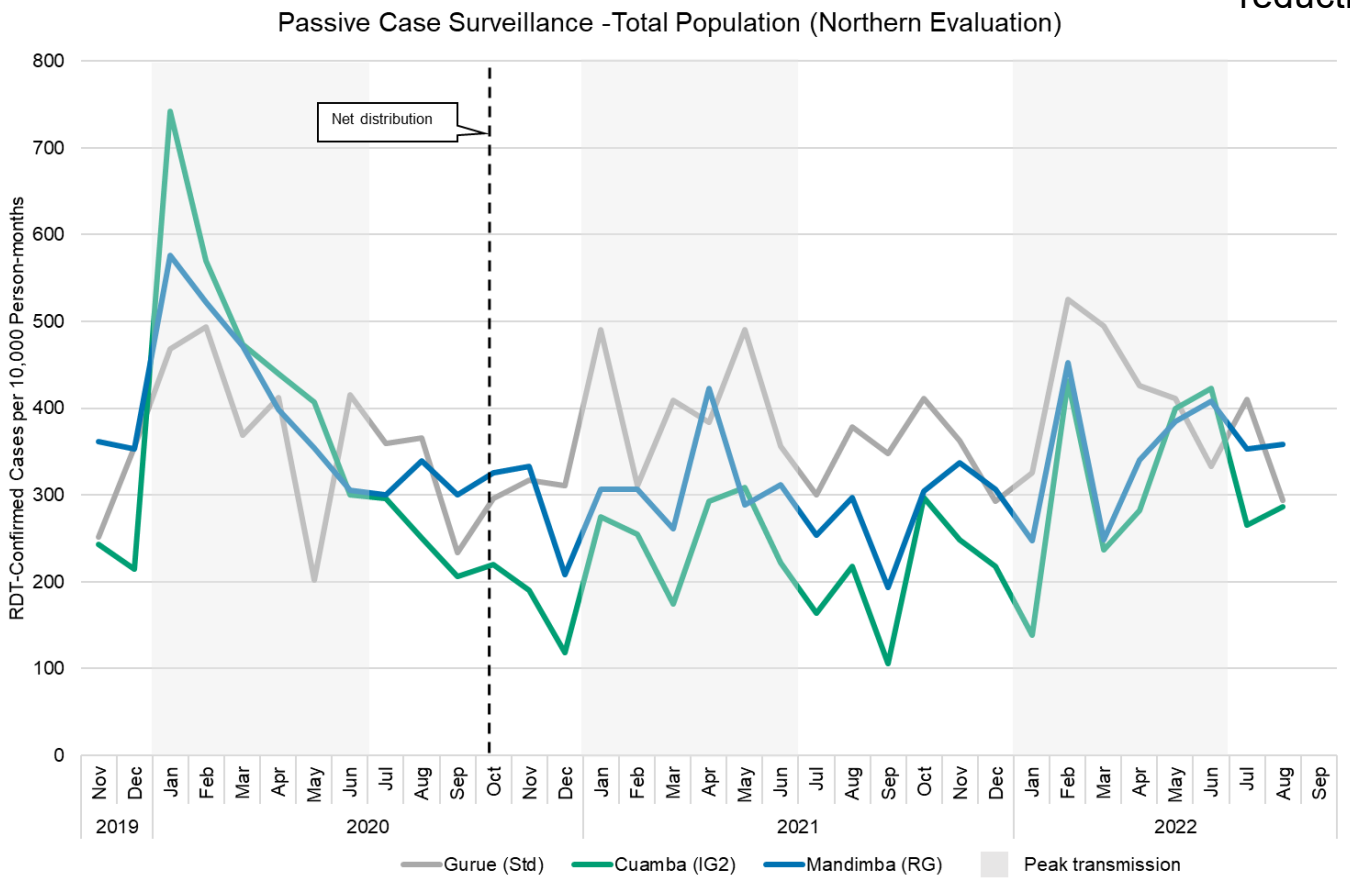
These trends were relatively short-lived, not sustained through the second year.

The formal model will adjust for ITN use, socioeconomic status (Malaria Indicator Survey Wealth Index), and other relevant covariables.

Malaria case incidence

through August 2022

After controlling for rainfall, clustering, and other covariables, the formal difference in differences analysis suggests that **there were greater reductions in all ages malaria incidence reported in the routine health system in the IG2 and PBO districts** compared to the standard ITN district (though only the year 2 IG2 reduction was statistically significant at p=0.05).



43% greater reduction in the IG2 district

9% greater reduction in the RG district

Through year 1

59%* greater reduction in the IG2 district

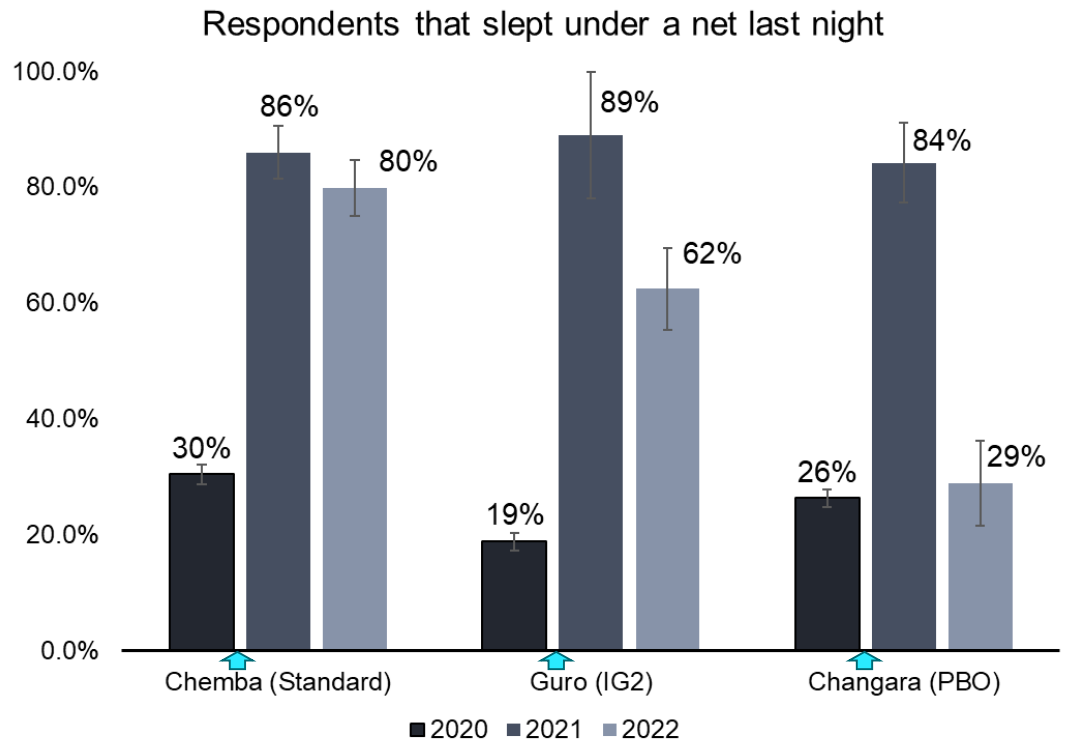
11% greater reduction in the RG district

