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# Evaluation of the protective efficacy of Olyset®Plus ceiling nets for reduction of malaria incidence in children in Homa Bay County, Kenya: a cluster-randomized controlled study protocol

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# SCHOLARONE<sup>™</sup> Manuscripts

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8 9	3	children in Homa Bay County, Kenya: a cluster-randomized controlled study protocol
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### Abstract

Introduction: Malaria is still a major health problem in sub-Saharan Africa, where 98% of global malaria mortality occurs. In addition, the spread of *Plasmodium falciparum* with partial artemisinin resistance in East Africa and beyond is a great concern. The establishment of more effective vector control, in addition to the current long-lasting insecticide-treated net (LLIN) distribution program, is an urgent task in these areas. One novel vector control candidate is the Olyset®Plus ceiling nets which can overcome the problems of variations in net use behaviors and metabolic resistance to insecticide in vectors. Our preliminary study suggests the protective efficacy and high acceptability of this tool. With this proposed second trial, we aim to evaluate the impact of this tool in a different eco-epidemiological setting in the lake endemic region of Kenya.

Methods: A cluster randomized controlled trial is designed to evaluate the impact of Olyset®Plus ceiling nets in Ndhiwa Sub-County, Homa Bay County, Kenya. A total of 44 clusters will be randomly assigned in a 1:1 ratio to the intervention group (Olyset®Plus ceiling nets) and the control group. The assignment will be accomplished through covariate-constrained randomization of clusters. For the primary outcome of clinical malaria incidence, 38 children from each cluster will be enrolled in a cohort and followed for 18 months. We will also evaluate the effects of the intervention on entomological indicators as well as its acceptance by communities and cost-effectiveness.

Ethics and dissemination: Ethics approval was provided by the Mount Kenya University Institutional Scientific Ethics Review Committee. Study results will be shared with study participants and communities, the Homa Bay County Government and the Kenya National Malaria Control Programme. Results will also be disseminated through publications, conferences and workshops to help the development of novel malaria control strategies in other malaria-endemic countries.

Trial registration: UMIN000053873

Keywords

Malaria, Anopheles mosquito, vector control, Pyrethroid resistance, Ceiling net, Kenya, Cluster-randomized controlled trial

#### Administrative information

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Role of sponsor {5c}	OMU will support project management oversight, trial management,
	data management, statistical analysis, and research governance. MKU
	also holds overall authority together with project management and
	analysis.

1 2			
3 4	73	Streng	th and limitations of this study
5 6	74	•	This study is a cluster-randomized controlled trial (CRCT) to evaluate the efficacy of the
7 8	75		Olyset®Plus ceiling net as a novel vector control tool and a complement to current malaria control
9 10	76		tools in sub-Saharan Africa.
11 12	77		
13 14	78	•	This marks the second CRCT of the Olyset®Plus ceiling net intervention in the lake endemic region
15 16	79		of Kenya, expanding the evidence base to a different eco-epidemiological setting from the previous
17 18	80		CRCT, where promising results were observed on Mfangano Island.
19 20	81		
21 22 23	82	•	Collaboration with local Kenyan institutions such as the Kenya National Bureau of Statistics
23 24 25	83		(KNBS), the National Malaria Control Programme (NMCP), the Kenya Medical Research Institute
26 27	84		(KEMRI), and Homa Bay County from the research planning stage is one of the strengths of this
28 29	85		trial, allowing for a seamless transition from research implementation in the field to policy
30 31	86		development.
32 33	87		
34 35	88	٠	One of the anticipated limitations is the possible contamination between intervention and control
36 37	89		clusters because we will not set a buffer zone due to the geographical proximity of each cluster. We
30 39 40	90		will try to account for such contamination effects by integrating spatial data into our statistical
41 42	91		model.
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# 01 Introduction

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## 02 Background and rationale {6a}

Malaria is still a major health problem, particularly in sub-Saharan Africa, where 98% of global malaria mortality occurs [1]. Although the morbidity and mortality of malaria declined from the 2000s to 2015 owing to many investments and interventions, such as long-lasting insecticide-treated nets (LLINs), malaria rapid diagnostic tests (RDTs), and artemisinin-based combination therapies (ACTs), progress has stalled since 2015. Moreover, the spread of *Plasmodium falciparum* partially resistant to ACT in Africa is an enormous concern. Currently five African countries, Rwanda [3], Uganda [4], Eritrea [5], Ethiopia [6], and the United Republic of Tanzania [2] have reported delayed clearance of *P. falciparum* after treatment with ACTs. Kenya's proximity to these countries highlights the urgent need to establish effective vector control, in addition to maintaining antimalarial drug efficacy and strengthening resistance surveillance.

Among several vector control measures, LLIN is the most widely adopted tool to prevent mosquito bites and interrupt malaria transmission. However, suboptimal uses of LLIN are key factors in reducing the impact of LLIN on the malaria burden. In the Lake Victoria basin, alternative uses of LLIN for fishing and protecting crops and chicks are well-known local behaviors [7,8]. In fact, in many areas including our study sites in Homa Bay County, Kenya, malaria prevalence remains high despite widespread distribution of LLINs and their periodic replacements for more than a decade. This suggests that LLIN alone is insufficient to interrupt malaria transmission in this region.

Recently, we have proposed a novel vector control tool that covers the ceiling and the gap between the ceiling and the walls of residential structures with co-formulated pyrethroid and piperonyl butoxide (PBO) bed net material, called the Olyset®Plus ceiling net. The benefit of installing the Olyset®Plus ceiling net in addition to conventional LLINs is detailed elsewhere [9]. Briefly, the Olyset®Plus ceiling net provides a combination of physical and chemical protection against mosquitoes which seek human bloodmeal in the house. Furthermore, the ceiling net is semi-permanently installed and requires no further action from end users, thus its protective efficacy is consistently extended to all who sleep in the house and less affected by the variation in conventional LLIN use.

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2 3 129	
4 5 130	The aim of this study is to evaluate the efficacy, acceptability, and cost-effectiveness of Olyset®Plus ceiling
7 8 131	nets on malaria morbidity and transmission in the Lake Victoria basin of Kenya. Preliminary data from our
9 10 <sup>132</sup>	previous study on Mfangano Island in Lake Victoria [9] suggest a substantial reduction in malaria prevalence
$^{11}_{12}$ 133	among school children and high community acceptance of this tool (unpublished data). With this proposed
13 14 134	second trial, we aim to evaluate the impact of this tool in a different eco-epidemiological setting with
16 135 17	relatively higher malaria transmission, more frequent human and vector movement, and synergistic impact
18 136 19	from other interventions such as indoor residual spraying (IRS) and the RTS,S malaria vaccine. Since
20 137 21	effective malaria controls need to be tailored to the local context, evidence of the effectiveness of
22 138 23	Olyset®Plus ceiling nets from various transmission settings will increase the appeal of this intervention.
<sup>24</sup> 139 25	Furthermore, considering the recent increase in choices of malaria control tools and the necessity of
<sup>26</sup> 140 27	combining various tools to maximize the impact of the malaria control program, it is important to understand
<sup>28</sup> 29 141	the acceptability and cost-effectiveness of each intervention to guide its future deployment.
$30 \\ 31 \\ 142 \\ 32 \\ 33 \\ 33 \\ 33 \\ 34 \\ 35 \\ 35 \\ 35 \\ 35$	
32 33 143 34	To achieve these objectives, our collaboration with local institutions including the Kenya National Bureau of
35 144 36	Statistics (KNBS), the National Malaria Control Programme (NMCP), the Kenya Medical Research Institute
37 145 38	(KEMRI), and Homa Bay County, started from the research planning stage. This collaboration is crucial to
39 146 40	the seamless transition from field trial to expanded implementation and policy development.
41 147 42	
43 44 148	Objectives {7}
45 46	The study has four research domains: epidemiology, entomology, social aspects, and cost-effectiveness.
47 48 150	
<sup>49</sup> 50 151	For the epidemiology domain, the primary objective is to determine the protective efficacy of Olyset®Plus
51 52 152 53	ceiling net in reducing malaria clinical incidence in children 6 months to 14 years old over 18 months post-
54 153 55	intervention. The secondary objectives are (1) to determine the protective efficacy of Olyset®Plus ceiling
56 154 57	nets in reducing <i>Plasmodium</i> infection prevalence by PCR in all age groups at 6-, 12-, and 18- months post-
58 155 59	intervention; (2) to determine the protective efficacy of Olyset®Plus ceiling nets against the time-to-first
60 156	Plasmodium infection; (3) to determine the spillover effects of Olyset®Plus ceiling nets in reducing

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*Plasmodium* infection prevalence in all age groups at 6-, 12-, and 18-months post-intervention; and (4) to determine the protective efficacy of Olyset®Plus ceiling net in reducing *Plasmodium* infection incidence in children 6 months to 14 years old over 18 months post-intervention.

For the entomology domain, the primary objective is to evaluate the impact of Olyset®Plus ceiling nets on the mosquito density of the primary malaria vector species. The secondary objectives are (1) to determine the impact of Olyset®Plus ceiling nets on entomological inoculation rate (EIR) and (2) to determine the prevalence of knockdown resistance (*kdr*) mutations in vectors.

For the social aspects domain, the primary objective is to assess the determinants of social acceptability of the Olyset®Plus ceiling net in both the intervention and control arms. The secondary objectives are (1) to determine the feasibility of installing the Olyset®Plus ceiling and (2) to determine the appropriateness of fit of the Olyset®Plus ceiling net in the context of households in Ndhiwa Sub-County.

For the cost-effectiveness domain, the primary objective is to determine the incremental cost effectiveness ratios (ICERs) of adding the Olyset®Plus ceiling net to existing malaria control interventions under field trial conditions. The secondary objectives are (1) to establish the relative contribution to costs of the distinct programmatic elements and identify the inputs that contribute the most to overall costs, and (2) to estimate the potential cost of providing Olyset®Plus ceiling net at a larger scale over 3 and 5 years under operational scenarios.

## 78 Trial design {8}

The study is an open-label, cluster-randomized controlled trial (CRCT) with 44 clusters evenly divided between the intervention and the control arms. Each cluster will include one or two villages and consist of at least 50 households. A baseline survey will be conducted to determine the pre-intervention *Plasmodium* prevalence and *Anopheles* density, and to collect demographic and socioeconomic data for covariateconstrained randomization of clusters. The baseline survey will be conducted one month before cluster randomization. The post-intervention follow-up period will be 18 months. For the evaluation of the primary Page 9 of 50

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3 185 4	objective, 38 children aged 6 months to 14 years from each cluster will be recruited and followed for 18
5 186	months as a cohort. Cross-sectional surveys will be conducted after 6, 12, and 18 months of the intervention
7 8 187	targeting 50 individuals of all ages from each cluster to estimate the overall <i>Plasmodium</i> prevalence.
9 10 <sup>188</sup>	
11 12 189	Methods: Participants, interventions and outcomes
13 14 190 15	Study setting {9}
15 16 191 17	Location and administrative structure
18 192 19	Ndhiwa (713.5 km <sup>2</sup> ) is one of nine sub-counties in Homa Bay County in Kenya. The sub-county has seven
20 193 21	administrative wards: Kanyamwa Kologi, Kanyamwa Kosewa, Kabuoch North, Kwabwai, Kanyadoto,
<sup>22</sup> 194 23	Kanikela, and Kabuoch South/Pala. Based on the number of malaria cases reported in the Kenya Health
<sup>24</sup> 195 25	Information System (KHIS), the accessibility of the site, and population size, we selected Kanyamwa Kologi
<sup>26</sup> 196 27	Ward as the target area (Figure 1). Agriculture is the primary economic activity, with sugarcane as a main
28 29 197	commercial crop. County residents also keep animals such as dairy cattle, beef cattle, sheep, goats, and
30 31 198	poultry [10]. The ward experiences a long rainy season from March to June and a short rainy season from
32 33 199	October to December. As of 2019, the mean annual precipitation is 228.64 mm and the mean annual
35 200	temperature is 26.7°C. The relative humidity remains elevated year-round, fluctuating between 75% to 85%
37 201 38	[11].
39 202 40	
<sup>41</sup> 203 42	Demographics
<sup>43</sup> 204	The population of Kanyamwa Kologi Ward is approximately 33,000 according to the 2019 national census
45 46 205	[12]. The dominant ethnic group in the region is Luo and the primary languages are DhoLuo, Kiswahili, and
47 48206	English. There are 172 primary and 36 secondary schools in Ndhiwa Sub-County [13]. Within Kanyamwa
49 50 207	Kologi Ward, there are 28 primary and 7 secondary schools.
52 208	
53 54 209	Malaria epidemiology and control measures
56 210	Based on the KHIS, there were 429.1 and 457.2 confirmed malaria cases per 1,000 population in Ndhiwa
58 211 59	Sub-County and Kanyamwa Kologi Ward , respectively, in 2023. The primary malaria vector in the sub-
50 212	county is Anopheles funestus, which prefers feeding on humans. An. arabiensis is also an important malaria

health centers.

vector [14]. In Homa Bay County, LLINs have been distributed every three years since the early 2000s, and

214 IRS and the RTS,S malaria vaccine have been piloted in several areas since 2018 and 2019, respectively

215 [15]. Notably PBO-incorporated LLINs (Veeralin®LN, manufactured by VKA Polymers, Tamil Nadu, , 10 216 India) were distributed in late 2023. In Kanyamwa Kologi Ward, there is one level four hospital and seven 11 12 217

#### 16219 **Eligibility criteria {10}**

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As the ceiling nets are installed per structure, we set the inclusion criteria on a structural basis. The inclusion 18 2 2 0 20 22 1 criteria for the installation of the ceiling nets are (1) residential structures with at least one permanent 22 222 resident aged 18 years or older in the household, (2) informed consent provided by a resident in the <sup>24</sup> 223 25 household, and (3) house structure amenable to ceiling net installation in terms of size of the structure, <sup>26</sup> 224 presence of eave, ceiling board, and vertical beams, and material of the top part of the wall. The applicability <sup>28</sup> 22 225 of the ceiling net installation will be assessed by experienced field staff. The exclusion criteria are (1) vacant 31 226 structure, confirmed by at least two visits by community health promoters (CHPs), (2) dwelling structure to 33 227 be vacated or destroyed within the study period, (3) not applicable house structure for the ceiling net 35 228 installation, and (4) non-residential structures (school, shop, kitchen, storage, and toilet). The inclusion 37 229 criteria for the prospective cohort are (1) children aged 6 months to 12 years old at the time of enrolment, (2) 39 2 3 0 living in the study area at the time of Olyset®Plus ceiling net installation, (3) having no plan to leave or stay 41 231 outside the study area for an extended period (longer than one month) over the 18-month follow-up period, <sup>43</sup> 232 and (4) informed consent provided by the participants or the parent or legal guardian. The exclusion criterion <sup>45</sup> 233 is having severe chronic illnesses. The inclusion criteria for cross-sectional malaria surveys for all age 47 48 234 groups are (1) living in the study area during the study period, and (2) informed consent being provided by 49 50 235 the participants or the parent or legal guardian before each survey. The exclusion criteria are (1) having <sub>52</sub>236 severe chronic illnesses and (2) pregnancy known at the time of the surveys.