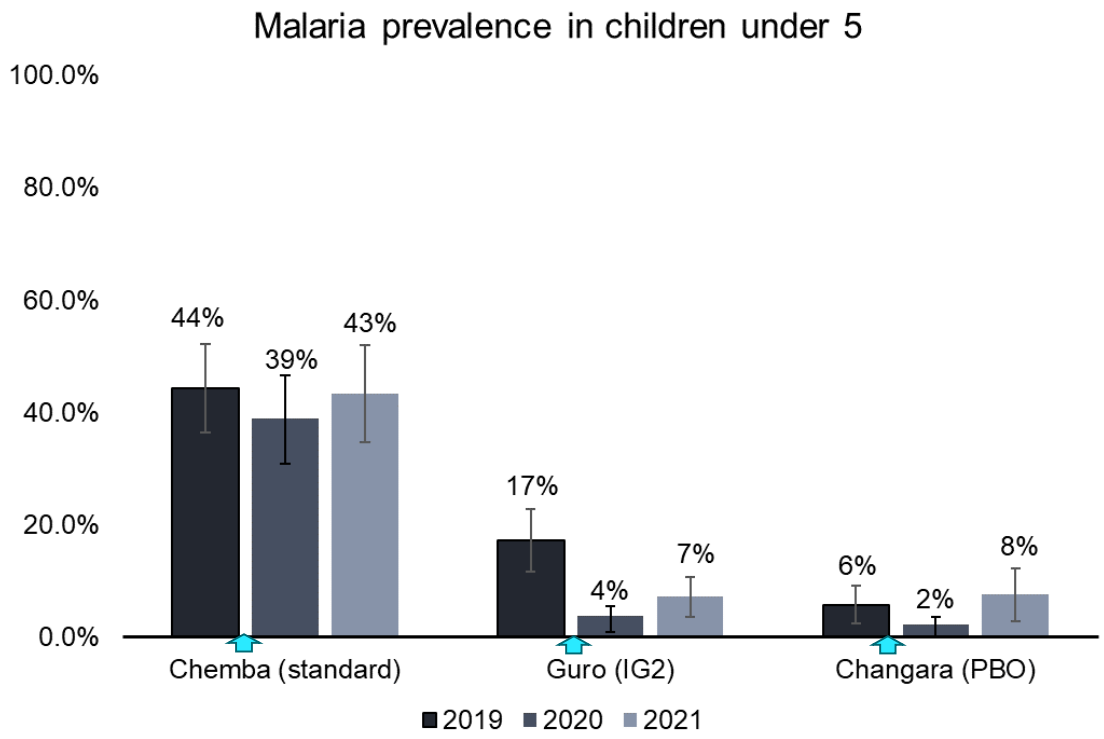
Through year 2

Western Mozambique

Malaria prevalence and ITN use

Cross-sectional surveys 2020–2022

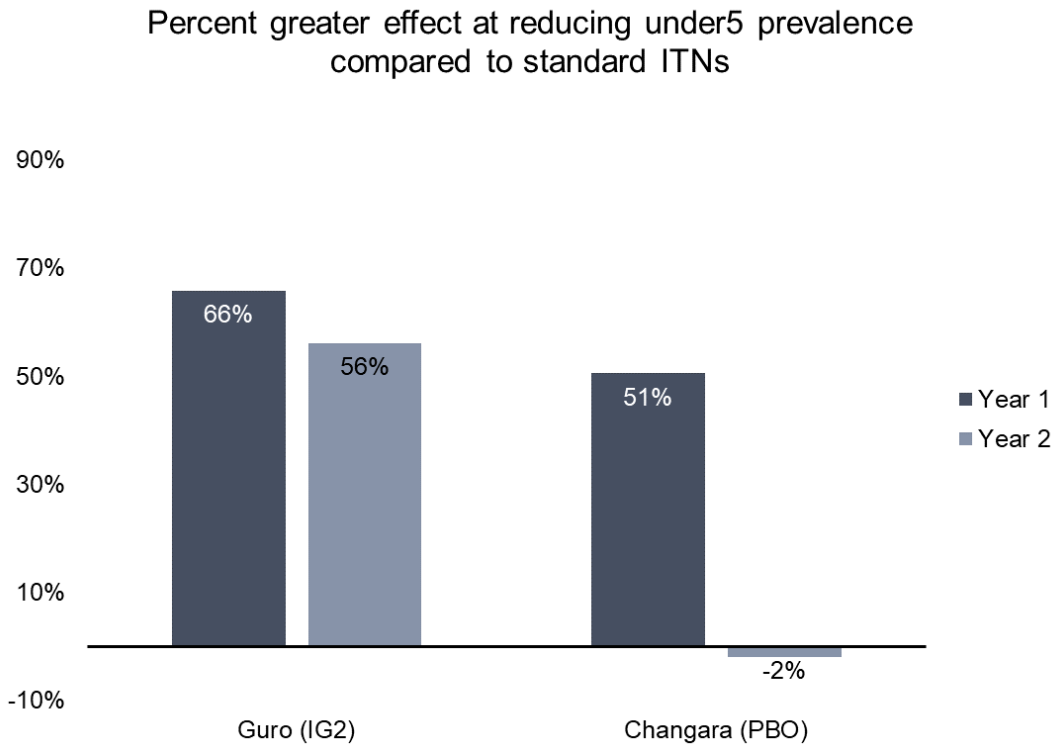




Net distribution

Comparative changes in malaria prevalence

Preliminary results of the logistic differences in differences model



These are the preliminary, unadjusted differences in differences results, which suggest that **there were substantially greater reductions in u5 prevalence in the IG2 and the PBO districts.**

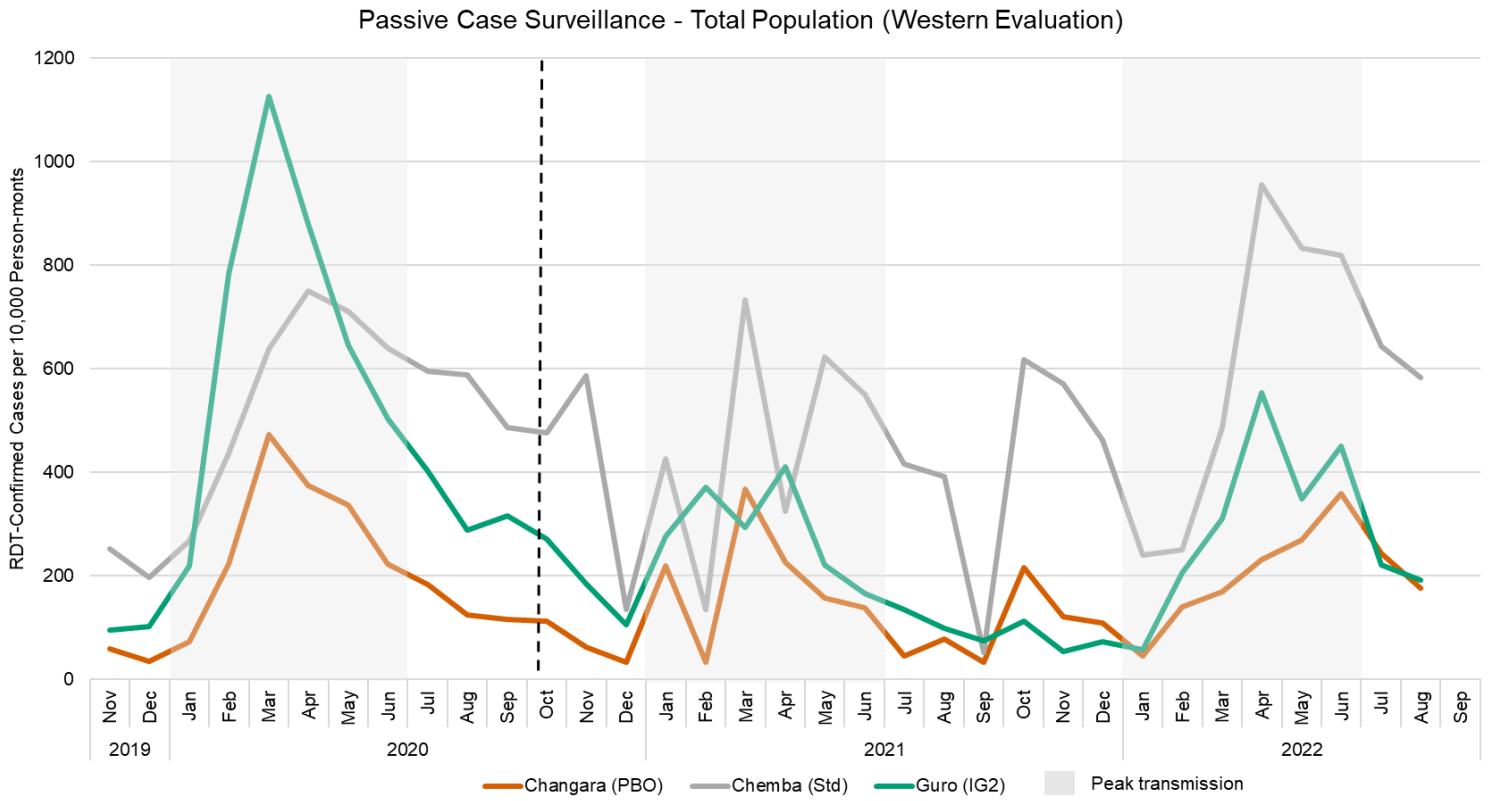
In the IG2 district, these gains were sustained through 2 years.

The formal model will adjust for ITN use, socioeconomic status (Malaria Indicator Survey Wealth Index), and other relevant covariables.

Malaria case incidence

through August 2022

After controlling for rainfall, clustering, and other covariables, the formal difference in differences analysis suggests that **there were greater reductions in all ages malaria incidence reported in the routine health system in the IG2 and PBO districts** compared to the standard ITN district (though only the year 2 IG2 reduction was statistically significant at p=0.05).



29% greater reduction in the IG2 district

2% greater reduction in the PBO district

Through year 1

41%* greater reduction in the IG2 district

17% greater reduction in the PBO district

Through year 2

Estimates of ITN durability

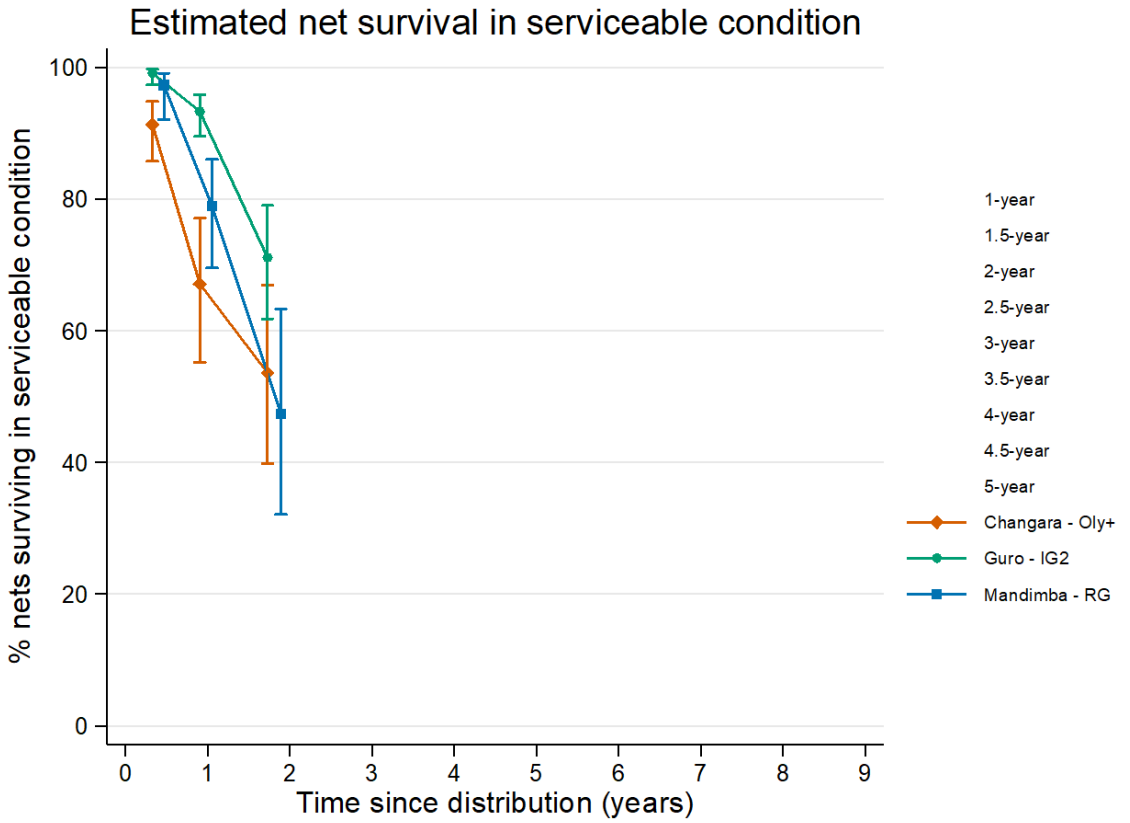
24-month

Estimates for the survival of campaign nets in serviceable condition after 24 months:

- **54% in Changara (PBO)**
- **71% in Guro (IG2)**
- **47% in Mandimba (RG)**

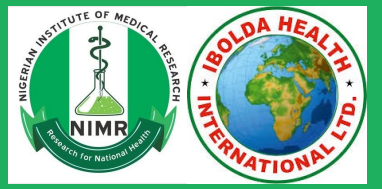
Estimated median lifespan:

- **Changara (PBO) – 1.8 years**
- **Guro (IG2) – 2.5 years**
- **Mandimba (RG) – 1.8 years**



Nigeria


FEDERAL MINISTRY OF
HEALTH


NIGERIAN INSTITUTE OF MEDICAL RESEARCH
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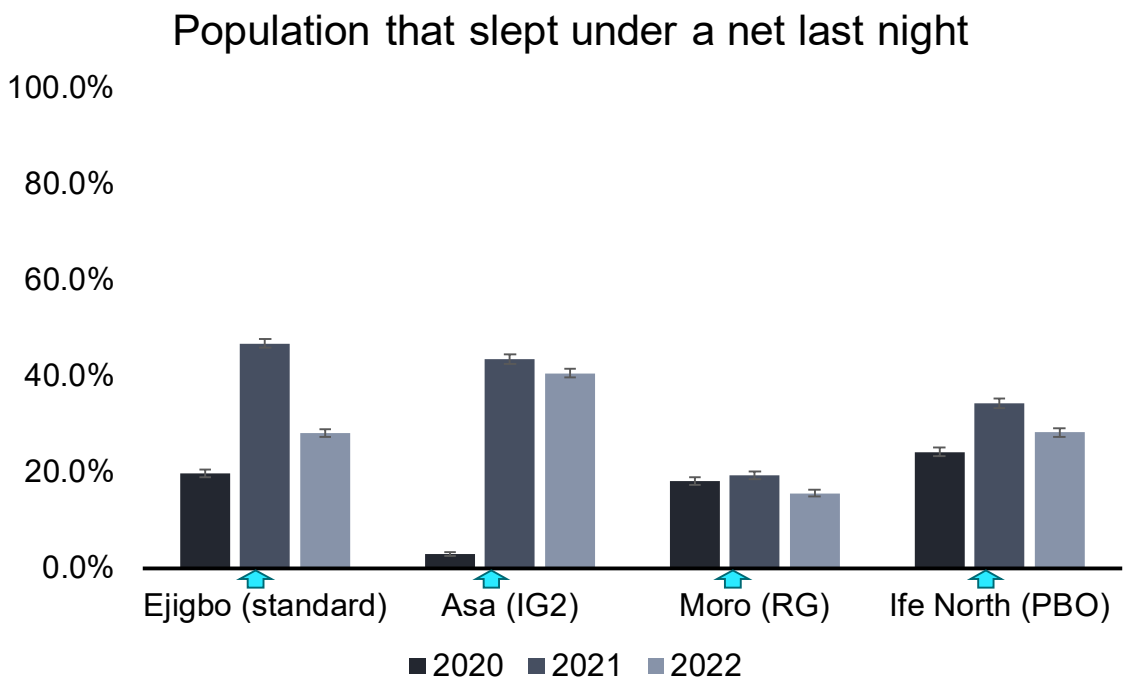
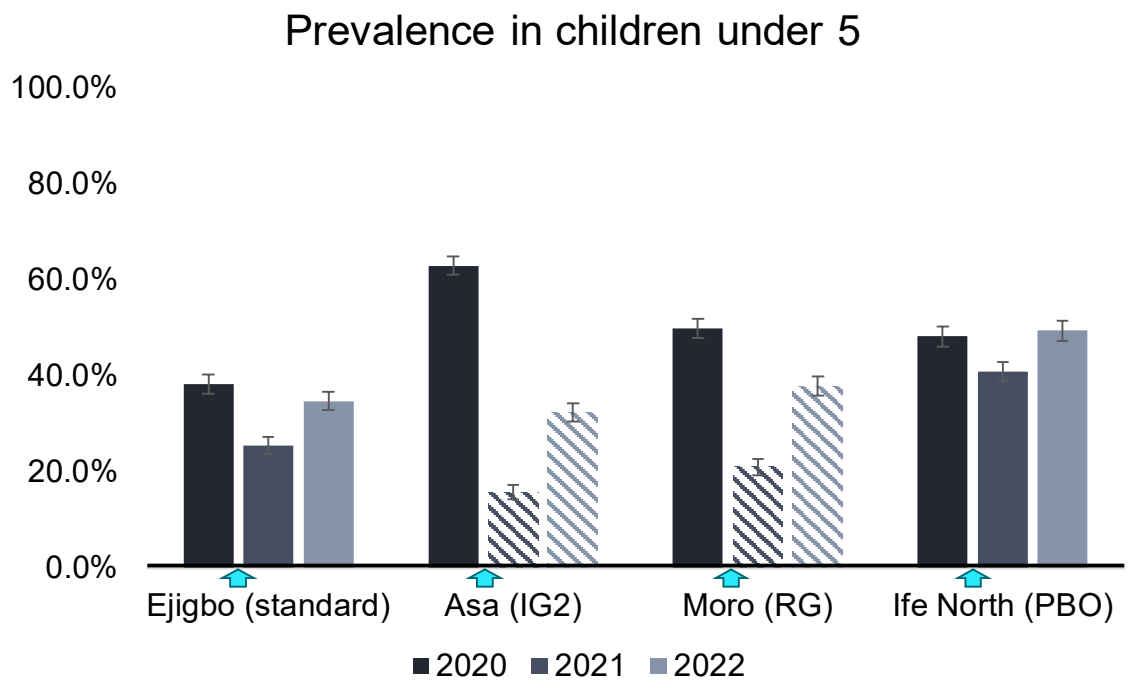
Malaria prevalence and ITN use