56 238 Who will take informed consent? {26a}

58 2 3 9 Written informed consent will be obtained by the study team members who fully understand the study 59 60 2 4 0 protocol. After eligibility is confirmed, the study team members will present to the potential participant a

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241 document containing all relevant information about the study in Luo and English. If the participant cannot 242 read, study information will be conveyed verbally in Luo, Kiswahili, and/or English by the study team 243 members. The potential participant will have opportunities to ask any questions. Agreement to participate j<sub>10</sub>244 will be sought only after the participant indicates complete understanding of the study.

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14 2 4 6 Additional consent provisions for collection and use of participant data and biological specimens {26b} 16 2 47 The study information document for ceiling net installation contains the study overview. In addition, the 18 2 4 8 documents for cross-sectional and cohort surveys contain details on collecting, storing, and using personal 20 2 4 9 data and biological specimens during the study.

<sup>24</sup> 251 25 Interventions

#### <sup>26</sup> 252 Explanation for the choice of comparators {6b}

<sup>28</sup><sub>29</sub> 253 In Kenya, LLIN is the most widely used malaria preventive measure. The Division of National Malaria 30 31 254 Programme coordinates free LLIN distribution, and the county governments deliver LLINs to residents in all <sub>33</sub> 255 endemic counties every three years. In Homa Bay County, the RTS, S malaria vaccine has been implemented 35 256 since 2019. The primary purpose of this trial is to demonstrate the superiority in malaria prevention of 37 257 adding Olyset®Plus ceiling nets to the standard malaria control program. Thus, in the control arm, no 39 2 58 Olyset®Plus ceiling nets will be installed, but LLIN use and RTS,S immunization will be allowed in the 41 259 control and intervention arms as the current best practice. There is no plan for new LLIN distribution during <sup>43</sup> 260 the study period.

#### 47 48 262 **Intervention description {11a}**

<sup>49</sup><sub>50</sub> 263 In the intervention arm, Olyset®Plus ceiling nets will be installed in all dwelling units where residents sleep, 51 <sub>52</sub> 264 free of charge to the households. All participants will be encouraged to continue to use LLINs, distributed by 53 54 265 the Homa Bay County government. In each intervention cluster, 1 CHP and 2 community volunteers will be 55 56 266 recruited from the intervention cluster and another 1 CHP from the control cluster will join the team to 57 58 267 enable future knowledge dissemination. The net installation team will be trained to install ceiling nets by 59 60 268 skilled local research assistants who participated in previous trials. The head (or another adult) of the

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household eligible to a ceiling net will be notified at least 24 hours before the scheduled installation time. The cost of the ceiling nets and their installation will be covered by the research team. Details of the installation procedure are described in the previous study protocol [9]. Briefly, the ceiling net is a rectangular sheet of Olyset®Plus net with loops sewn along the diagonal seams. The loops are roped to the support beams under the roof and the edges of the net are stapled to the wall.

75 Criteria for discontinuing or modifying allocated interventions {11b}

As the ceiling net is semi-permanently installed, the intervention will only be discontinued if the participant specifically requests the removal of the ceiling net by the study team. There will be no crossover from the control arm to the intervention arm during the follow-up period. Those who migrate between the arms or emigrate from the study areas will be dropped from the study follow-up.

#### 81 Strategies to improve adherence to interventions {11c}

Adherence to the intervention cohort in this study is defined as sleeping in houses with Olyset®Plus ceiling nets. Adherence is monitored indirectly by assessing the number of nights each participant spends outside their house during the bi-weekly interview. During each house visit, CHPs will visually inspect the condition of the ceiling nets. Any visible tear and damage to the ceiling net will be reported to the research team, who will assess the size and location of the damage and perform repair or replace the ceiling net if necessary.

288 Relevant concomitant care permitted or prohibited during the trial {11d}

9 There is no specific concomitant care prohibited during the trial. All participants in both arms will continue
0 to receive and use free LLIN and have access to standard medical care, including malaria testing by RDT,
1 treatment with ACT and RTS,S malaria vaccination.

#### 293 **Provisions for post-trial care {30}**

All participants will be under the normal healthcare system in the study setting. No perceived health risks for
 the intended population are expected with the intervention. Our plan of continuous cross-sectional malaria
 surveillance after the study period allows us to monitor further parasite transmission in the population.

2 3 297	,
4 5 298	Outcomes {12}
7 8 299	Epidemiological domain: The primary outcome will be symptomatic malaria case incidence, defined as
9 10 300 11	axillary temperature of $\geq 37.5^{\circ}$ C or a history of fever in the preceding 48 hours, and positive mRDT, in
12 13 301	children aged 6 months to 14 years enrolled in the cohort, monitored with biweekly visit and passive case
15 302	detection in the health facilities during an 18-month follow-up. The secondary outcomes will be (1) the
16 17 303	prevalence of <i>Plasmodium</i> infections by PCR in all age groups at 6, 12, and 18 months post-intervention, (2)
18 19 304 20	time to first infection defined as the number of days between the start of the intervention and the first PCR
21 305 22	positive diagnosis in the cohort of children during the 18-month follow-up period, (3) spillover effect
<sup>23</sup> 306	measured with the above-mentioned prevalence parameter, and (4) infection incidence by PCR in the
$\frac{25}{26}307$	prospective cohort of children aged 6 months to 14 years over 18 months.
27 28 308	
29 30 309	Entomological domain: The primary outcome will be the density of the primary malaria vectors, species
31 32 310	composition and sporozoite infection rates. Malaria vector density will be determined using CDC light trap,
33 34 31 1	and species composition and sporozoite infection rates will be determined by microscopy and PCR. The
35 36 312	secondary outcomes of the entomology domains will be (1) changes in EIR as a measure of malaria
37 38 313 39	transmission and (2) prevalence of kdr mutations associated with insecticide resistance in Anopheles
40 314	mosquitoes captured by light trap.
<sup>42</sup> 315	
44 45 316	Social aspect domain: The primary outcome will be the percentage of households consenting to Olyset®Plus
46 47 317	ceiling net installation when offered. In addition, we will include observations and discussions about
48 49 318	individual attitudes toward the ceiling net. The secondary outcomes of the social aspect domain will be the
50 51 319	percentage of the intact ceiling net, description of damaged net, and the impact on the living environment at
52 53 320	6, 12, and 18 months post-intervention.
54 55 321	
56 57 322 58	Cost-effectiveness domain: The primary outcome will be the incremental cost-effectiveness of adding
59 323 60	Olyset®Plus ceiling net to existing malaria control interventions under field trial conditions from the societal

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1	
2 3 324 4	and provider perspectives. The secondary outcomes of the cost-effectiveness domains will be (1) the costs of
<sup>5</sup> 325	the distinct programmatic elements and the inputs that contribute the most to overall costs, and (2) the cost of
<sup>7</sup> 326	providing Olyset®Plus ceiling net at a larger scale over three and five years under operational scenarios.
9 10 327	
11 12 328	Participant timeline {13}
13 14 329 15	The schedule of trial activities is presented in Figure 2. The detail of each survey is described in Figure 3.
16 330	
18 331 19	Sample size {14}
20 332 21	The sample size was calculated using the method of Hayes and Moulton [16]. All the sample sizes will be
22 333 23	recalculated based on the baseline data, which will be collected about one month before the ceiling net
<sup>24</sup> 334 25	installation.
$\frac{26}{27}335$	
<sup>28</sup> 29 336	Epidemiological survey
30 31 337	The following calculations were based on the historical data collected from the Lake Victoria region in
32 33 338	Kenya with a clinical malaria incidence rate of 0.5 per person-year in children under 14 years old by RDT
34 35 339	(unpublished data on Mfangano island), 40% parasite prevalence for all age groups by PCR and a between-
36 37 340	cluster coefficient of variation (CV) in incidence rate of 0.24 in both groups. In the study site, RTS,S malaria
39 341	vaccination began in 2019, with a mass distribution of PBO-incorporated LLINs at the end of 2023.
40 41 342 42	Therefore, the intervention effect is expected to be smaller than those in previous studies and is
<sup>43</sup> 343 44	conservatively assumed to be 25%. Assuming 38 individuals per cluster to be followed for up to 18 months
45 46344	with 20 % loss-to-follow up rate, we require 22 clusters per arm to achieve 80% power to detect a significant
47 48345	incidence rate ratio of 0.75 (25% protective efficacy) at a two-sided type 1 error of 5%. With the number of
49 50 346	clusters with 50 individuals per cluster, for the secondary outcome of malaria prevalence by PCR for all age
51 52 347	groups, we would achieve 5% type 1 error and 80% power to detect 23.5 % relative reduction. We do not
53 54 348	specify the sample size for identifying spillover effects because spillovers tend to have smaller effect sizes
55 56 349 57	relative to total or overall effects, so typically larger sample sizes are required to detect them. Although our
58 350 59	study may be underpowered to detect spillovers, we will report the results as an exploratory analysis.
60 351	

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#### 352 Entomological survey

Based on the previous study, we assume a mean vector density (number of mosquitoes per CDC light traps) of 3.3, a standard deviation (SD) of 3.3, and CV of 0.192. For 80% power to detect a 50% decrease in mean mosquito densities at 5% type 1 error level, we need to capture mosquitoes from five houses per cluster.

## **Recruitment {15}**

Thirty-eight eligible children in each cluster will be randomly recruited into our cohort. Recruitment will be limited to children aged 12 or younger, to avoid children aging out during the 18-month monitoring period. Study team staff will obtain informed consent from the parents or caregivers of the children before enrolling the children in the cohort. For the cross-sectional survey at each time point, we will randomly select from each cluster 50 individuals of all age groups. To guarantee the representativeness for all age groups, the selection will be done with following age category stratifications; 0-4, 5-9, 10-14, 15-19, and 20 and above.

Assignment of interventions: allocation

**Sequence generation {16a}** 

Random numbers will be generated using the sample function in R software.

## **Concealment mechanism {16b}**

The individual, household, and villages (clusters) are all given unique IDs at the beginning of the baseline. Any following steps handle only these anonymized IDs.

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# **Implementation {16c}**

After the baseline survey, covariate-constrained randomization will be used to allocate the 44 clusters across <sub>53</sub> 375 the two study arms. The following factors will be constrained: baseline malaria infection prevalence by RDT 55 376 in children aged 0.5–14 years, LLIN usage, malaria vaccine coverage, socioeconomic status (SES), 57 377 population size, the proportion of eligible houses for the ceiling net installation, and vector densities. An 58 59 378 independent statistician will perform the randomization. Local study assistants will perform participant 60

1	
2 3 270	
4 5	enronment.
6 380 7	
8 381 9	Assignment of interventions: Blinding
10 382 11	Who will be blinded {17a}
12 383 13	Due to the visibility of the Olyset®Plus ceiling net, neither the trial participants nor the members of the study
<sup>14</sup> 384 15	team who take part in field activities can be blinded. However, laboratory- and office-based personnel (e.g.,
16 385 17	microscopists, laboratory technicians, and data analysts) will be blinded to the identity and intervention
<sup>18</sup> 19 <sup>386</sup>	status of the trial participants since all biological specimens will be identified by a unique numeric study
20 21 387	identifier, and personal information will be removed before analyses.
22 23 388 24	
<sup>25</sup> 389 26	Procedure for unblinding if needed {17b}
<sup>27</sup> 390 28	This is an open-label trial, and only the data measurers are blinded. Therefore, there is no circumstance that
<sup>29</sup> <sub>30</sub> 391 <sup>31</sup> <sub>32</sub> 392	they need to be unblinded.
33 34 393	Data collection and management
35 36 394 37	Plans for assessment and collection of outcomes {18a}
38 395 39	Baseline survey
40 396 41	A baseline survey targeting 50 enumeration areas (comprising one or two villages) in the study area will be
42 397 43	conducted shortly before the ceiling net intervention to obtain data to assure the balance of the cluster
<sup>44</sup> 398 45	allocation and obtain basic demographic data. The baseline survey includes a questionnaire for all
46 47 399	households, mRDT testing of all children aged 6 months to 14 years, and an entomological survey of
48 49400	randomly sampled households. We modified the questionnaire used in the 2020 Kenya Malaria Indicator
50 51 401	Survey (KMIS) mainly to quantify the SES of each household and bed net usage. In addition, we add
52 53 402 54 55 403	questions to quantify the favorability of ceiling nets before the intervention.
56 57 404	Cohort monitoring
58 59 405 60	Incidence of clinical malaria in the prospective cohort will be estimated by both active and passive case

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detections. For active case detection, we will conduct home visits every two weeks. Axillary temperature will be measured using a digital thermometer. Participants with fever (>37.5°C) or other malaria-related symptoms listed in the Kenya National Malaria Treatment Guideline at the time of home visit or within the previous 48 hours will be tested for malaria by RDT. History of travel, confirmed malaria episode, and visit to local health facilities since the previous visit is recorded. *Plasmodium* infection status will be determined by RDT and PCR from all cohort participants during every other biweekly home visit i.e. every four weeks. For passive case detection, we ask all cohort participants to visit designated health facilities in case they suspect malaria between home visits. The designated facilities are asked to record all malaria tests performed regardless of their results together with the cohort ID. The cost of RDT and anti-malarial treatment will be covered by the research team to encourage cohort participants to use only designated facilities.

Cross-sectional malariometric surveys

Malaria prevalence in children and adults will be estimated using cross-sectional malariometric surveys in communities. These surveys will be conducted at 6, 12, and 18 months post-installation. Community surveys will be conducted by house visits.