Cross-sectional surveys 2020–2022



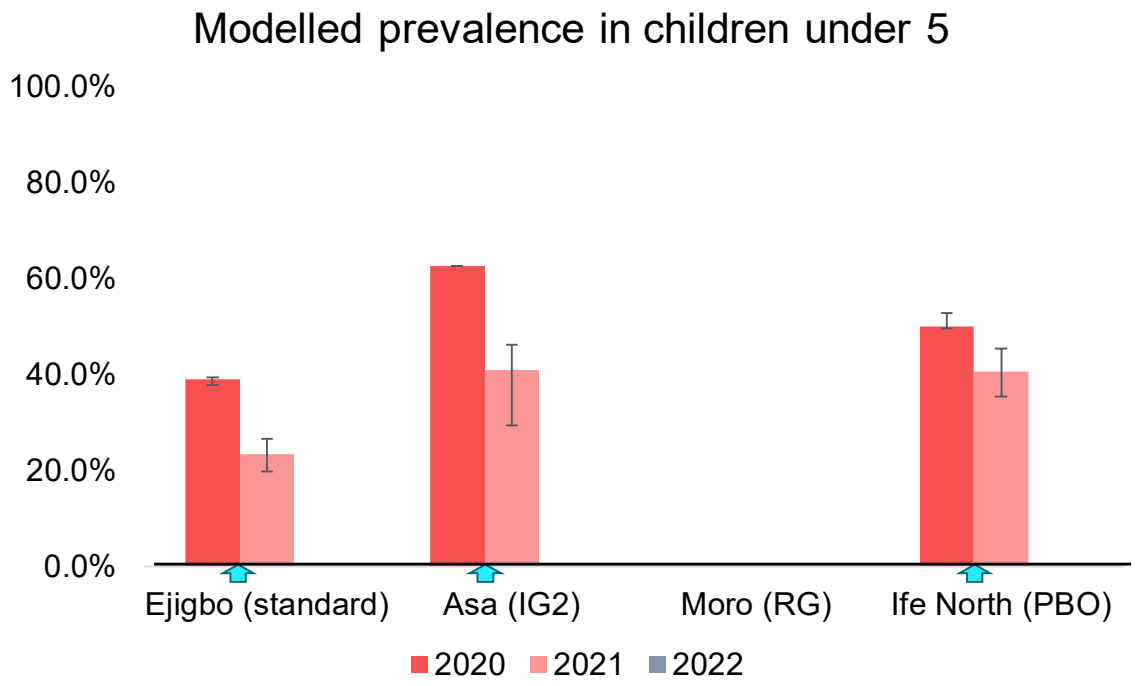


* 2021 and 2022 results include expanded SMC in Asa and Moro

Net distribution

Modelled malaria prevalence

Cross-sectional surveys 2020–2022



- Modelled prevalence assuming no SMC in Asa and Moro.
- Moro estimates not yet available—validation for pyriproxyfen model ongoing.

Net distribution

Estimates of ITN durability

12-month

Estimates for the survival of campaign nets in serviceable condition after 12 months:

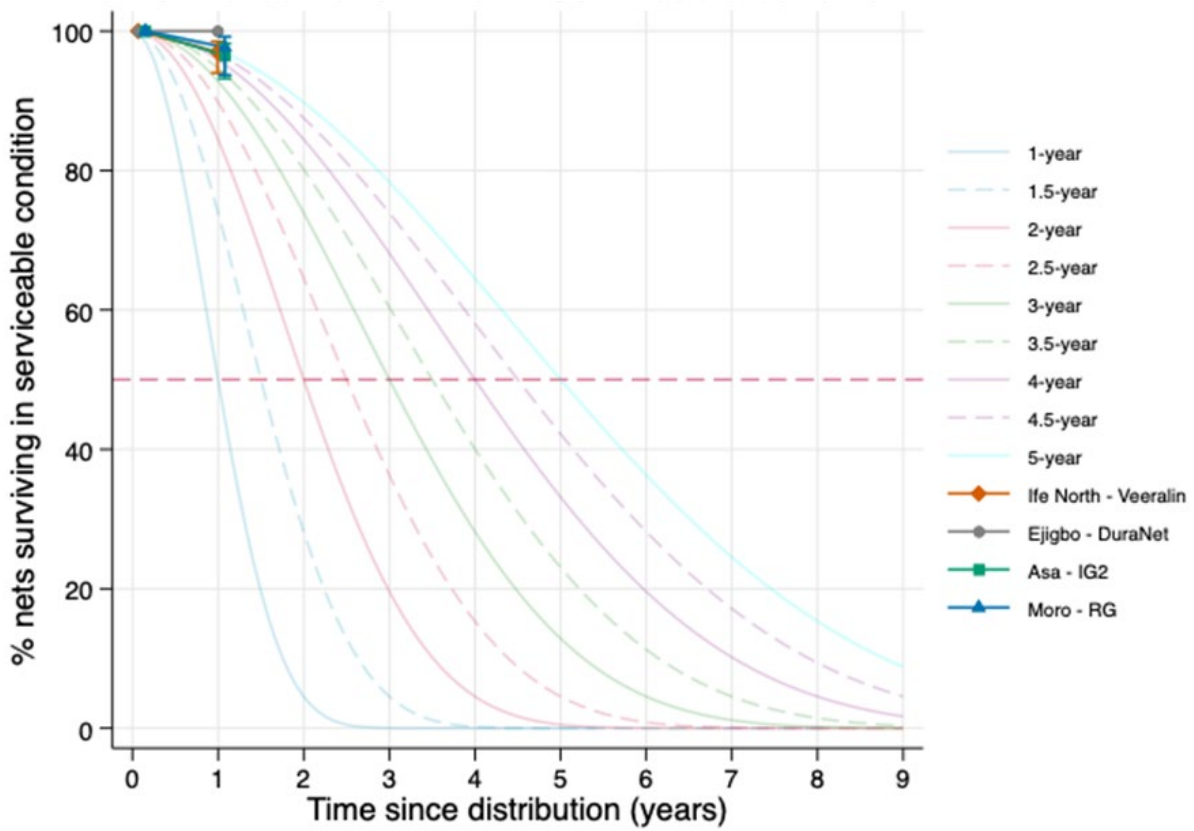
100% in Ejigbo

96.5% in Asa

97.7% in Moro

97.0% in Ife North

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.

Rwanda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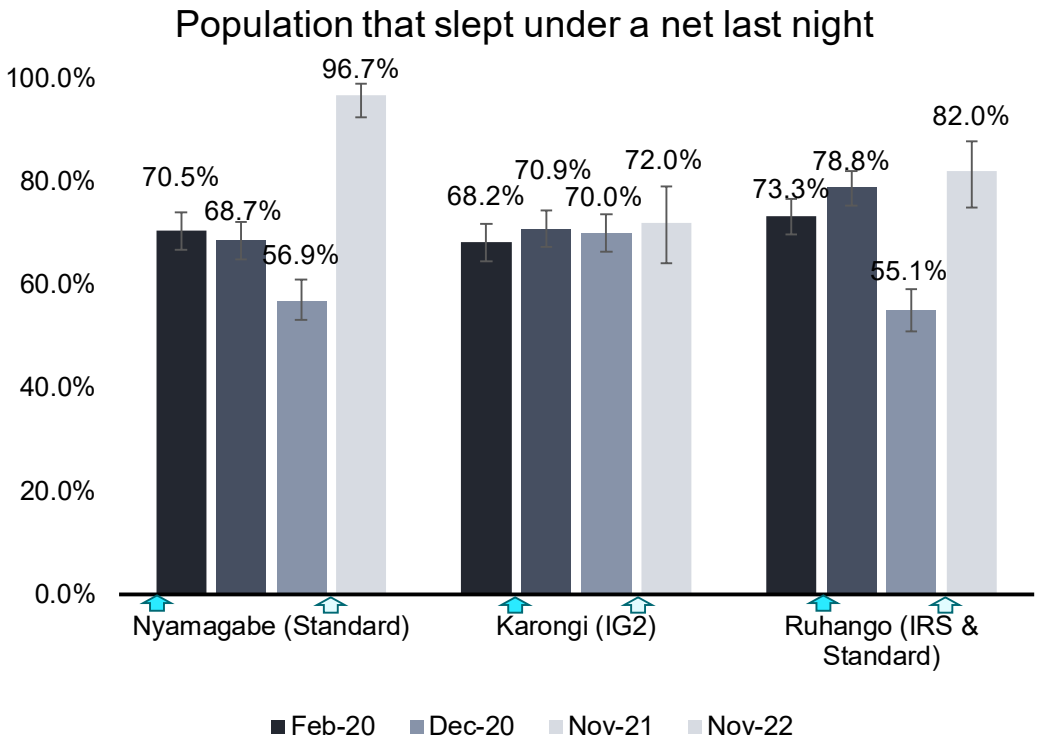
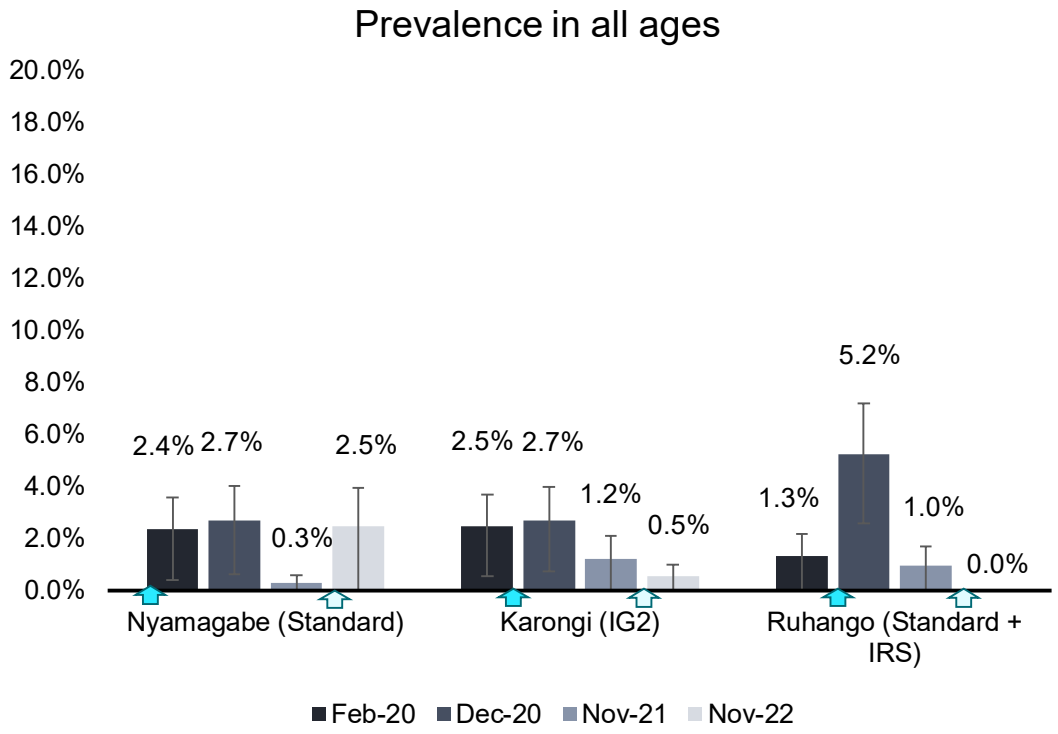
Malaria prevalence and ITN use

Cross-sectional surveys Feb. 2020, Dec. 2020, Nov. 2021, Nov. 2022



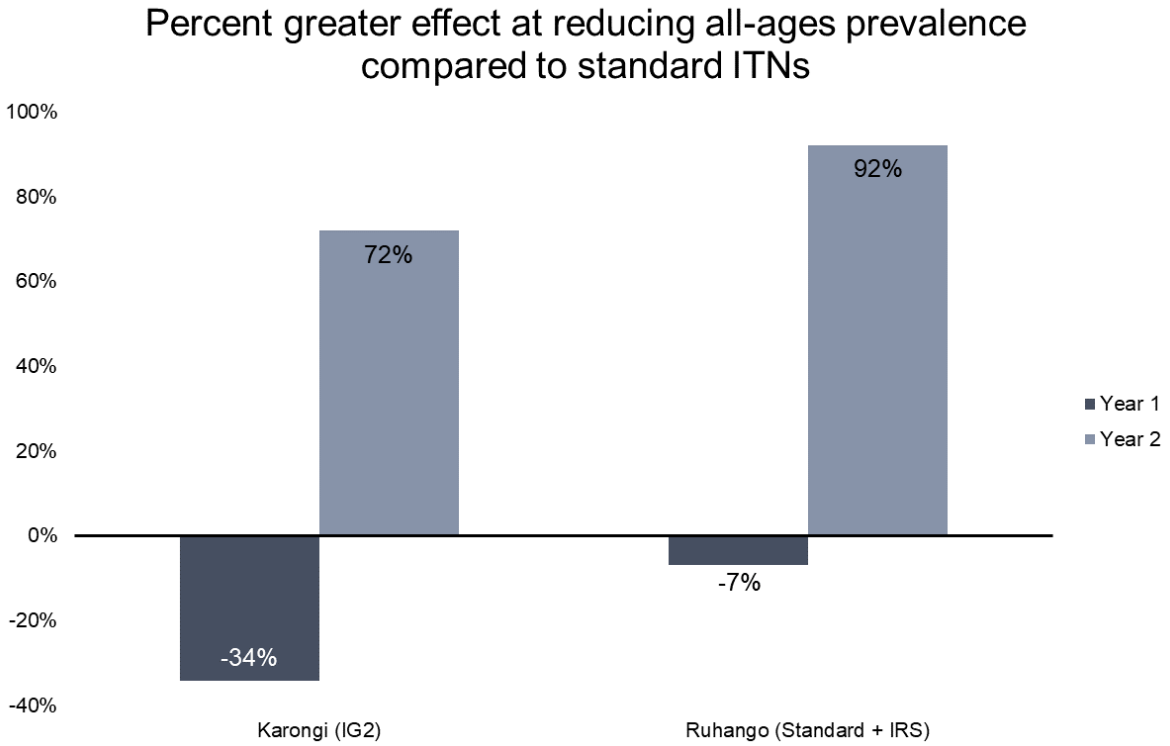


2020 Net distribution

2022 Supplemental net distribution

Comparative changes in malaria prevalence

Preliminary results of the logistic differences in differences model



These are the preliminary, unadjusted differences in differences results, which suggest that **there were significant reductions in all ages prevalence in all districts at year one in this very low burden setting.**

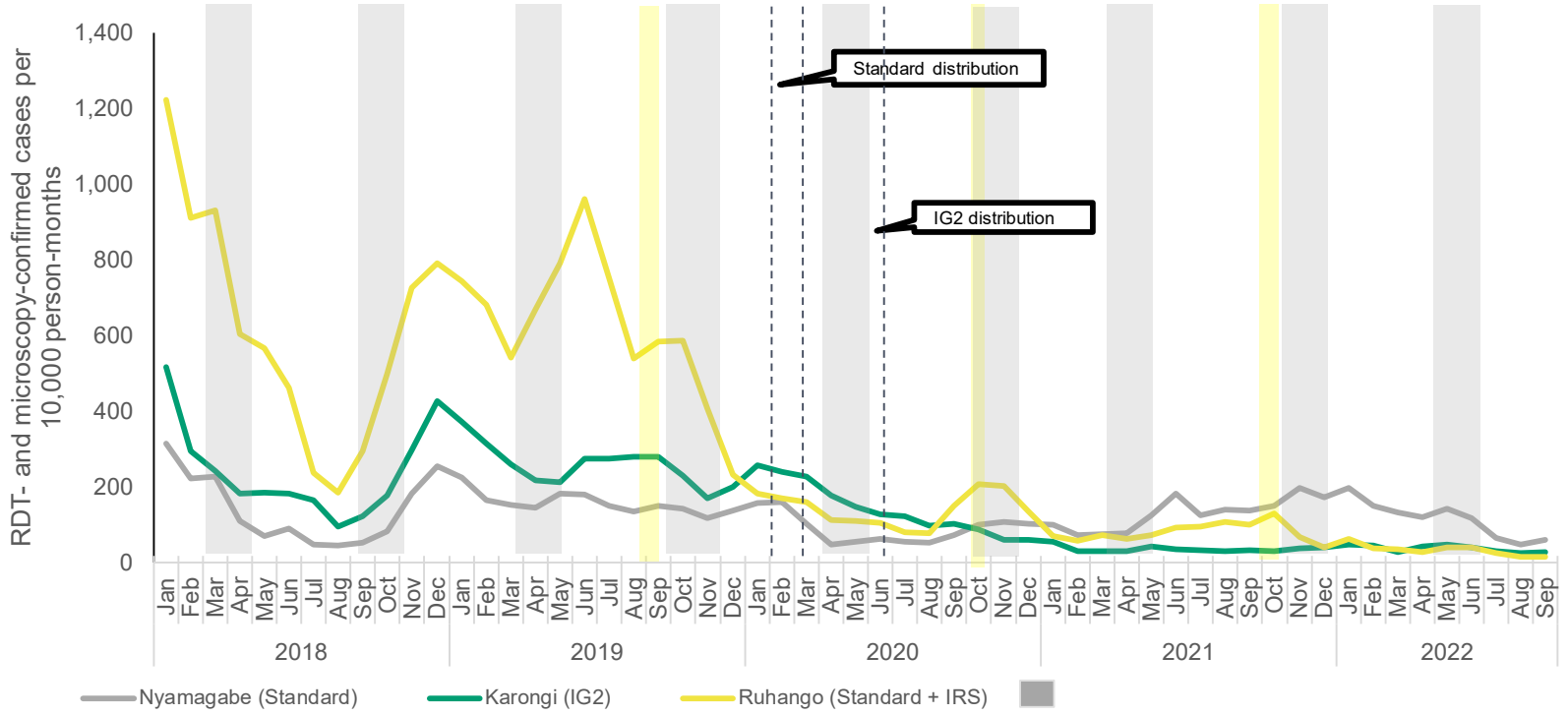
During the second year, there were substantially greater reduction in all-ages prevalence in the IG2 and the Standard + IRS districts

The formal model will adjust for ITN use, socioeconomic status (Malaria Indicator Survey Wealth Index), and the presence of an extra SMC round.

Malaria case incidence

January 2018–September 2022

After controlling for rainfall, clustering, and other covariables, the formal difference in differences analysis suggests that **there were greater reductions in all ages malaria incidence reported in the routine health system in the IG2 and IRS districts** compared to the standard ITN district.