Plasmodium infection status will be determined using three methods: RDT, microscopy, and PCR. A fingerprick blood sample will be collected for on-site diagnosis using the Bioline Malaria Ag P.f/Pan RDT (Abbott Diagnostics Korea Inc., Republic of Korea). Survey participants with positive test results will be provided with a treatment course of artemether-lumefantrine with dosing instructions in accordance with guidelines from the Ministry of Health in Kenya after checking their recent treatment history. Blood smears will be prepared on site and transported to the main laboratory in Homa Bay where thin smears are fixed with methanol and all smears are stained with 3% Giemsa solution for 30 minutes, then examined by experienced microscopists. Two blood samples (70 µl each) will be collected with a 75-mm heparinized micro-hematocrit capillary tube (Thermo Fisher Scientific, MA, USA) and spotted on Whatman ET31 Chr filter paper (Whatman International. Maidstone, UK). The blood samples will be allowed to dry at ambient temperature and stored in individual zipped plastic bags at -20°C. The dried blood spots will be used for the determination of malaria status by PCR [17].

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#### 434 Entomological surveys

Indoor resting mosquitoes will be collected from five sentinel houses within each cluster using the CDC light trap method. Samples will be preserved in 96% ethanol and placed in a cool box with ice. Specimens will be examined for sex determination by microscopy and species identification by microscopy and PCR. Indoor resting mosquitoes will be collected at baseline, 6, 12 and 18 months post ceiling net installation.

#### 40 Social aspects

We will conduct an exploratory sequential research design using integrated mixed methods (qualitative and quantitative). Qualitative assessment of community perceptions on the Olyset®Plus ceiling nets, community facilitators, and concerns of Olyset®Plus ceiling net use will be implemented, followed by quantitative assessments every 6 months and routine monitoring to evaluate durability and appropriateness of fit of Olyset®Plus ceiling nets using observation checklists. At the end of the study, other qualitative case studies, such as focus group discussions and key informant interviews, will be conducted to document success stories and inform the sustainability and scalability of the intervention.

#### 49 Cost-effectiveness analysis

Incremental financial and economic cost data of Olyset®Plus ceiling net will be collected alongside the intervention. In cases where resources, such as staff, are shared among multiple elements, the allocation of costs will be carried out using an appropriate proxy. Costs related to research activities will be excluded from this allocation. Financial costs will be derived from project expenditure records, while economic costs, which encompass financial expenditures and donated resources, will be identified through project records and social aspects activities. The value of donated resources will be credited based on prevailing market rates. Furthermore, capital costs will be annualized over their useful life for financial costing and annualized at a discount rate of 3% for economic costing.

## 459 Plans to promote participant retention and complete follow-up {18b}

All surveys planned for the epidemiological and entomological domains will be conducted by house visits.
CHPs will make an appointment with eligible participants before each visit to confirm the participants'

available date and time. Small remunerations will be provided to survey participants to compensate for their time. CHPs will receive detailed instructions and participatory training for all field procedures and will be actively supervised by the research team throughout the duration of the study. Feedback will be regularly sought from CHPs regarding any issues raised by study participants, and discussions will be held to resolve issues from the field.

#### Data management {19}

All data from the baseline, cohort, and cross-sectional surveys will be captured using the Research Electronic Data Capture (REDCap) software on electronic tablets. Data will be uploaded daily to a highly secure server hosted by Mount Kenya University (MKU). All data from the quantitative surveys will also be stored securely and backed up regularly to prevent data loss. Data access and management of databases will be limited to authorized study investigators and collaborators. After validation of data uploaded to the MKU server, data stored locally on the tablet computers will be permanently deleted to minimize unauthorized Ne access.

#### 36 477 **Confidentiality {27}**

38 4 7 8 To maintain confidentiality, each participant in cross-sectional surveys, the longitudinal cohort, and the 40 479 quantitative surveys is assigned a unique identifier. The data collected will be labelled using the unique 42 4 8 0 identifier and stored separately from the key linking personal information (name, date of birth, GPS of each <sup>44</sup> 481 household, and phone number). The data will be kept on a secure server that is only accessible to the <sup>46</sup>/<sub>-</sub> 482 research staff. Publications will contain only aggregated data, and no personal information will be included.

Plans for collection, laboratory evaluation and storage of biological specimens for genetic or molecular analysis in this trial/future use {33}

55 486 Anonymized blood samples from study participants will be stored and analyzed for *Plasmodium* infections 57 487 by microscopy and PCR in our laboratory in Homa Bay. Microscopic examinations of adult mosquito 59488 specimens will be conducted in our field laboratory in Mbita, while PCR analyses will be conducted in our

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laboratories in Homa Bay and MKU. Laboratory data outputs will be entered in Microsoft Excel and imported into the database. No human genetic analysis is planned for this study. However, remaining biological materials will be stored indefinitely for future studies unless the participants opt out during the informed consent process. Participants are provided with contact information of the research team and can remove themselves from this study or any future studies at any time without penalty ore prejudice.

Statistical methods

#### Statistical methods for primary and secondary outcomes {20a}

We will follow the CONSORT guidelines extended for CRCT for statistical analysis and result reporting. The intention-to-treat (ITT) analysis is the primary analysis approach for both the primary and secondary objectives for the epidemiological and entomological studies. The per-protocol (PP) analysis is included as a supplementary analysis for the primary and secondary objectives for the epidemiological and entomological studies. Detailed methodologies for the epidemiological part are described in the supplementary file of statistical analysis plan. er.

#### Clinical malaria incidence

We will determine the protective efficacy of Olyset®Plus ceiling nets against malaria case incidence by comparing clinical malaria incidence rates between arms. We will use mixed effects negative binomial regression accounting for within-cluster correlation of outcomes. Possible confounding factors such as age, sex, bed net usage, house structure, malaria vaccination history, and SES will be adjusted as well as covariates used in the covariate-constrained randomization. In addition, because we will not set a buffer zone, the distance to the nearest household in the other arm will be adjusted in the following analysis to reduce the contamination between two arms. The variable was selected from the previous study [18].

Prevalence of malaria infection

56 514 The secondary outcome, the prevalence of malaria infection by PCR and microscopy measured at 6, 12, and 57 58 5 1 5 18 months after the ceiling net installation will be analyzed using mixed effects logistic regression adjusting 59 60 5 1 6 for the above-mentioned confounding factors.

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2 3 517	
4	
5 518 6	Time to first malaria infection
7 8 519	A Cox proportional hazards model and other survival models will be used to compare time to first malaria
9 10 520	infection between arms adjusting for the above-mentioned confounding factors. In addition, we will account
11 12 521	for the within-cluster correlation of responses.
13 14 522	
16 523	Exploratory analysis for spillover effects
18 524 19	Evidence for positive spillover effects of the ceiling net on malaria infection prevalence of all age group will
20 525 21	be assessed by comparing individuals with no intervention conditioning 1) the distance to ceiling net
22 526 23	installed household, and 2) the coverage of surrounding households with ceiling net within 400 m. The
<sup>24</sup> 527 25	distance of 400 m was chosen as the spillover effect appears to attenuate at this distance based on previous
<sup>26</sup> 528 <sup>27</sup> 528 <sup>28</sup> 529	reports [19].
<sup>30</sup> <sub>31</sub> 530	Entomology
33 531	Differences in vector density and EIR between arms will be evaluated by random effects negative binomial
35 532 36 37 533 38	regression taking into account the intracluster correlation.
39 534 40	Social aspects
41 535 42	We will employ the Framework for Reporting Adaptations and Modifications to Evidence-based
<sup>43</sup> 536 44	Implementation Strategies (FRAME-IS) [20] to document the implementation processes of the ceiling nets,
<sup>45</sup> 537 46	and the Evidence integration triangle framework[21] to align the evidence generated to policy and vector
<sup>47</sup> 538	control strategies from the health systems aspect. The theoretical framework in qualitative research will be
<sup>49</sup> 539	grounded theory[22]. Data from ethnographic, focus group discussions, key informant interview will be
52 540	summarized using content thematic analysis. Pre- and post-intervention acceptability to install Olyset®Plus
54 541 55 56 542	ceiling net intervention will be compared to actual consent using logistic regressions.
57 58 543 59 60	Cost-effectiveness

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The economic and financial costs associated with the Olyset®Plus ceiling net intervention will be presented in total and disaggregated forms, highlighting the relative contribution of each program element to the overall program costs. To facilitate comparisons with other malaria vector control interventions, the costs will be converted into cost per household and per person receiving the intervention annually. Various program scenarios, such as different scales and durations, will be presented to estimate operational implementation costs. Compared to the control group, we will utilize the number of malaria cases averted in the Olyset®Plus ceiling net arm to calculate the DALYs averted using standard methods.

#### Interim analyses {21b}

No interim analysis is planned because neither the insecticide permethrin nor the synergist PBO as formulated in Olyset®Plus LLINs are known to pose significant health and safety risks [9,23].

### Methods for additional analyses (e.g. subgroup analyses) {20b}

We will perform the same analysis for three age subgroups ( $\leq$  59 months old; 5 years old to 14 years old; 15 years old or older) to examine if the effects of Olyset®Plus ceiling net differ by age groups. In addition, we will perform other machine learning based approach such as causal forest and super learner to estimate the conditional average treatment effect.

# Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data {20c}

564 In the cohort, non-adherence to the intervention can be identified by bi-weekly interviews. Participants who 565 regularly sleep outside their homes will be removed from the analyses. The extent and patterns of missing data will be assessed once all data collection has been completed. If necessary, we will apply simple hotdeck imputation methods if the missing fraction for the covariate is <5% or appropriate multiple imputation approaches if the missing fraction for a covariable are  $\geq 5\%$ . If a non-ignorable portion of the subjects have missing values on a covariate (due to missing at random or missing completely at random), that covariate may be excluded in the model.

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1 2	
<sup>3</sup> 572 4	Plans to give access to the full protocol, participant level-data and statistical code {31c}
<sup>5</sup> 573	This manuscript is the full protocol. The corresponding author will make the de-identified datasets or any
<sup>7</sup> 574	future statistical code available upon reasonable request.
9 10 575	
11 12 576	Oversight and monitoring
13 14 577	Composition of the coordinating centre and trial steering committee {5d}
15 16 578	The sampling team, composed of CHPs and laboratory technicians, set up a day-to-day communication
17 18 579	group and exchanged their experiences. A local management team of study investigators from Kenya and
19 20 580 21	Japan also joined this, leading and advising the activities and monitoring the sample and data integrity. A
<sup>22</sup> 581	monthly meeting will be held by the steering committee composed of all key researchers from Kenya and
<sup>24</sup> 582	Japan, including the principal investigator (PI) and co-PI, which aim to monitor the progress of the trial.
$\frac{26}{27}$ 583	
<sup>28</sup> 29 584	Composition of the data monitoring committee, its role and reporting structure {21a}
30 31 585	Because this intervention is considered to be of a low-risk nature, this study does not have a data monitoring
32 33 586	committee. For additional credibility about study quality, the researchers will consult a third statistician, if
34 35 587	necessary.
36 37 588	
38 39 589	Adverse event reporting and harms {22}
40 41 590	All unanticipated problems will be reported to the research team and Homa Bay County Ministry of Health
43 43 591	(MOH) through CHPs. Medical officers from Homa Bay County will assess the relatedness of the reported
<sup>45</sup> 46 592	events to the study and report to the research team, including the PI. In the event of a study-related serious
47 48 593	adverse event, the study team will convene a meeting immediately with the MOH and Homa Bay County
49 50 594	Teaching and Referral Hospital representatives to review the case and take necessary action. Also, the
51 52 595	ceiling net is made of the same materials and chemicals as LLIN already on the market, and is therefore not
53 54 596	expected to have significant environmental impact.
55 56 597	
57 58 598	Frequency and plans for auditing trial conduct {23}
59 60 599	A monthly meeting will be held during the follow-up period to ensure that all surveys and investigations are

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2 3 600 conducted according to the study protocol. The study is required to submit annual reports and renewal to 4 5 601 ethical review boards of Osaka Metropolitan University, Japan, and Mount Kenya University, Kenya. 6 7 602 8 9 -10<sup>603</sup> Plans for communicating important protocol amendments to relevant parties (e.g. trial participants, 11 12<sup>604</sup> ethical committees) {25} 13 14 605 Decisions on important trial amendments must be made through a formal procedure and will be approved by 15 16 606 institutional review boards (IRB) at Mount Kenya University and Osaka Metropolitan University. The 17 18 607 protocol in the clinical trials registry will also be updated accordingly. 19 20 608 21 22 609 **Dissemination plans {31a}** 23 <sup>24</sup> 610 25 Study results will be shared with the study participants and communities, the Homa Bay County Government 26 27 611 and the Kenya National Malaria Control Programme. Results will also be disseminated through publications, <sup>28</sup> 29 612 conferences and workshops to help the development of novel malaria control strategies in other malaria-30 <sub>31</sub> 613 endemic countries. Suggestions from the participants will also help shape the future improvement of the 32 33 614 intervention. 34 35 615 36 37 6 1 6 Discussion 38 39617 Global malaria progress has flatlined in recent years: targets of reductions in malaria morbidity and mortality 40 41 618 and required funding by 2030 are all off track as of 2023[6]. In addition, P. falciparum with partial 42 <sup>43</sup> 619 artemisinin resistance, which has been a problem in the Great Mekong Subregion (GMS) for more than a 44 45 620 decade [24] [2-6]. Novel interventions that are cost-effective and widely accepted by local communities are 46 **4**8 621 47 urgently needed to contain the spread of artemisinin-resistant P. falciparum in sub-Saharan Africa. 49 .) 50 622 51 <sub>52</sub> 623 Early results from our cluster randomized controlled trial of Olyset®Plus ceiling nets on Mfangano Island in 53 54 624 Lake Victoria, Kenya suggest that ceiling nets can reduce *Plasmodium* prevalence and are positively 55 56 625 received by the local communities. Nevertheless, there are regional differences in housing design, vector 57 58 6 2 6 abundance and composition, and availability of malaria control interventions. As such the feasibility and 59 60 627 acceptability of the ceiling net intervention are likely to depend on local eco-epidemiological context [25].

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628 Furthermore, one of the secondary objectives in this study is to measure the spillover effects, i.e. how much a 629 household that does not have a ceiling net benefits from living near a house with a ceiling net. This enables a 630 broader understanding of the impact of the ceiling nets at the community level.

12 632 This trial has several limitations. First, although the study is designed as a cluster-randomized controlled 14 633 trial, contamination between intervention and control clusters cannot be excluded, as buffer zones between 16 6 34 intervention and control clusters cannot be created due to geographic proximity of houses and villages in the 18 6 3 5 ward. A recent study, however, has shown that the spillover effect of interventions on malaria can extend to 20 6 3 6 3 km [26], so buffer zones of a few hundred meters, as set out in many studies, may not be sufficient. We 22 637 will try to eliminate such contamination effects by integrating spatial data into our statistical model. Second, <sup>24</sup> 638 25 because of the visible nature of the ceiling net, we cannot exclude open-label and observer biases. It is <sup>26</sup> 639 conceivable that participants receiving ceiling nets may reduce their usage of conventional LLIN, as both <sup>28</sup> 29 640 interventions are made of the same materials and may be perceived to protect against malaria in the same <sub>31</sub> 641 manner. We aim to reduce such bias as much as possible through repeated reminders by CHPs that ceiling 33 642 nets serve as an addition to and not a replacement of conventional LLINs. We will conduct surveys and in-35 643 depth interviews to elicit participants' perceptions of the ceiling net, which can guide future messaging and 37 644 implementation. To reduce observer bias, laboratory investigators and data analysts will be blinded. Third, in 39 6 4 5 the study area, pyrethroid+PBO-incorporated LLINs were distributed in 2023. It may reduce the effect of our 41 646 ceiling net intervention because pyrethroid+PBO-incorporated LLINs are more effective than non-PBO-<sup>43</sup> 647 incorporated LLINs by targeting both Anopheles vectors with and without metabolic resistance to <sup>45</sup> 648 pyrethroids. Pyrethroid+PBO incorporated LLINs received a conditional endorsement from the World 47 48 649 Health Organization (WHO) in 2017, and approximately half of the LLINs distributed in sub-Saharan Africa ... 50 650 in 2022 were of this type [2]. Given the abundance of PBO-incorporated LLINs in the region, it is important <sub>52</sub> 651 to assess the effectiveness of the Olyset®Plus ceiling net as an addition to these LLINs to inform policy 54 652 recommendations. Recently LLINs combining two different classes of insecticides have been shown to be 56 653 superior to pyrethroid-based LLINs [27]. When these new LLINs become widely available, the effectiveness 58 6 5 4 of pyrethroid-PBO ceiling nets needs to be re-investigated. 59 60 6 5 5

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3 656 4	Trial status
${}^{5}_{6}$ 657	The Baseline survey was started on April 8, 2024. The recruitment of the intervention participants will be in
$\frac{7}{8}$ 658	June 2024. The current protocol is version 5.0 as of April 18.
9 10 659	
11 12 660	Abbreviations
13 14 661	ACT: artemisinin-based combination therapy
15 16 17 662	CHP: community health promoter
<sup>18</sup> 19 <sup>663</sup>	CRCT: cluster-randomized controlled trial
<sup>20</sup> 21 664	CV: coefficient of variation
22 23 665	<i>kdr</i> : knockdown resistance
24 25 666	KHIS: Kenya Health Information System
20 27 667 28	ITN: insecticide treated nets
29 668 30	IRS: indoor residual spraying
31 669 32	LLIN: long-lasting insecticidal nets
<sup>33</sup> 670 34	MKU: Mount Kenya University
<sup>35</sup> 671 36	PBO: piperonyl butoxide
<sup>37</sup> 38 672	RDT: rapid diagnosis tests
39 40 673	
41 42 674 43	Declarations
<sup>44</sup> 675 45	Acknowledgements
46 47676	We would like to express our sincere gratitude to this study's participants, field, and laboratory staff. In
48 49 677	addition, we acknowledge the collaboration and support of health offices in Homa Bay County, Kenya.
<sup>50</sup> 51 678	
52 53 679	Authors' contributions {31b}
54 55 680	AK and JG are co-principal investigators. YKK, WK, and AK developed the original concept. All authors
56 57 681	discussed and contributed to the study protocol. YKK, WK, PO, BM, TO, CWC, JK, SM, and MK drafted
59 682 60	the manuscript. YKK, WK, CWC, MK, GO, and JG contributed to the revisions of the draft of the

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3 711 4	The	samples collected in this study may potentially be used for other research purposes. This is clearly stated
5 712 6	in th	ne informed consent form. In such cases, we will obtain the necessary ethical approval and provide
7 713	part	icipants with the chance to opt-out from this. All experiments will be carried out in adherence to WHO
9 10 <sup>714</sup>	requ	irements and the Declaration of Helsinki.
11 12 715		
13 14 716	Con	sent for publication {32}
15 16 717	We	will not present identifying images or other personal or clinical details of participants. The participant
17 18 718	info	rmation materials and informed consent form are available from the corresponding author on request.
19 20 719		
21 22 22 720	Con	nnating interests (28)
23 7 20	Con	
25 721 26	This	s study was partially supported by a research grant from Sumitomo Chemical Corporation.
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Map of the study area. Inset shows the locations of the level four hospital and seven health centers (HC) in Kanyamwa Kologi Ward.

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CONSORT flow diagram and the detail of each survey.

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Evaluation of the protective efficacy of Olyset®Plus ceiling nets for reduction of malaria incidence children in Homa Bay County, Kenya: statistical analysis plan for clinical and epidemiological outcomes

# **SAP** version

Version 4.0

Apr 9, 2024 prepared by Yura K Ko (yongra.ko@ki.se)

# SAP revisions

Version	Date	Summary of Changes
1.0	Jan 23, 2024	First draft
2.0	Feb 5, 2024	Added more details based on collaborators' feedback
3.0	Mar 4, 2024	Revised by the senior statistician (Dr. Daisuke Yoneoka)
4.0	April 9, 2024	Revised based on collaborators' feefback

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# Introduction

Objectives

# Primary objective:

• To determine the protective efficacy of Olyset®Plus ceiling nets in reducing malaria case incidence in children 6 months-14 years for 18 months post-intervention

# Secondary objectives:

- 1. To determine the protective efficacy of Olyset®Plus ceiling nets in reducing malaria infection prevalence in all age groups at 6-, 12-, and 18-months post-intervention
- 2. To determine the protective efficacy of Olyset®Plus ceiling nets against the time to first malaria infection for 18 months post-intervention
- 3. To determine the spillover effects of Olyset®Plus ceiling nets in reducing malaria infection prevalence in all age groups at 6-, 12-, and 18-months post-intervention
- 4. To determine the protective efficacy of Olyset®Plus ceiling net in reducing *Plasmodium* infection incidence in children 6 months to 14 years old over 18 months post-intervention.

## Study Methods

#### Trial design

The study is a cluster-randomized controlled trial (CRCT) with 44 clusters evenly divided between the intervention and the control arms. Each cluster will be one or two villages consisting of at least 50 households. A baseline survey will be conducted to determine pre-intervention *Plasmodium* prevalence and to collect demographic and socioeconomic data for covariate-constrained randomization of clusters. The baseline survey will be conducted approximately one month before randomization. The post-intervention follow-up period will be 18 months. Thirty-eight children aged 6 months to 14 years from each cluster will be recruited and followed for 18 months as a cohort to determine the protective efficacy of the Olyset®Plus ceiling net on clinical malaria incidence (primary objective), time to first *Plasmodium* infection incidence (secondary objectives). Cross-sectional surveys will be conducted at 6, 12, and 18 months post-intervention targeting 50 individuals of all ages from each cluster to determine the overall *Plasmodium* prevalence and to estimate the spillover effect (secondary objectives).

#### Randomization

After the baseline survey, covariate-constrained randomization will be used to allocate the 44 clusters across the two study arms. Covariate-constrained allocation ensures that the arms are balanced overall by excluding allocations where predetermined factors are not balanced within set margins. The following factors will be constrained: baseline malaria infection prevalence by RDT in children aged 0.5–14 years, LLIN usage, malaria vaccine coverage, socioeconomic status (SES), population size, the proportion of eligible houses for the ceiling net installation, and vector densities.

For the proportions of interest, we require the average difference between the arms of no more than 10% for the means of interest, and we require the difference in means to be no more than a quarter of the standard deviation of the variable among individuals in the population. After enumerating the allocations that fulfil the criteria, we may relax or tighten up the balance criteria when the allocated number is too small or very large. One allocation will be selected randomly among all possible allocations meeting the balancing constraints. Data on any additional potentially confounding ecological factors not included in the covariate-constrained randomization will be collected and adjusted for in the analysis. An independent statistician will perform the randomization.

#### Sample size

The sample size was calculated using the method of Hayes and Moulton<sup>1</sup>. All the sample sizes will be recalculated based on the baseline data, which will be collected before the ceiling net installation.

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The following calculations were based on the historical data collected from the same Lake Victoria region in Kenya with a clinical malaria incidence rate of 0.5 per person-year for children under 14 years old by RDT (personal communication), 40% parasite prevalence for all age groups by PCR, and a betweencluster coefficient of variation (CV) of incidence rate = 0.24 in both arms. In the study site, RTS, S vaccination began in 2019, with an additional mass distribution of pyrethroid-PBO LLINs at the end of 2023. Therefore, the intervention effect is expected to be smaller than in previous studies and was conservatively assumed to be 25%. Assuming 38 individuals per cluster to be followed for up to 18 months with 20 % loss-to-follow up rate, we require 22 clusters per arm to achieve 80% power to detect a significant incidence rate ratio of 0.75 (25% protective efficacy) at a two-sided type 1 error of 5%. With 44 clusters and 50 individuals per cluster, for the outcome of *Plasmodium* prevalence by PCR, we would achieve 80% power to detect a 23.5 % relative reduction. We do not specify the sample size for identifying spillover effects because spillovers tend to have smaller effect sizes relative to total or overall effects, so typically larger sample sizes are required to detect them. Although our study may be underpowered to detect spillovers, we will report the results as an exploratory analysis.

# Framework

Our null hypothesis for the primary outcome is that Olyset®Plus ceiling nets + standard malaria treatment and prevention measures do not reduce the clinical malaria incidence compared to standard malaria treatment and prevention measures in children 6 months to 14 years at 18 months post-intervention.

### Statistical interim analyses and stopping guidance

Neither the ceiling nets nor synergist PBO are known to pose significant health and safety risks. This has also been demonstrated in our previous CRT on Mfangano Island<sup>2</sup>. Therefore, no interim analysis is planned.

#### Timing of final analysis

We will conduct the final analysis after 18 months of follow-up. Results will immediately be submitted for publication in peer-reviewed journals.

# Timing of outcome assessments



### Figure1: Timetable of trial activities

# **Statistical Principles**

# Confidence intervals and P values

We will use a two-sided significance level of  $\alpha = 0.05$  for hypothesis testing. All statistical tests will be conducted at this predetermined level of significance unless otherwise specified. For each estimated parameter, 95% confidence intervals will be calculated and reported.

# Adherence and protocol deviations

Since the intervention (ceiling net) will be installed in trial participants' houses, participants not sleeping in their own houses will not benefit from the intervention. In the cohort, non-adherence to the intervention can be inferred from travel history during bi-weekly interviews. Therefore, participants who regularly sleep outside their homes will be removed from the analyses. In addition, if a cohort participant is absent for three consecutive visits or for more than half of all visits, the child will be excluded from the analysis. Other protocol deviations will be carefully documented and categorized during the study.

# Analysis populations

The intention to treat (ITT) analysis is the primary analysis approach for both the primary and secondary objectives. The per-protocol (PP) analysis is included as a supplementary analysis for the primary and secondary objectives.

# Trial population

## Screening data

Screening data will be collected during the cohort enrollment and each cross-sectional survey to assess the eligibility of potential participants. This information will include demographic characteristics such as age, sex, SES, and other relevant parameters outlined in the study protocol.

# Eligibility

The inclusion criteria for the installation of the Olyset®Plus ceiling net are (1) residential structures housing at least one permanent resident aged 18 years or older in the household, (2) informed consent provided by at least one adult in the household and (3) applicable house structure for the ceiling net in terms of size of the structure, presence of eave, ceiling board, and vertical beams, and material of the top part of the wall. The applicability of the ceiling net installation will be assessed by experienced field staff. The exclusion criteria are (1) vacant dwelling structure (confirmed by at least two visits by CHPs), (2) dwelling structure to be vacated or destroyed within the study period and (3) not applicable house structure for the ceiling net installation.

The inclusion criteria for prospective cohorts of children aged 6 months to 14 years old are (1) living in the study area at the time of Olyset®Plus ceiling net installation, (2) having no plan to leave or stay outside the study area for an extended period (longer than 1 month) over the 18-month follow-up period, and (3) informed consent provided by the participant's parent or guardian. The exclusion criterion is having severe chronic illnesses.

The inclusion criteria for cross-sectional malaria surveys for all age groups are (1) living in the study area during the study period, and (2) informed consent being provided by the parent or legal guardian before each survey. The exclusion criterion is having severe chronic illnesses.

# Recruitment

For the baseline survey, we will randomly choose 50 enumeration areas (comprising one or two villages) in Kanyamwa Kologi Ward, Ndhiwa Sub-County. The survey includes a questionnaire for all households, mRDT testing of all children aged 6 months to 14 years. We will not create buffer zones to minimize contamination since a buffer zone of 400–600 m from the boundary will greatly reduce the number of houses in the core area available for analysis in many clusters. Thirty-eight eligible children will be randomly recruited into our cohort in each cluster. Recruitment will be limited to children aged 12 or younger, to prevent children from aging out during the 18 months monitoring period. For the cross-sectional survey at each time point, we will randomly select 50 individuals of all age groups from each

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cluster. To reflect the age structure of the populations, the selection will be done with age category stratifications.

### Withdrawal/follow-up

Those who migrate between the arms or emigrate from the study areas, or those who dismount the ceiling net from their house structure will be dropped from the intervention. For the cohort, those who are absent for three consecutive visits or for more than half of all visits will be excluded from the analysis as lost to follow-up. A summary of study participant selection is shown in Figure 2.



Figure 2: A schematic flow diagram of cluster allocation and study participant selection.

# **Baseline characteristics**

We will report a list of baseline characteristics of the intervention and control arms. The list will include population, mean number of people per household, median age of population, number of selected children

for the cohort monitoring, number of selected individuals for each cross-sectional survey, malaria infection prevalence by RDT in children aged 0.5–14 years, LLIN usage, malaria vaccine coverage among children, SES, the proportion of suitable houses for the ceiling net installation, the mean indoor vectors per household per night.

## Analysis

# Endpoints

# Primary endpoint:

• Overall malaria case incidence in children 6 months-14 years among intervention and control clusters during the 18-month follow-up period.

# Secondary endpoints:

- 1. Malaria infection prevalence at 6, 12, and 18 months post-intervention in all age groups among intervention and control clusters.
- 2. Time to first malaria infections in children 6 months-14 years among intervention and control clusters during the 18-month follow-up period.