32%* greater reduction in the IG2 district

85%* greater reduction in the Std + IRS district

Through year 1

54%* greater reduction in the IG2 district

81%* greater reduction in the Std + IRS district

Through year 2

Cost and cost-effectiveness approaches

Cost and cost-effectiveness

Methods

- Costings of distribution conducted in (Mozambique, Rwanda, Nigeria).
    - Additional cost data from (Uganda, Mali in collaboration with IFRC)
- Updated review of ITN cost distribution literature
- Effectiveness estimates conducted from new observational studies in (Moz., Rwanda, Nigeria, Burkina Faso).
- Effectiveness from generalized models, plus country specific models
- **Incremental Cost effectives of switch from standard ITN (LLIN) to Next Generation Nets calculated using observational studies and modelling. Generalized (vs. no-ITN) calculated from modeled data.**

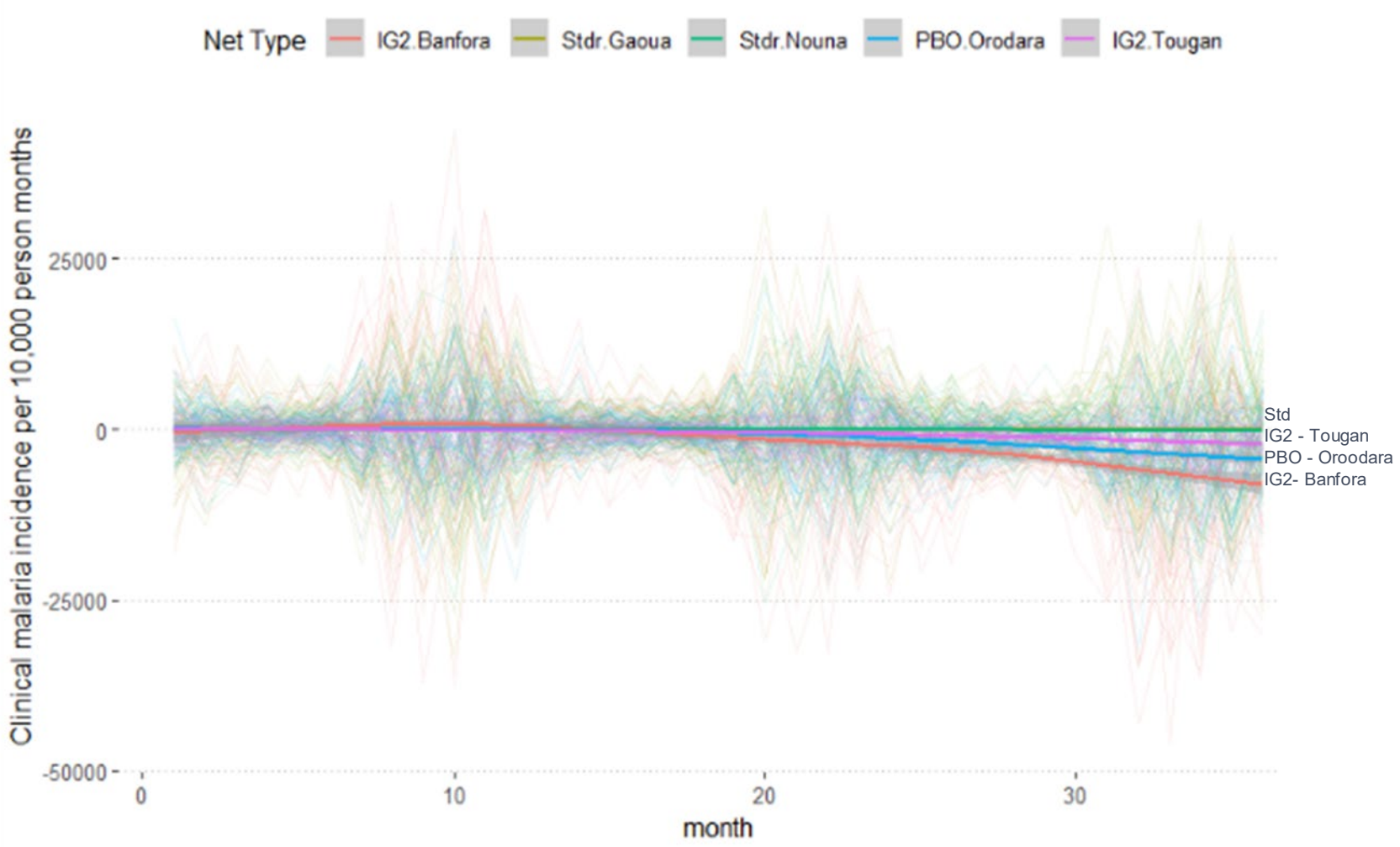
Preliminary results to date

- No indications of major changes required to distribution systems to accommodate new net types
- **Costs of distribution remain driven by costs of net products**
- New products can be price competitive with Standard LLIN with subsidy
- CE of new nets will depend on ***sustained price reductions*** and ***deployment in places with enhanced effect***

Preliminary cost and cost-effectiveness work

Framework

- Provider perspective cost estimates (Including distribution cost per ITN)
- Effectiveness estimates from observational study data (example from Burkina Faso →)
- Incremental cost per case averted is the final output



Key findings to date

Key findings

- Mass ITN distributions (universal coverage campaigns) are **strongly associated with increases in ITN access and use and decreases in malaria transmission - regardless of ITN type**.

- In areas with moderate to high transmission and pyrethroid-resistant vectors:
    - Distribution of **IG2, PBO, or RG ITNs seem more effective at controlling malaria** than distribution of standard, pyrethroid-only ITNs (through 1 year)
    - This improved control is **more sustained with IG2 (and with PBO in Burkina Faso)**

- Increased impact may be **less pronounced in settings like Rwanda** with overall low malaria burden and low levels of pyrethroid resistance.

- ITN durability likely affecting the duration of effect for RG and PBO (polyethylene) ITNs – at least in Southeastern Africa

- **These pilot study results align well with results from the cluster randomized trials in Tanzania and Benin**

- No indications of major changes required to distribution systems to accommodate new net types
- Costs of distribution remain driven by costs of net products
- New products can be price competitive with Standard LLIN with copayment
    - Dual-AI nets are currently price-competitive without a copayment
- CE of new nets will depend on ***sustained price reductions*** and ***deployment in places with enhanced effect***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Backup Slides & Additional Info

The New Nets Project is supporting research and enhanced surveillance to evaluate the impact of different ITN types in operational settings (2019–2022)

- Interceptor® G2 ITN
- Royal Guard® ITN
- PBO ITN
- Standard ITN

Epidemiology

- Measure impact of new nets and standard ITNs, and if feasible PBO ITNs, through observational studies comparing trends in:
  - Malaria prevalence in community surveys
  - Malaria prevalence in antenatal care
  - Malaria case incidence

Entomology

- Understand the transmission landscape in each setting
- Evaluate the impact of new nets and standard ITNs, and if feasible PBO ITNs, on vector population density, behavior, infection and resistance status

Anthropology

- Examine barriers, facilitators, and patterns of ITN access and use.
- Measure time spent under an ITN and correlate use patterns with vector behaviors to explore transmission risks and understand the limitations of ITN interventions.

Durability monitoring

- Estimate survivorship, attrition, physical integrity and insecticidal content throughout the study time period

Cost-effectiveness

- Estimate the cost and cost-effectiveness through data on product price, delivery and deployment costs and effectiveness based on incidence rates

Entomological landscape

Year 1 context

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

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

- Mix of *An. gambiae* s.s., *An. coluzzii,* and *An. funestus*
- High levels of pyrethroid resistance by multiple mechanisms—partially mitigated by PBO
- Roughly equal rates of indoor and outdoor biting – no shifts noted after ITN distribution

- Only *An. gambiae* s.l. specimens have tested positive for *P. falciparum* sporozoites
  - *An. gambiae* s.s., *An. coluzii*, and *An. arabiensis* are all positive
  - Transmission detected both indoors and outdoors