# Definition of malaria case incidence

Incidence of clinical malaria in the prospective cohort will be estimated by both active and passive case detections. For active case detection, we will visit the home of cohort participants every two weeks. At each biweekly visit, axillary temperature will be taken from each cohort participant. If the participant has fever (>37.5°C) or any malaria-related symptoms during or within 48 hours of the home visit, the child will be tested by mRDT. A clinical case is defined as positive mRDT accompanied by fever and/or any malaria-related symptoms and will be treated with artemether-lumefantrine (artemisinin-based combination therapy [ACT]). For passive case detection, we ask all cohort participants to visit designated health facilities in case they suspect malaria between home visits.

If two consecutive RDTs are positive, there are two patterns: active case detection or passive case detection for the detection of the second positive. If the second positive RDT is detected by active case detection, we will refer the child to a health facility and regard it as a new malaria infection if subsequent microscopy or PCR confirms parasites after 15 days or more passed from the first RDT test. If not, it is considered a carryover from the previous infection. For the passive case detection of a second RDT positive, we will regard it as a new malaria infection if more than 14 days have passed since the first RDT test.

For the overall incidence rate calculation, the time at the risk will be adjusted by subtracting the 14 days of "protection period" of ACT. If a participant misses a particular visit or a second positive is considered a carryover from the previous infection, the period is not included in the at-risk period.

If the cohort children visit health care facility and get tested for malaria between each visit, both positive and negative results will be utilized for our analysis. Specifically, the 14 days prior to the test result will be incorporated into the denominator of the incidence calculation as the at-risk period. Specific patterns for incidence rate calculation are shown in Figure 3.

If a participant is absent for three consecutive visits or for more than half of all visits, the child will be excluded from the analysis.

# Definition of malaria infection incidence

In addition, we will test all cohort children by RDT and PCR every month. For the secondary outcome of time to first malaria infection and infection incidence, because our focus is only on infection, not symptomatic infection. We therefore use passive case detection differently to the above. If the cohort children visit health care facility because of any symptom and get negative RDT results for malaria, this data point is removed as it does not provide any additional information. If the RDT results in the facility is positive, the passive positive is assigned to either the active visit immediately before or after the passive case detection, whichever is closer in time to the passive case detection.

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#### Analysis methods

We will follow the CONSORT guidelines extended for CRT<sup>3</sup> for the statistical analysis and results reporting.

#### Clinical malaria incidence

We will determine the protective efficacy of Olyset®Plus ceiling nets against malaria case incidence by comparing clinical malaria incidence rates between arms. We will use mixed effects negative binomial regression accounting for within-cluster correlation of responses by following equations:

$$\mu_{k,i} = \exp \left(\beta_0 + \boldsymbol{x}_{k,i}^T \boldsymbol{\beta} + z_k\right)$$
$$z_k \sim N(0,\sigma^2),$$

where  $\mu_{k,i}$  is the mean incidence rate of individual *i* in cluster *k*,  $x_{k,i}$  is the covariate vector including individual and cluster level data,  $z_k$  is the Gaussian-type random effect at the cluster level. The protective efficacy will be estimated by  $(1 - \exp(\hat{\beta})) \times 100\%$ , where  $\hat{\beta}$  is the estimated regression coefficient of the treatment. Possible confounding factors such as age, sex, bed net usage, house structure, and SES will be adjusted as well as the covariates used in the covariate-constrained randomization. In addition, because we will not set a buffer zone, the distance to the nearest household in the other arm will be adjusted as a covariate to reduce the contamination between two arms. The variable was selected from the previous study<sup>4</sup>.

#### Prevalence of malaria infection

The secondary outcome, prevalence of malaria infection by PCR and microscopy measured at 6-, 12-, and 18-months after the ceiling net installation will be analyzed using mixed effects logistic regression adjusting for the above-mentioned confounding factors.

#### Time to first malaria infection

A Cox proportional hazards model and other survival models will be used to compare time to first malaria infection between arms adjusting for the above-mentioned confounding factors. In addition, we will account within-cluster correlation of responses.

Exploratory analysis for spillover effects

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Evidence for positive spillover effects of the ceiling net on malaria infection prevalence of all age group will be assessed by comparing individuals with no intervention conditioning 1) the distance to ceiling net installed household, and 2) the coverage of surrounding households with ceiling net within 400 m (Figure 4). The distance of 400 m was chosen as the spillover effect appears to attenuate at this distance based on previous reports<sup>5</sup>. As there may be a bias that households without a ceiling net in the intervention cluster have different characteristics (e.g. preventive behaviour against malaria), we will include only control clusters for the spillover analysis to ensure comparability.



- d: the distance to the nearest discordant household
- c: the coverage of surrounding households with ceiling net within 400 m Household with ceiling net

Figure 4: The distance to the nearest discordant household and the coverage of treatment.

#### Missing data

We will make substantial effort to avoid having missing values on outcome (malaria infection status and visit dates) by encouraging individual participants and CHPs repeatedly. When missing values occur for an outcome for reasons not related to the outcome, reasons for missingness and the missing fraction by treatment arm and cluster will be reported. Per protocol, the subjects are screened actively on their malaria status (the outcome) every four weeks.

In both cases, all the available data from the subject will be included in the primary and secondary analysis, without employing any specific missing data analysis techniques, due to the ignorability of the missing mechanisms. Missing baseline covariates (individual-level, household-level, and cluster-level) that are a part of the regression models for the outcome of interest will be imputed using simple hot-deck imputation methods if the missing fraction for the covariate is <5%. If the missing fraction for a covariable is  $\geq5\%$ , appropriate multiple imputation approaches will be applied. If a non-ignorable portion

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of the subjects have missing values on a covariate (due to missing at random or missing completely at random), that covariate may be excluded in the model.

#### Additional analysis

We will perform the same analysis for three age subgroups ( $\leq$  59 months old; 5 years old to 14 years old; 15 years old or older) to examine if the effects of Olyset®Plus ceiling net differ by age groups. In addition, we will perform other machine learning based approach such as causal forest and super learner to estimate the conditional average treatment effect.

# Harms

Since the chance of having adverse event due to this intervention is very low based on the preceding study, all the details of unanticipated problems will be narratively reported, if any.

#### Statistical software

For all data handling and analysis, we will use R software version 4.3.2 (R Core Team (2021). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <u>https://www.R-project.org/</u>.)

4.2

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# Evaluation of the protective efficacy of Olyset®Plus ceiling nets for reduction of malaria incidence in children in Homa Bay County, Kenya: a cluster-randomized controlled study protocol

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6 7	2	Evaluation of the protective efficacy of Olyset®Plus ceiling nets for reduction of malaria incidence in
8 9	3	children in Homa Bay County, Kenya: a cluster-randomized controlled study protocol
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31	Abstract
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Introduction: Malaria is still a major health problem in sub-Saharan Africa, where 98% of global malaria mortality occurs. In addition, the spread of *Plasmodium falciparum* with partial artemisinin resistance in East Africa and beyond is a great concern. The establishment of more effective vector control, in addition to the current long-lasting insecticide-treated net (LLIN) distribution program, is an urgent task in these areas. One novel vector control candidate is the pyrethroid-PBO ceiling nets (Olyset®Plus ceiling nets) which can overcome the problems of variations in net use behaviors and metabolic resistance to insecticide in vectors. Our preliminary study suggests the protective efficacy and high acceptability of this tool. With this proposed second trial, we aim to evaluate the impact of this tool in a different eco-epidemiological setting in the lake endemic region of Kenya.

41 Methods: A cluster randomized controlled trial is designed to evaluate the impact of pyrethroid-PBO ceiling 42 nets in Ndhiwa Sub-County, Homa Bay County, Kenya. A total of 44 clusters will be randomly assigned in a 43 1:1 ratio to the intervention group (pyrethroid-PBO ceiling nets) and the control group. The assignment will 44 be accomplished through covariate-constrained randomization of clusters. For the primary outcome of 45 clinical malaria incidence, 38 children from each cluster will be enrolled in a cohort and followed for 18 46 months. We will also evaluate the effects of the intervention on entomological indicators as well as its 47 acceptance by communities and cost-effectiveness.

Ethics and dissemination: Ethics approvals were provided by the Mount Kenya University Institutional Scientific Ethics Review Committee and the Ethics Committee Osaka Metropolitan University. Study results will be shared with study participants and communities, the Homa Bay County Government and the Kenya National Malaria Control Programme. Results will also be disseminated through publications, conferences and workshops to help the development of novel malaria control strategies in other malaria-endemic countries.

54 Trial registration: UMIN000053873

# 56 Keywords

Malaria, *Anopheles* mosquito, vector control, Pyrethroid resistance, Ceiling net, Kenya, Cluster-randomized
 controlled trial

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# Administrative information

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Role of sponsor {5c}	OMU will support project management oversight, trial managem
	data management, statistical analysis, and research governance. N
:	also holds overall authority together with project management an
;	analysis.
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2 3 4	72	
5 6	73	
7 8	74	Strength and limitations of this study
9 10	75	
11 12	76	• This is a second cluster-randomized controlled trial of a novel vector control tool, pyrethroid-PBO
13 14 15	77	ceiling net, to evaluate its efficacy in reducing malaria incidence among children.
16 17	78	
18 19	79	• The implementation of monthly active screening within the prospective cohort population
20 21	80	established in each cluster facilitates the assessment of infection incidence.
22 23	81	
24 25	82	• The incorporation of multidisciplinary outcomes, encompassing social aspects and cost-effectiveness
26 27 28	83	analyses, provides valuable insights for the potential future deployment of this intervention within
20 29 30	84	integrated malaria control strategies.
31 32	85	
33 34	86	• One of the anticipated limitations is the possible contamination between intervention and control
35 36	87	clusters because we will not set a buffer zone due to the geographical proximity among clusters.
37 38	88	
39 40	89	
41 42 42	90	
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1 2	
3 100 4	
5 6 101	Introduction
8 102	Background and rationale {6a}
10 103	Malaria is still a major health problem, particularly in sub-Saharan Africa, where 98% of global malaria
<sup>12</sup> 104	mortality occurs [1]. Although the morbidity and mortality of malaria declined from the 2000s to 2015
<sup>14</sup> 105 15	owing to many investments and interventions, such as long-lasting insecticide-treated nets (LLINs), malaria
16 17 106	rapid diagnostic tests (RDTs), and artemisinin-based combination therapies (ACTs), progress has stalled
18 19 107	since 2015. Moreover, the spread of <i>Plasmodium falciparum</i> partially resistant to ACT in Africa is an
20 21 108	enormous concern. Currently five African countries, Rwanda [2], Uganda [3], Eritrea [4], Ethiopia [5], and
22 23 109	the United Republic of Tanzania [6] have reported delayed clearance of <i>P. falciparum</i> after treatment with
24 25 110 26	ACTs. Kenya's proximity to these countries highlights the urgent need to establish effective vector control,
27 111 28	in addition to maintaining antimalarial drug efficacy and strengthening resistance surveillance.
29 112 30	
<sup>31</sup> 113 32	Among several vector control measures, LLIN is the most widely adopted tool to prevent mosquito bites and
<sup>33</sup> 114 34	interrupt malaria transmission. However, suboptimal uses of LLIN are one of the key factors in reducing the
<sup>35</sup> 36 115	impact of LLIN on the malaria burden, together with insufficient provision in the mass net distribution
<sup>37</sup> 38 116	program or shortening durability of nets [7]. In the Lake Victoria basin, alternative uses of LLIN for fishing
39 40 117	and protecting crops and chicks are well-known local behaviors [8,9] as reported in other endemic areas [10].
41 42 118	In fact, in many areas including our study sites in Homa Bay County, Kenya, malaria prevalence remains
43 44 119 45	high despite widespread distribution of LLINs and their periodic replacements for more than a decade. This
46 120 47	suggests that LLIN alone is insufficient to interrupt malaria transmission in this region.
48 121 49	
<sup>50</sup> 122 51	Recently, we have proposed a novel vector control tool that covers the ceiling and the gap between the
<sup>52</sup> 123 53	ceiling and the walls of residential structures with co-formulated pyrethroid and piperonyl butoxide (PBO)
54 55 124	bed net material, called the Olyset®Plus (Sumitomo Chemical) ceiling net. The benefit of installing the
56 57 125	pyrethroid-PBO ceiling net in addition to conventional LLINs is detailed elsewhere [11]. Briefly, the
58 59 126 60	pyrethroid-PBO ceiling net provides a combination of physical and chemical protection against mosquitoes

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which seek human bloodmeal in the house. Recent reports have demonstrated that a substantial proportion of residual biting exposure occurs between the hours of entering indoor spaces and retiring to bed [12], pyrethroid-PBO ceiling nets may have a significant impact. Furthermore, the ceiling net is semi-permanently installed and requires no further action from end users, thus its protective efficacy is consistently extended to all who stay in the house and less affected by factors such as discomfort or sleeping arrangement that contribute to variations in conventional LLIN use [13]. The concept of ceiling net was previously investigated [14], and in this study, by integrating it with pyrethroid-PBO bed net material, this tool is anticipated to be effective even against pyrethroid-resistant mosquitoes, which are widely reported across Africa.

The aim of this study is to evaluate the efficacy, acceptability, and cost-effectiveness of pyrethroid-PBO 138 ceiling nets on malaria morbidity and transmission in the Lake Victoria basin of Kenya. Preliminary data 139 from our previous study on Mfangano Island in Lake Victoria [11] suggest a substantial reduction in malaria prevalence among school children and high community acceptance of this tool (unpublished data). With this proposed second trial, we aim to evaluate the impact of this tool in a different eco-epidemiological setting with relatively higher malaria transmission, more frequent human and vector movement, and synergistic impact from other interventions such as indoor residual spraying (IRS) and the RTS, S malaria vaccine. Since effective malaria controls need to be tailored to the local context, evidence of the effectiveness of pyrethroid-PBO ceiling nets from various transmission settings will increase the appeal of this intervention. Furthermore, considering the recent increase in choices of malaria control tools and the necessity of 147 combining various tools to maximize the impact of the malaria control program, it is important to understand 148 the acceptability and cost-effectiveness of each intervention to guide its future deployment.

To achieve these objectives, our collaboration with local institutions including the Kenya National Bureau of Statistics (KNBS), the National Malaria Control Programme (NMCP), the Kenya Medical Research Institute (KEMRI), and Homa Bay County, started from the research planning stage. This collaboration is crucial to the seamless transition from field trial to expanded implementation and policy development.

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# 55 **Objectives** {7}

6 The study has four research domains: epidemiology, entomology, social aspects, and cost-effectiveness.

For the epidemiology domain, the primary objective is to determine the protective efficacy of pyrethroid-PBO ceiling net in reducing malaria clinical incidence in children 6 months to 14 years old over 18 months post-intervention. This age range was selected to include both children under five years who are at high risk of malaria-related morbidity and mortality, and the school-age children who have the highest prevalence of *Plasmodium* infections[15]. The secondary objectives are (1) to determine the protective efficacy of pyrethroid-PBO ceiling nets in reducing *Plasmodium* infection prevalence by PCR in all age groups at 6-, 12-, and 18- months post-intervention; (2) to determine the spillover effects of pyrethroid-PBO ceiling nets in reducing *Plasmodium* infection prevalence in all age groups at 6-, 12-, and 18-months post-intervention; and (3) to determine the protective efficacy of pyrethroid-PBO ceiling net in reducing *Plasmodium* infection incidence in children 6 months to 14 years old over 18 months post-intervention.

For the entomology domain, the primary objective is to evaluate the impact of pyrethroid-PBO ceiling nets on the indoor mosquito density of the primary malaria vector species captured by CDC light traps. The secondary objectives are (1) to determine the impact of pyrethroid-PBO ceiling nets on the entomological inoculation rate (EIR) and (2) to determine the prevalence of voltage gated sodium channel (VGSC) mutations in vectors.

For the social aspects domain, the primary objective is to assess the determinants of social acceptability of the pyrethroid-PBO ceiling net in both the intervention and control arms. The secondary objectives are (1) to determine the feasibility of installing the pyrethroid-PBO ceiling nets and (2) to measure attitudes,

emotions, knowledge, and beliefs relating to the ceiling net in Ndhiwa Sub-County.

For the cost-effectiveness domain, the primary objective is to determine the incremental cost effectiveness
ratios (ICERs) of adding the pyrethroid-PBO ceiling net to existing malaria control interventions under field

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trial conditions. The secondary objectives are (1) to establish the relative contribution to costs of the distinct programmatic elements and identify the inputs that contribute the most to overall costs, and (2) to estimate the potential cost of providing pyrethroid-PBO ceiling net at a larger scale over 3 and 5 years under operational scenarios.

# 87 Trial design {8}

The study is an open-label, cluster-randomized controlled trial (CRCT) with 44 clusters evenly divided between the intervention and the control arms. Each cluster will include one or two villages and consist of at least 50 households. A baseline survey will be conducted to determine the pre-intervention *Plasmodium* prevalence and *Anopheles* density, and to collect demographic and socioeconomic data for covariateconstrained randomization of clusters. The baseline survey will be conducted one month before cluster randomization. The post-intervention follow-up period will be 18 months. For the evaluation of the primary objective, 38 children aged 6 months to 14 years from each cluster will be recruited and followed for 18 months as a cohort. Cross-sectional surveys will be conducted after 6, 12, and 18 months of the intervention targeting 50 individuals of all ages from each cluster to estimate the overall *Plasmodium* prevalence.

# 98 Methods: Participants, interventions and outcomes

# 199 Study setting {9}

200 Location and administrative structure

Ndhiwa (713.5 km<sup>2</sup>) is one of nine sub-counties in Homa Bay County in Kenya. The sub-county has seven administrative wards: Kanyamwa Kologi, Kanyamwa Kosewa, Kabuoch North, Kwabwai, Kanyadoto, Kanikela, and Kabuoch South/Pala. Based on the number of malaria cases reported in the Kenya Health Information System (KHIS), the accessibility of the site, and population size, we selected Kanyamwa Kologi Ward as the target area (Figure 1). Agriculture is the primary economic activity, with sugarcane as a main commercial crop. County residents also keep animals such as dairy cattle, beef cattle, sheep, goats, and popultry [16]. The ward experiences a long rainy season from March to June and a short rainy season from October to December. As of 2019, the average monthly precipitation is 228.64 mm and the mean annual temperature is 26.7°C. The relative humidity remains elevated year-round, fluctuating between 75% to 85%

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<sup>2</sup> <sup>3</sup> 210 4	[17].
<sup>5</sup> 211	
<sup>7</sup> 212	Demographics
9 10 <sup>213</sup>	The population of Kanyamwa Kologi Ward is approximately 33,000 according to the 2019 national census
$^{11}_{12}214$	[18]. The dominant ethnic group in the region is Luo and the primary languages are DhoLuo, Kiswahili, and
13 14 215	English. There are 172 primary and 36 secondary schools in Ndhiwa Sub-County [19]. Within Kanyamwa
16 216 17	Kologi Ward, there are 28 primary and 7 secondary schools.
18 217 19	
20 218 21	Malaria epidemiology and control measures
<sup>22</sup> 219 23	Based on the KHIS, there were 429.1 and 457.2 confirmed malaria cases per 1,000 population in Ndhiwa
<sup>24</sup> 220 25	Sub-County and Kanyamwa Kologi Ward, respectively, in 2023. The primary malaria vector in the sub-
<sup>26</sup> 221 27	county is Anopheles funestus, which prefers feeding on humans. Although An. arabiensis exhibits
<sup>28</sup> <sub>29</sub> 222	predominantly zoophilic behavior, it is also a significant malaria vector in our study area [20]. In Homa Bay
<sup>30</sup> 31 223	County, LLINs have been distributed every three years since the early 2000s, and IRS and the RTS, S malaria
32 33 224	vaccine have been piloted in several areas since 2018 and 2019, respectively [21]. Notably PBO-
35 225 36	incorporated LLINs (Veeralin®LN, manufactured by VKA Polymers, Tamil Nadu, India) were distributed in
37 226 38	late 2023. In Kanyamwa Kologi Ward, there is one level four hospital and seven health centers.
39 <u>22</u> 7	
41 228 42	Eligibility criteria {10}
43 229 44	As the ceiling nets are installed per structure, we set the inclusion criteria on a structural basis. The inclusion
45 46 230	criteria for the installation of the ceiling nets are (1) residential structures with at least one permanent
47 48 231	resident aged 18 years or older in the household, (2) informed consent provided by a resident in the
<sup>49</sup> <sub>50</sub> 232	household, and (3) house structure amenable to ceiling net installation in terms of size of the structure,
51 52 233	presence of eave, ceiling board, and vertical beams, and material of the top part of the wall. The applicability
54 234	of the ceiling net installation will be assessed by experienced field staff. The exclusion criteria are (1) vacant
56 235 57	structure, confirmed by at least two visits by community health promoters (CHPs), (2) dwelling structure to
58 236 59	be vacated or destroyed within the study period, (3) non-eligible house structure for the ceiling net
60 237	installation, and (4) non-residential structures (school, shop, kitchen, storage, and toilet). The inclusion

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criteria for the prospective cohort are (1) children aged 6 months to 12 years old at the time of enrolment, (2) living in the study area at the time of pyrethroid-PBO ceiling net installation, (3) having no plan to leave or stay outside the study area for an extended period (longer than one month) over the 18-month follow-up period, and (4) informed consent provided by the participants or the parent or legal guardian. The exclusion criterion is having severe chronic illnesses. The inclusion criteria for cross-sectional malaria surveys for all age groups are (1) living in the study area during the study period, and (2) informed consent being provided by the participants or the parent or legal guardian before each survey. The exclusion criteria are (1) having severe chronic illnesses and (2) pregnancy known at the time of the surveys.

47 Who will take informed consent? {26a}

Written informed consent will be obtained by the study team members who fully understand the study protocol. After eligibility is confirmed, the study team members will present to the potential participant a document containing all relevant information about the study in Luo and English. If the participant cannot read, study information will be conveyed verbally in Luo, Kiswahili, and/or English by the study team members. The potential participant will have opportunities to ask any questions. Agreement to participate will be sought only after the participant indicates complete understanding of the study.

Additional consent provisions for collection and use of participant data and biological specimens {26b} The study information document for ceiling net installation contains the study overview. In addition, the documents for cross-sectional and cohort surveys contain details on collecting, storing, and using personal data and biological specimens during the study.

- 260 Interventions
- **Explanation for the choice of comparators {6b}**

In Kenya, LLIN is the most widely used malaria preventive measure. The Division of National Malaria
Programme coordinates free LLIN distribution, and the county governments deliver LLINs to residents in all
endemic counties every three years. In Homa Bay County, the RTS,S malaria vaccine has been implemented
since 2019. The primary purpose of this trial is to demonstrate the superiority in malaria prevention of

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adding pyrethroid-PBO ceiling nets to the standard malaria control program. Thus, in the control arm, no pyrethroid-PBO ceiling nets will be installed, but LLIN use and RTS,S immunization will be allowed in the control and intervention arms as the current best practice. There is no plan for new LLIN distribution during the study period.

# 271 Intervention description {11a}

In the intervention arm, pyrethroid-PBO ceiling nets will be installed in all dwelling units where residents sleep, free of charge to the households. All participants will be encouraged to continue to use LLINs, distributed by the Homa Bay County government. In each intervention cluster, 1 CHP and 2 community volunteers will be recruited from the intervention cluster and another 1 CHP from the control cluster will join the team to enable future knowledge dissemination. The net installation team will be trained to install ceiling nets by skilled local research assistants who participated in previous trials. The head (or another adult) of the household eligible to a ceiling net will be notified at least 24 hours before the scheduled installation time. The cost of the ceiling nets and their installation will be covered by the research team. Details of the installation procedure are described in the previous study protocol [11]. Briefly, the ceiling net is a rectangular sheet of pyrethroid-PBO net with loops sewn along the diagonal seams. The loops are roped to the support beams under the roof and the edges of the net are stapled to the wall.

# 284 Criteria for discontinuing or modifying allocated interventions {11b}

As the ceiling net is semi-permanently installed, the intervention will only be discontinued if the participant specifically requests the removal of the ceiling net by the study team. There will be no crossover from the control arm to the intervention arm during the follow-up period. Those who migrate between the arms or emigrate from the study areas will be dropped from the study follow-up.

290 Strategies to improve adherence to interventions {11c}

Adherence to the intervention cohort in this study is defined as sleeping in houses with pyrethroid-PBO
 ceiling nets. Adherence is monitored indirectly by assessing the number of nights each participant spends
 outside their house during the monthly interview. During each house visit, CHPs will visually inspect the

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3 294 4	condition of the ceiling nets. Any visible tear and damage to the ceiling net will be reported to the research	
5 295 6	team, who will assess the size and location of the damage and perform repair or replace the ceiling net if	
7 8 296	necessary.	
9 10 297		
11 12 298	Relevant concomitant care permitted or prohibited during the trial {11d}	
13 14 299	There is no specific concomitant care prohibited during the trial. All participants in both arms will continue	
15 16 300	to receive and use free LLIN and have access to standard medical care, including malaria testing by RDT,	
17 18 301	treatment with ACT and RTS,S malaria vaccination.	
19 20 302		
21 22 303	Provisions for post-trial care {30}	
23	Trovisions for post trial cure (co)	
<sup>24</sup> 304 25	All participants will be under the normal healthcare system in the study setting. No perceived health risks for	
<sup>26</sup> 305	the intended population are expected with the intervention. To monitor the long-term impact of the	
<sup>28</sup> <sub>29</sub> 306	intervention, the research team may conduct additional cross-sectional surveys 2 and 3 years post-	
30 31 307	intervention to monitor further parasite transmission in the population.	
32 33 308		
34 35 309	Outcomes {12}	
36 37 310	Epidemiological domain: The primary outcome will be symptomatic malaria case incidence, defined as	
38 39 311	axillary temperature of $\geq$ 37.5°C or a history of fever in the preceding 48 hours, and positive RDT, in	
40 41 312 42	children aged 6 months to 14 years enrolled in the cohort, monitored with a monthly visit and passive case	
<sup>43</sup> 313 44	detection in the health facilities during an 18-month follow-up. The secondary outcomes will be (1) the	
45 46314	prevalence of <i>Plasmodium</i> infections by PCR in all age groups at 6, 12, and 18 months post-intervention, (2)	
47 48 315	the prevalence of <i>Plasmodium</i> infections by PCR among individuals without the ceiling net in all age groups	
49 50 316	at 6, 12, and 18 months post-intervention, and (3) infection incidence by PCR in the prospective cohort of	
51 52 317	children aged 6 months to 14 years over 18 months.	
53 54 318		
55 56 319 57	Entomological domain: The primary outcome will be the density of the primary malaria vectors, species	
58 320 59	composition and sporozoite infection rates. Indoor malaria vector density will be determined using CDC	
60 321	light trap, and species composition and sporozoite infection rates will be determined by microscopy and	

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PCR. The secondary outcomes of the entomology domains will be (1) changes in EIR as a measure of malaria transmission and (2) prevalence of VGSC mutations associated with insecticide resistance in Anopheles mosquitoes captured by light trap.

Social aspect domain: The primary outcome will be the percentage of households consenting to pyrethroid-PBO ceiling net installation when offered. In addition, we will include observations and discussions about individual attitudes toward the ceiling net. The secondary outcomes of the social aspect domain will be the percentage of the intact ceiling net, description of damaged net, and the impact on the living environment such as perceived temperature in the house, dirt/debris trapped by the ceiling net, loss of storage space at the top of the wall, and rewiring of power lines. They will be evaluated by questionnaires at 6, 12, and 18 months post-intervention.

Cost-effectiveness domain: The primary outcome will be the incremental cost-effectiveness of adding pyrethroid-PBO ceiling net to existing malaria control interventions under field trial conditions from the societal and provider perspectives. The secondary outcomes of the cost-effectiveness domains will be (1) the costs of the distinct programmatic elements and the inputs that contribute the most to overall costs, and (2) the cost of providing pyrethroid-PBO ceiling net at a larger scale over three and five years under operational scenarios.

Participant timeline {13}

The schedule of trial activities is presented in Figure 2. The detail of each survey is described in Figure 3.

# Sample size {14}

The sample size was calculated using the method of Hayes and Moulton [22]. All sample sizes will be recalculated based on the baseline data, which will be collected about one month before the ceiling net installation.