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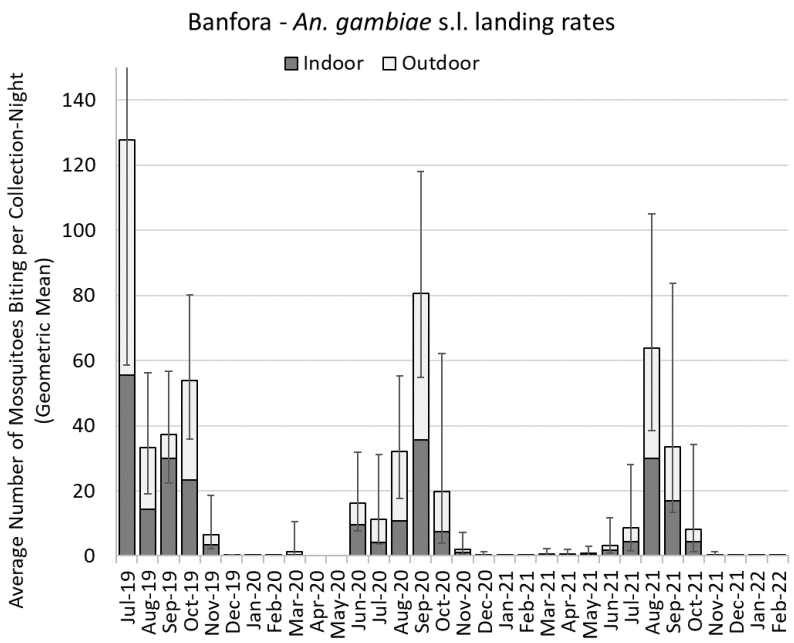
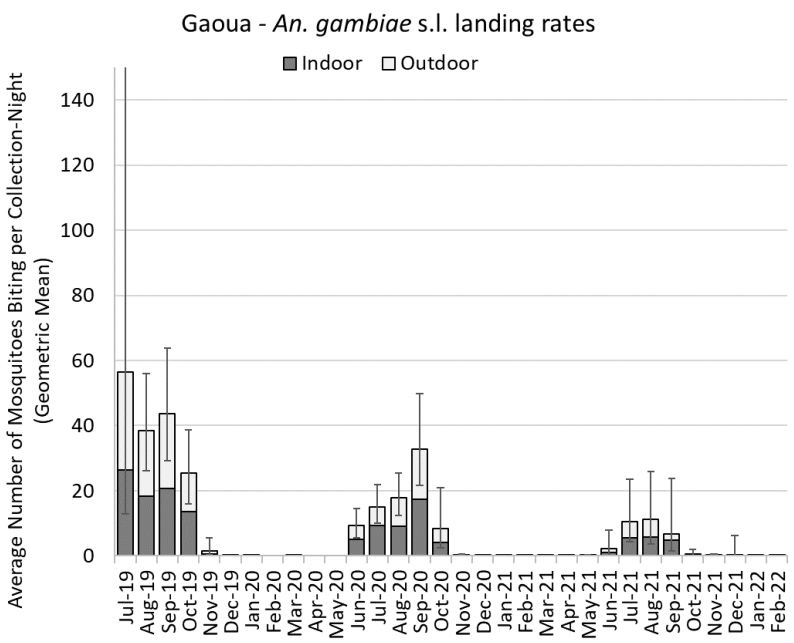
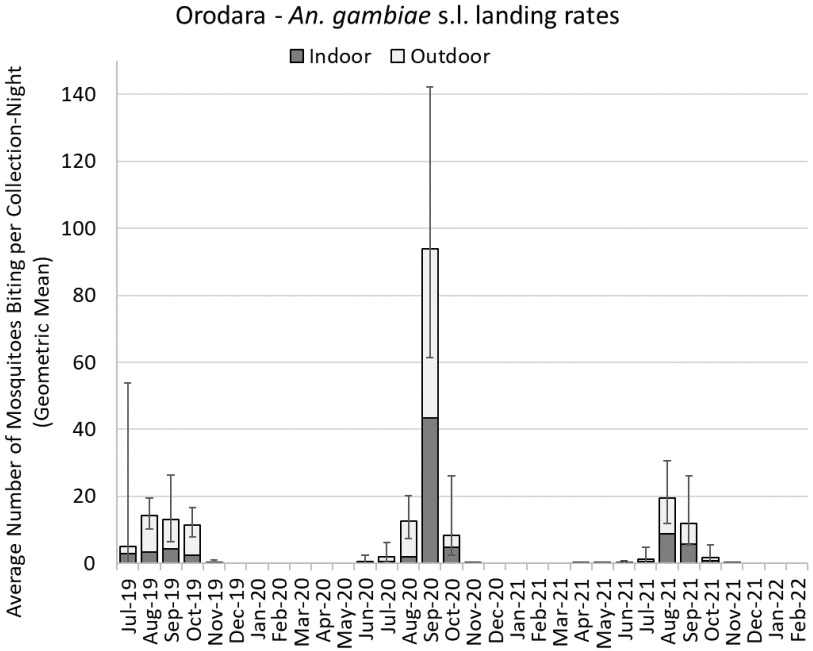
Entomological landscape - Burkina Faso

Trends in human landing rates for An. gambiae *s.l.*







- Trend towards lower landing rates following ITN distribution – both indoor and outdoor
- Not as evident in Orodara, the PBO district, where overall mosquito densities are lowest

Entomological landscape

Through September 2022

	Gurue (standard ITNs)	Cuamba (IG2 ITNs)	Mandimba (RG ITNs)
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*)*		

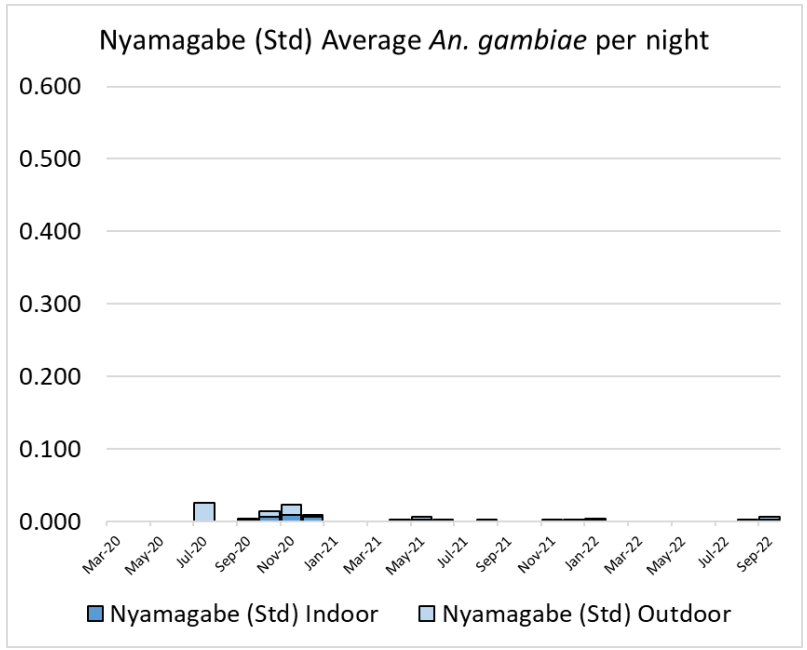
*Historical data, 2018 and 2019.

- Mix of *An. gambiae* s.s. and *An. funestus*
- Moderate to High levels of pyrethroid resistance—mitigated by PBO
- Roughly equal rates of indoor and outdoor biting

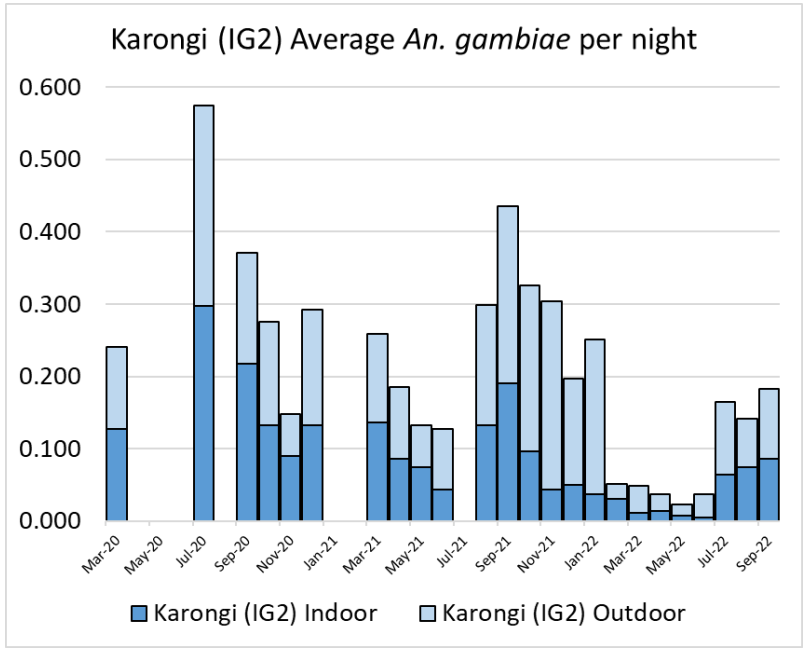
- Both *An. funestus* and *An. gambiae* have tested positive for *P. falciparum*
- Transmission detected both indoors and outdoors

Entomological landscape - Rwanda

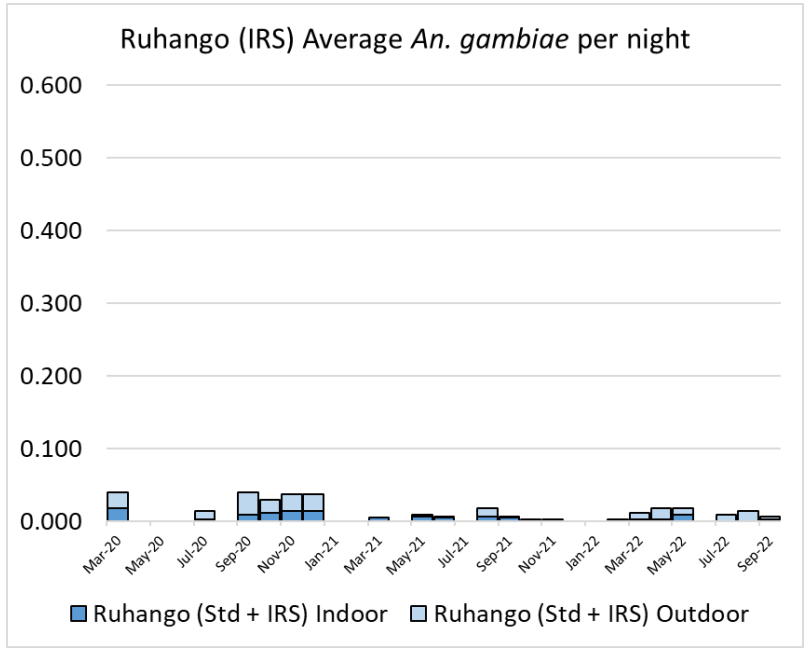
Trends in human landing rates for An. gambiae *s.l.*