- 5 5
- 5
- Epidemiological survey

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The following calculations were based on the historical data collected from the Lake Victoria region in Kenya with a clinical malaria incidence rate of 0.5 per person-year in children under 14 years old by RDT (unpublished data on Mfangano island), 40% parasite prevalence for all age groups by PCR and a betweencluster coefficient of variation (CV) in incidence rate of 0.24 in both groups. In the study site, RTS, S malaria vaccination began in 2019, with a mass distribution of PBO-incorporated LLINs at the end of 2023. Therefore, the intervention effect is expected to be smaller than those in previous studies and is conservatively assumed to be 25%. Assuming 38 individuals per cluster to be followed for up to 18 months with 20 % loss-to-follow up rate, we require 22 clusters per arm, a total of 1,672 children, to achieve 80% power to detect a significant incidence rate ratio of 0.75 (25% protective efficacy) at a two-sided type 1 error of 5%. With 50 individuals per cluster (2,200 total individuals) for the secondary outcome of *Plasmodium* prevalence by PCR in all age groups, we would achieve 5% type 1 error and 80% power to detect 23.5 % relative reduction. We do not specify the sample size for identifying spillover effects because spillovers tend to have smaller effect sizes relative to total or overall effects, so typically larger sample sizes are required to detect them. Although our study may be underpowered to detect spillovers, we will report the results as an exploratory analysis.

Entomological survey

Based on the previous entomological study conducted in Homa Bay County, we assume a mean vector density (number of mosquitoes per CDC light traps) of 3.3, a standard deviation (SD) of 3.3, and CV of 0.192 [14]. For 80% power to detect a 50% decrease in mean mosquito densities at 5% type 1 error level, we need to capture mosquitoes from five houses in each of 44 clusters.

# **Recruitment {15}**

Thirty-eight eligible children in each cluster will be randomly recruited into our cohort. Recruitment will be limited to children aged 12 or younger, to avoid children aging out during the 18-month monitoring period. Study team staff will obtain informed consent from the parents or caregivers of the children before enrolling the children in the cohort. For the cross-sectional survey at each time point, we will randomly select from 60 377 each cluster 50 individuals of all age groups. To guarantee the representativeness for all age groups, the

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3 378 4	selection will be done with following age category stratifications; 0-4, 5-9, 10-14, 15-19, and 20 and above.	
5 379 6		
<sup>7</sup> 380	Assignment of interventions: allocation	
9 10 <sup>381</sup>	Sequence generation {16a}	
11 12 382	Random numbers will be generated using the sample function in R software.	
<sup>13</sup> <sup>14</sup> 383		
16 17 17	Concealment mechanism {16b}	
18 19 385 20	The individual, household, and villages (clusters) are all given unique IDs at the beginning of the baseline.	
21 386 22	Any following steps handle only these anonymized IDs.	
23 387 24		
<sup>25</sup> 388 26	Implementation {16c}	
<sup>27</sup> 389 28	After the baseline survey, covariate-constrained randomization will be used to allocate the 44 clusters across	
<sup>29</sup> 30 390	the two study arms. The following factors will be constrained: baseline malaria infection prevalence by RDT	
<sup>31</sup> 32 391	in children aged 0.5-14 years, LLIN usage, malaria vaccine coverage, socioeconomic status (SES),	
33 34 392	population size, the proportion of eligible houses for the ceiling net installation, and vector densities. An	
35 36 393	independent statistician will perform the randomization. Local study assistants will perform participant	
38 394 39	enrollment.	
40 41 395		
42 43 396	Assignment of interventions: Blinding	
44 45 397	Who will be blinded {17a}	
46 47 398	Due to the visibility of the pyrethroid-PBO ceiling net, neither the trial participants nor the members of the	
48 49 399 50	study team who take part in field activities can be blinded. However, laboratory- and office-based personnel	
51 400 52	(e.g., microscopists, laboratory technicians, and data analysts) will be blinded to the identity and intervention	
53 401 54	status of the trial participants since all biological specimens will be identified by a unique numeric study	
<sup>55</sup> 402 56	identifier, and personal information will be removed before analyses.	
57 58 403		
59 60 404	Procedure for unblinding if needed {17b}	

This is an open-label trial, and only the data measurers are blinded. Therefore, there is no circumstance that

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they need to be unblinded.

6 7 407 8 9 -10<sup>408</sup> **Data collection and management** 11 12 409 Questionnaires for the baseline survey, cohort surveys, and post-intervention cross-sectional surveys are 13 14410 provided in the supplementary file. 15 16411 17 18412 Plans for assessment and collection of outcomes {18a} 19 20 4 1 3 Census and baseline cross-sectional survey 21 22 414 In Kanyamwa Kologi Ward, 85 census enumeration areas (EAs) are defined by the 2019 Kenya Population 23 <sup>24</sup> 415 and Housing Census. Births, deaths, and migrations in each EA are regularly updated by CHPs using the 25 <sup>26</sup> 416 integrated community health system maintained by the Ministry of Health. Fifty EAs are randomly selected <sup>28</sup> 22 417 for our baseline survey, during which demographic information of all individuals is updated. To ensure 30 418 balanced cluster allocation, the baseline survey includes a questionnaire for all households, RDT testing of 31 32 <sub>33</sub> 419 all children aged 6 months to 14 years, and an entomological survey of randomly sampled households. We 34 35 420 modified the questionnaire used in the 2020 Kenya Malaria Indicator Survey (KMIS) mainly to quantify the 36 37 421 SES of each household and bed net usage. In addition, we add questions to quantify the favorability of 38 39 4 2 2 ceiling nets before the intervention. 40 41 423 42 <sup>43</sup> 424 Cohort monitoring 44 <sup>45</sup> 425 Incidence of clinical malaria in the prospective cohort will be estimated by both active and passive case 46 47 426 detections. For active case detection, we will conduct home visits every four weeks. From all cohort 48 49 .) 50 427 participants, axillary temperature will be measured using a digital thermometer, and Plasmodium infection 51 <sub>52</sub> 428 status will be determined by RDT and PCR. Participants with fever (>37.5°C) or other malaria-related 53 54 429 symptoms listed in the Kenya National Malaria Treatment Guideline at the time of home visit or within the 55 56 4 30 previous 48 hours will be tested for malaria by RDT. History of travel, confirmed malaria episode, and visit 57 58 4 3 1 to local health facilities since the previous visit is recorded. For passive case detection, we ask all cohort 59 60 4 3 2 participants to visit designated health facilities in case they suspect malaria between home visits. The

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433 designated facilities are asked to record all malaria tests performed regardless of their results together with 434 the cohort ID. The cost of RDT and anti-malarial treatment will be covered by the research team to 435 encourage cohort participants to use only designated facilities.

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#### 12 437 Cross-sectional malariometric surveys

14 4 38 Malaria prevalence in children and adults will be estimated using cross-sectional malariometric surveys in 16 4 39 communities. These surveys will be conducted at 6, 12, and 18 months post-installation. Community surveys 18 4 4 0 will be conducted by house visits.

20 4 4 1 *Plasmodium* infection status will be determined using three methods: RDT, microscopy, and PCR. A finger-21 22 442 prick blood sample will be collected for on-site diagnosis using the Bioline Malaria Ag P.f/Pan RDT (Abbott 23 <sup>24</sup> 443 Diagnostics Korea Inc., Republic of Korea). Survey participants with positive test results will be provided 25 <sup>26</sup> with a treatment course of artemether-lumefantrine with dosing instructions in accordance with guidelines 27 28 445 from the Ministry of Health in Kenya after checking their recent treatment history. Blood smears will be 29 30 446 prepared on site and transported to the main laboratory in Homa Bay where thin smears are fixed with 31 32 <sub>33</sub> 447 methanol and all smears are stained with 3% Giemsa solution for 30 minutes, then examined by experienced 34 35 448 microscopists. Two blood samples (70 µl each) will be collected with a 75-mm heparinized micro-hematocrit 36 37 449 capillary tube (Thermo Fisher Scientific, MA, USA) and spotted on Whatman ET31 Chr filter paper 38 39 4 5 0 (Whatman International. Maidstone, UK). The blood samples will be allowed to dry at ambient temperature 40 <sup>41</sup> 451 and stored in individual zipped plastic bags at -20°C. The dried blood spots will be used for the determination 42 <sup>43</sup> 452 of malaria status by PCR [23]. 44

**4**8 454 454 Entomological surveys

50 455 Indoor mosquitoes will be collected from five randomly selected houses within each cluster using the CDC <sub>52</sub> 456 light trap method. Samples will be preserved in 96% ethanol and placed in a cool box with ice. Specimens 54 4 57 will be examined for sex determination by microscopy and species identification by microscopy and PCR. 56 4 58 Indoor mosquitoes will be collected at baseline, 6, 12 and 18 months post ceiling net installation.

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60 4 60 Social aspects

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We will conduct an exploratory sequential research design using integrated mixed methods (qualitative and quantitative). Qualitative assessment of community perceptions on the pyrethroid-PBO ceiling nets, community facilitators, and concerns of pyrethroid-PBO ceiling net use will be implemented, followed by quantitative assessments every 6 months and routine monitoring to evaluate the durability of pyrethroid-PBO ceiling nets using observation checklists in randomly sampled houses. At the end of the study, other qualitative case studies, such as focus group discussions and key informant interviews, will be conducted to document any remarks related to the study and inform the sustainability and scalability of the intervention.

Cost-effectiveness analysis

Incremental financial and economic cost data of pyrethroid-PBO ceiling net will be collected alongside the intervention. In cases where resources, such as staff, are shared among multiple elements, the allocation of costs will be carried out using an appropriate proxy. Costs related to research activities will be excluded from this allocation. Financial costs will be derived from project expenditure records, while economic costs, which encompass financial expenditures and donated resources, will be identified through project records and social aspects activities. The value of donated resources will be credited based on prevailing market rates. Furthermore, capital costs will be annualized over their useful life for financial costing and annualized at a discount rate of 3% for economic costing.

Plans to promote participant retention and complete follow-up {18b}

All surveys planned for the epidemiological and entomological domains will be conducted by house visits. CHPs will make an appointment with eligible participants before each visit to confirm the participants' 482 available date and time. Small remunerations will be provided to survey participants to compensate for their time. CHPs will receive detailed instructions and participatory training for all field procedures and will be actively supervised by the research team throughout the duration of the study. Feedback will be regularly sought from CHPs regarding any issues raised by study participants, and discussions will be held to resolve issues from the field.

- Data management {19}
All data from the baseline, cohort, and cross-sectional surveys will be captured using the Research Electronic Data Capture (REDCap) software on electronic tablets. Data will be uploaded daily to a highly secure server hosted by Mount Kenya University (MKU). All data from the quantitative surveys will also be stored securely and backed up regularly to prevent data loss. Data access and management of databases will be limited to authorized study investigators and collaborators. After validation of data uploaded to the MKU server, data stored locally on the tablet computers will be permanently deleted to minimize unauthorized access.

**Confidentiality {27}** 

To maintain confidentiality, each participant in cross-sectional surveys, the longitudinal cohort, and the quantitative surveys is assigned a unique identifier. The data collected will be labelled using the unique identifier and stored separately from the key linking personal information (name, date of birth, GPS of each household, and phone number). The data will be kept on a secure server that is only accessible to the research staff. Publications will contain only aggregated data, and no personal information will be included.

## Plans for collection, laboratory evaluation and storage of biological specimens for genetic or molecular analysis in this trial/future use {33}

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Anonymized blood samples from study participants will be stored and analyzed for Plasmodium infections by microscopy and PCR in our laboratory in Homa Bay. Microscopic examinations of adult mosquito specimens will be conducted in our field laboratory in Mbita, while PCR analyses will be conducted in our 509 laboratories in Homa Bay and MKU. Laboratory data outputs will be entered in Microsoft Excel and imported into the database. No human genetic analysis is planned for this study. However, remaining biological materials will be stored indefinitely for future studies unless the participants opt out during the informed consent process. Participants are provided with contact information of the research team and can remove themselves from this study or any future studies at any time without penalty or prejudice.

- 58 515 Statistical methods

#### 60 5 1 6 Statistical methods for primary and secondary outcomes {20a}

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We will follow the CONSORT guidelines extended for CRCT for statistical analysis and result reporting. The intention-to-treat (ITT) analysis is the primary analysis approach for both the primary and secondary objectives for the epidemiological and entomological studies. The per-protocol (PP) analysis is included as a supplementary analysis for the primary and secondary objectives for the epidemiological and entomological studies. Detailed methodologies for the epidemiological part are described in the supplementary file of statistical analysis plan.

#### Clinical malaria incidence

We will determine the protective efficacy of pyrethroid-PBO ceiling nets against malaria case incidence by comparing clinical malaria incidence rates between arms. We will use mixed effects negative binomial regression accounting for within-cluster correlation of outcomes. Possible confounding factors such as age, sex, bed net usage, house structure, malaria vaccination history, and SES will be adjusted as well as covariates used in the covariate-constrained randomization. In addition, because we will not set a buffer zone, the distance to the nearest household in the other arm will be adjusted in the following analysis to reduce the contamination between two arms. The variable was selected from the previous study [24].

Prevalence of malaria infection

The secondary outcome, the prevalence of malaria infection by PCR and microscopy measured at 6, 12, and 18 months after the ceiling net installation will be analyzed using mixed effects logistic regression adjusting for the above-mentioned confounding factors.

Exploratory analysis for spillover effects

Evidence for positive spillover effects of the ceiling net on malaria infection prevalence in all age groups will be assessed by comparing individuals with no intervention conditioning 1) the distance to the nearest ceiling net installed household, and 2) the coverage of surrounding households with ceiling net within 400 m. The distance of 400 m was chosen as the spillover effect appears to attenuate at this distance based on previous reports [25].

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#### 545 Entomology

546 Differences in vector density and EIR between arms will be evaluated by random effects negative binomial 547 regression taking into account the intracluster correlation.

#### 549 Social aspects

We will employ the Framework for Reporting Adaptations and Modifications to Evidence-based Implementation Strategies (FRAME-IS) [26] to document the implementation processes of the ceiling nets, and the evidence integration triangle framework [27] to align the evidence generated to policy and vector control strategies from the health systems aspect. The theoretical framework in qualitative research will be grounded theory [28]. Data from ethnographic, focus group discussions, key informant interview will be summarized using content thematic analysis. Pre- and post-intervention acceptability to install pyrethroid-PBO ceiling net intervention will be compared to actual consent using logistic regressions.

#### 58 Cost-effectiveness

The economic and financial costs associated with the pyrethroid-PBO ceiling net intervention will be presented in total and disaggregated forms, highlighting the relative contribution of each program element to the overall program costs. To facilitate comparisons with other malaria vector control interventions, the costs will be converted into cost per household and per person receiving the intervention annually. Various program scenarios, such as different scales and durations, will be presented to estimate operational implementation costs. Compared to the control group, we will utilize the number of malaria cases averted in the pyrethroid-PBO ceiling net arm to calculate the DALYs averted using standard methods. Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

#### 567 Interim analyses {21b}

No interim analysis is planned because neither the insecticide permethrin nor the synergist PBO as
formulated in pyrethroid-PBO LLINs is known to pose significant health and safety risks [11,14].