Low biting rates consistent over study



Moderate biting rates decreased over study



Low biting rates decreased over study

An. gambiae also fed readily both indoors and outdoors

- Consistent for *An. gambiae* s.s. and *An. arabiensis,* both of which are present throughout the study area (~70% *An. gambiae* s.s. to 30% *An. arabiensis*)

Feeding behaviors did not change after ITN campaigns, though biting rates tend to decrease somewhat after new nets are distributed

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Entomological landscape

through September 2022

	Chemba (standard ITNs)	Guro (IG2 ITNs)	Changara (PBO ITNs)
Most abundant vector (% of likely vector species collected)	*An. funestus* s.l. (79.7%)	*An. gambiae* s.l. (100%)	*An. gambiae* s.l. (100%)
Second most abundant vector (% of all likely vectors collected)	*An. gambiae* s.l. (20.31%)	–	–
***An. gambiae* molecular IDs**			
	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	**LOW 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*)*		

*Historical data, 2018 and 2019.

- Mix of *An. gambiae* s.s. and *An. funestus*
- Low to high levels of pyrethroid resistance—mitigated by PBO
- Roughly equal rates of indoor and outdoor biting

- Only *An. gambiae* s.l. have tested positive for *P. falciparum*
- Transmission detected both indoors and outdoors

Entomological landscape

Year 1

	Ejigbo (standard ITNs)	Asa (IG2 ITNs)	Moro (RG ITNs)	Ife North (PBO ITNs)
	Year 1	**Year 1**	**Year 1**	**Year 1**
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 all anophelines collected)	*An. funestus* s.l. (6%)	–	–	*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%	–
HLC 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%

- Mix of *An. gambiae* s.s., *An. funestus, An. coluzzii, An. arabiensis*
- Moderate to high levels of pyrethroid resistance—partially mitigated by PBO
- Tendency for higher indoor than outdoor biting rates in some districts

- Both *An. gambiae* s.s. and *An. coluzzii* have tested positive for *P. falciparum*

- Transmission detected both indoors and outdoors

Entomological landscape

Year 1

	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. (89.5%)	*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%

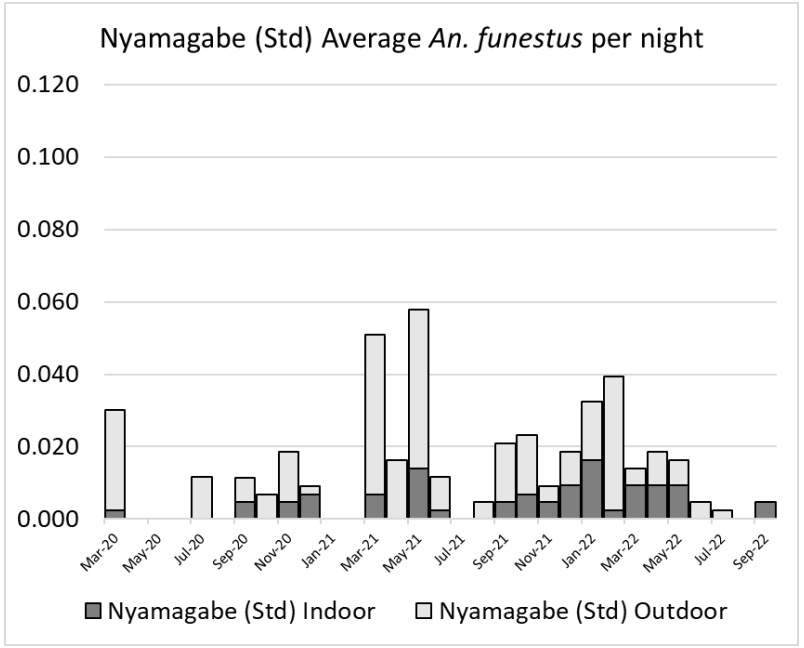
- Mix of *An. gambiae* s.s., *An. funestus* s.l., *An. arabiensis,* and *An. coustani*
- Low to moderate levels of pyrethroid resistance—mitigated by PBO
- Variable ratios of indoor to outdoor biting

- An. gambiae s.s., An. arabiensis, and An. funestus are all likely actively transmitting

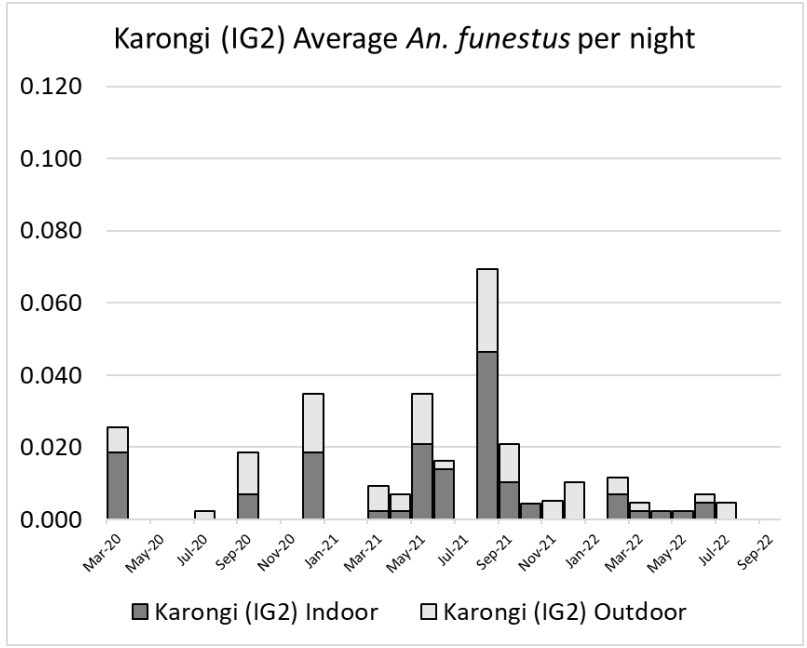
- Transmission detected both indoors and outdoors

Entomological landscape - Rwanda

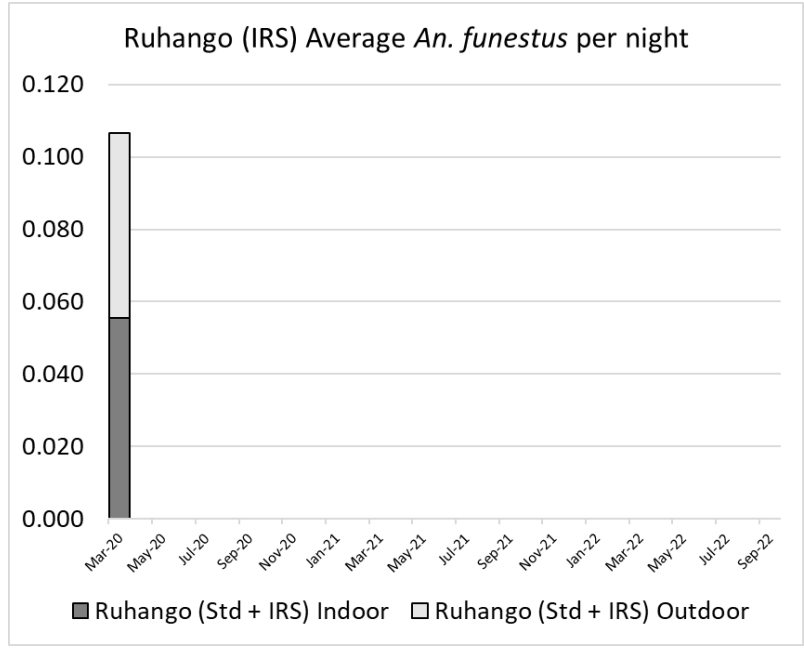
Trends in human landing rates for An. funestus *s.l.*



Low biting rates consistent over study



Low biting rates consistent over study



Low biting rates decreased to zero following IRS

- *An. funestus* fed readily both indoors and outdoors
- Feeding behaviors did not change after ITN distribution campaigns, though biting rates do decrease slightly
- **No *An. funestus* collected in Ruhango after the 2020 IRS campaign**

Preliminary cost-effectiveness

Rwanda

- Provider perspective cost estimates (preliminary): Distribution cost per ITN (0.40 – 0.70)

- Preliminary analysis indicates that in low burden, moderately pyrethroid resistant settings like Rwanda dual AI ITNs and standard ITNs + IRS are both more effective than standard ITNs alone
  - adding IRS to standard nets will likely avert more cases overall
  - switching from standard to pyrethroid + chlorfenapyr nets is likely to be more cost-effective per additional case averted