#### <sup>8</sup> 571 Methods for additional analyses (e.g. subgroup analyses) {20b}

<sup>50</sup> 572 We will perform the same analysis for three age subgroups ( $\leq$  59 months old; 5 years old to 14 years old; 15

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years old or older) to examine if the effects of pyrethroid-PBO ceiling net differ by age groups. In addition, we plan to use other machine learning methods to estimate the conditional average treatment effect (CATE), such as causal forests—which extend random forest algorithms for causal inference [29] —and the super learner algorithm, an ensemble method that combines multiple predictive models to improve accuracy [30].

## Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing

data {20c}

In the cohort, non-adherence to the intervention can be identified by monthly interviews. Participants who regularly sleep outside their homes will be removed from the analyses. The extent and patterns of missing data will be assessed once all data collection has been completed. If necessary, we will apply simple hotdeck imputation methods if the missing fraction for the covariate is <5% or appropriate multiple imputation approaches if the missing fraction for a covariable are  $\geq 5\%$ . If a non-ignorable portion of the subjects have missing values on a covariate (due to missing at random or missing completely at random), that covariate may be excluded in the model.

#### Plans to give access to the full protocol, participant level-data and statistical code {31c}

This manuscript is the full protocol. The corresponding author will make the de-identified datasets or any future statistical code available upon reasonable request.

**Oversight and monitoring** 

#### Composition of the coordinating centre and trial steering committee {5d}

The sampling team, composed of CHPs and laboratory technicians, set up a day-to-day communication group and exchanged their experiences. A local management team of study investigators from Kenya and Japan also joined this, leading and advising the activities and monitoring the sample and data integrity. A monthly meeting will be held by the steering committee composed of all key researchers from Kenya and Japan, including the principal investigator (PI) and co-PI, to monitor the progress of the trial.

Composition of the data monitoring committee, its role and reporting structure {21a}

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Our intervention is considered to be of a low-risk nature. The data safety monitoring committee will consist of two medical doctors who are independent from the project organizations and sponsor and have no competing interests. The primary responsibilities of this committee will be to periodically review selfreported adverse events derived from the monthly questionnaire in the cohort. All severe adverse events observed or reported during the study will be reported to the committee in a timely manner, and the committee will determine the relationship between the severe adverse events and the intervention. For additional credibility about study quality, the researchers will consult a third statistician, if necessary.

Adverse event reporting and harms {22}

In addition to the safety monitoring committee, researchers will compare self-reported non-serious adverse events such as coughs, rashes, and itches between the intervention and the control arms in the cohort and cross-sectional surveys. In the event of a study-related serious adverse event, the study team will convene a meeting immediately with the MOH and Homa Bay County Teaching and Referral Hospital representatives to review the case and take necessary action.

#### Frequency and plans for auditing trial conduct {23}

A monthly meeting will be held during the follow-up period to ensure that all surveys and investigations are conducted according to the study protocol. The study is required to submit annual reports and renewal to ethical review boards of Osaka Metropolitan University, Japan, and Mount Kenya University, Kenya.

Plans for communicating important protocol amendments to relevant parties (e.g. trial participants, ethical committees) {25}

Decisions on important trial amendments must be made through a formal procedure and will be approved by

institutional review boards (IRB) at Mount Kenya University and Osaka Metropolitan University. The

protocol in the clinical trials registry will also be updated accordingly.

#### 58 627 **Dissemination plans {31a}**

60 628 Study results will be shared with the study participants and communities, the Homa Bay County Government

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and the Kenya National Malaria Control Programme. Results will also be disseminated through publications,
 conferences and workshops to help the development of novel malaria control strategies in other malaria endemic countries. Suggestions from the participants will also help shape the future improvement of the
 intervention.

#### 34 Discussion

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Global malaria progress has flatlined in recent years: targets of reductions in malaria morbidity and mortality and required funding by 2030 are all off track as of 2023[6]. In addition, *P. falciparum* with partial artemisinin resistance, which has been a problem in the Great Mekong Subregion (GMS) for more than a decade, is emerging independently in sub-Saharan Africa [2–6,31]. Novel interventions that are costeffective and widely accepted by local communities are urgently needed to contain the spread of artemisininresistant *P. falciparum* in sub-Saharan Africa.

Early results from our cluster randomized controlled trial of pyrethroid-PBO ceiling nets on Mfangano Island in Lake Victoria, Kenya suggest that ceiling nets can reduce *Plasmodium* prevalence and are positively received by the local communities. Nevertheless, there are regional differences in housing design, vector abundance and composition, and availability of malaria control interventions. As such the feasibility and acceptability of the ceiling net intervention are likely to depend on local eco-epidemiological context [32]. Furthermore, one of the secondary objectives in this study is to measure the spillover effects, i.e. how much a household that does not have a ceiling net benefits from living near a house with a ceiling net. This enables a broader understanding of the impact of the ceiling nets at the community level.

This trial has several limitations. First, although the study is designed as a cluster-randomized controlled 51 <sub>52</sub> 652 trial, contamination between intervention and control clusters cannot be excluded, as buffer zones between 53 54 653 intervention and control clusters cannot be created due to geographic proximity of houses and villages in the 55 56 654 ward. A recent study, however, has shown that the spillover effect of interventions on malaria can extend to 57 58 6 5 5 3 km [33], so buffer zones of a few hundred meters, as set out in many studies, may not be sufficient. We 59 60 6 5 6 will try to eliminate such contamination effects by integrating spatial data into our statistical model. Second,

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because of the visible nature of the ceiling net, we cannot exclude open-label and observer biases. It is conceivable that participants receiving ceiling nets may reduce their usage of conventional LLIN, as both interventions are made of the same materials and may be perceived to protect against malaria in the same manner. We aim to reduce such bias as much as possible through repeated reminders by CHPs that ceiling nets serve as an addition to and not a replacement of conventional LLINs. We will conduct surveys and indepth interviews to elicit participants' perceptions of the ceiling net, which can guide future messaging and implementation. To reduce observer bias, laboratory investigators and data analysts will be blinded. Third, in the study area, pyrethroid+PBO-incorporated LLINs were distributed in 2023. It may reduce the effect of our ceiling net intervention because pyrethroid+PBO-incorporated LLINs are more effective than non-PBOincorporated LLINs by targeting both Anopheles vectors with and without metabolic resistance to pyrethroids. Pyrethroid+PBO incorporated LLINs received a conditional endorsement from the World Health Organization (WHO) in 2017, and approximately half of the LLINs distributed in sub-Saharan Africa in 2022 were of this type [6]. Given the abundance of PBO-incorporated LLINs in the region, it is important to assess the effectiveness of the pyrethroid-PBO ceiling net as an addition to these LLINs to inform policy recommendations. Recently LLINs combining two different classes of insecticides have been shown to be superior to pyrethroid-based LLINs [34]. When these new LLINs become widely available, the effectiveness of pyrethroid-PBO ceiling nets needs to be re-investigated.

#### 675 Trial status

The Baseline survey was started on April 8, 2024. The recruitment of the intervention participants and the
ceiling net installation were conducted in June 2024. The current protocol is version 6.0 as of November 11,
2024.

#### 2 680 Abbreviations

4 681 ACT: artemisinin-based combination therapy

<sup>6</sup>,682 CHP: community health promoter

683 CRCT: cluster-randomized controlled trial

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3 684 4	CV: coefficient of variation
<sup>5</sup> 685 6	KHIS: Kenya Health Information System
7 8 686	ITN: insecticide treated nets
9 10 <sup>687</sup>	IRS: indoor residual spraying
11 12 688	LLIN: long-lasting insecticidal nets
13 14 689 15	MKU: Mount Kenya University
16 690 17	PBO: piperonyl butoxide
18 691 19	RDT: rapid diagnosis tests
20 692 21	VGSC: Voltage gated sodium channel
22 22 693	
23 09 5	
25 694 26	Declarations
27 695 28	Acknowledgements
29 696 30	We would like to express our sincere gratitude to this study's participants, field, and laboratory staff. In
31 697 32 33 608	addition, we acknowledge the collaboration and support of health offices in Homa Bay County, Kenya.
34 34	
<sup>35</sup> 699 36	Authors' contributions {31b}
<sup>37</sup> 700	AK and JG are co-principal investigators. AK is the guarantor. YKK, WK, and AK developed the original
<sup>39</sup> 40 701	concept. All authors discussed and contributed to the study protocol. YKK, WK, PO, KBM, JK, VO, JO,
41 42 702	SMM, KNBS, KK, ES, GO, and AK contributed the preparation of the baseline survey. YKK, WK, PO, BM,
44 703 45	TO, CWC, JK, SM, and MK drafted the manuscript. YKK, WK, CWC, MK, GO, and JG contributed to the
46 704 47	revisions of the draft of the manuscript. DY participated as a senior statistician. YKK and MK drafted the
48 705 49	statistical analysis plan (SAP) and WK, CWC, and DY revised. The authors read and approved the final
50 706 51	manuscript and SAP.
52 707 53	
<sup>54</sup> 708 55	Funding {4}
<sup>56</sup> 709 57	AK and JG received support from JICA/AMED joint research project (SATREPS) (Grant no.
<sup>58</sup> 710 59 70	20JM0110020H0002), Hitachi Fund Support for Research Related to Infectious Diseases, and Sumitomo

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3 711 4	Chemical Corporation. The funding bodies play no role in the study design, data collection, analysis,
5 712 6	interpretation, and publication.
7 713	
9 10 <sup>714</sup>	Availability of data and materials {29}
11 12 12 12	The study regimes, consent forms, assent forms, and study-related materials are accessible from the
13 14 716	corresponding author. The final trial dataset will be available to all investigators. The corresponding author
16 717 17	will make the de-identified datasets and source codes for all analysis available upon reasonable request.
18 718 19	
20 719 21	Patient and public involvement
22 720 23	Although the study design was developed through discussions among the researchers, consultations with the
<sup>24</sup> 721 25	local population were conducted prior to initiating the baseline survey, and their input was incorporated into
<sup>26</sup> 722 27	the study. Community involvement will also be ongoing during the implementation of interventions and
<sup>20</sup> <sub>29</sub> 723	research activities.
31 724	
33 725 34	Ethics approval and consent to participate {24}
35 726 36	Ethics approvals were received from Mount Kenya University Institutional Scientific Ethics Review
37 727 38	Committee (MKU-ISERC) (approval number: 2565) and the Ethics Committee in Osaka Metropolitan
37 727 38 39 728 40	Committee (MKU-ISERC) (approval number: 2565) and the Ethics Committee in Osaka Metropolitan University (approval number: 2024-068).
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Evaluation of the protective efficacy of Olyset®Plus ceiling nets for reduction of malaria incidence children in Homa Bay County, Kenya: statistical analysis plan for clinical and epidemiological outcomes

#### Version 6.0

Nov 1, 2024 prepared by Yura K Ko (yongra.ko@ki.se)

#### **SAP** revisions

Version	Date	Summary of Changes
1.0	Jan 23, 2024	First draft
2.0	Feb 5, 2024	Added more details based on collaborators' feedback
3.0	Mar 4, 2024	Revised by the senior statistician (Dr. Daisuke Yoneoka)
4.0	April 9, 2024	Revised based on collaborators' feedback
5.0	Jun 4, 2024	Changed the cohort monitoring interval to one month due to
		feasibility after discussion with CHPs and local research staff.
6.0	Nov 1, 2024	1) Removed the secondary objective of time-to-first infection
		because it is impossible to ascertain the outcome without initial
		parasite clearance at enrollment.
		2) Modified the definition of infection incidence based on the
		journal reviewer's comments.
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#### Introduction

Objectives

#### Primary objective:

• To determine the protective efficacy of pyrethroid-PBO (Olyset®Plus) ceiling nets in reducing malaria case incidence in children 6 months-14 years for 18 months post-intervention

#### Secondary objectives:

- 1. To determine the protective efficacy of pyrethroid-PBO ceiling nets in reducing malaria infection prevalence in all age groups at 6-, 12-, and 18-months post-intervention
- 2. To determine the spillover effects of pyrethroid-PBO ceiling nets in reducing malaria infection prevalence in all age groups at 6-, 12-, and 18-months post-intervention
- 3. To determine the protective efficacy of pyrethroid-PBO ceiling net in reducing malaria infection incidence in children 6 months to 14 years old over 18 months post-intervention.

#### Study Methods

#### Trial design

The study is a cluster-randomized controlled trial (CRCT) with 44 clusters evenly divided between the intervention and the control arms. Each cluster will be one or two villages consisting of at least 50 households. A baseline survey will be conducted to determine pre-intervention *Plasmodium* prevalence and to collect demographic and socioeconomic data for covariate-constrained randomization of clusters. The baseline survey will be conducted approximately one month before randomization. The post-intervention follow-up period will be 18 months. Thirty-eight children aged 6 months to 14 years from each cluster will be recruited and followed for 18 months as a cohort to determine the protective efficacy of the pyrethroid-PBO ceiling net on clinical malaria incidence (primary objective) and *Plasmodium* infection incidence (secondary objectives). Cross-sectional surveys will be conducted at 6, 12, and 18 months post-intervention targeting 50 individuals of all ages from each cluster to determine the overall *Plasmodium* prevalence and to estimate the spillover effect (secondary objectives).

#### Randomization

After the baseline survey, covariate-constrained randomization will be used to allocate the 44 clusters across the two study arms. Covariate-constrained allocation ensures that the arms are balanced overall by excluding allocations where predetermined factors are not balanced within set margins. The following factors will be constrained: baseline malaria infection prevalence by RDT in children aged 0.5–14 years, LLIN usage, malaria vaccine coverage, socioeconomic status (SES), population size, the proportion of eligible houses for the ceiling net installation, and vector densities.

For the proportions of interest, we require the average difference between the arms of no more than 10% for the means of interest, and we require the difference in means to be no more than a quarter of the standard deviation of the variable among individuals in the population. After enumerating the allocations that fulfil the criteria, we may relax or tighten up the balance criteria when the allocated number is too small or very large. One allocation will be selected randomly among all possible allocations meeting the balancing constraints. Data on any additional potentially confounding ecological factors not included in the covariate-constrained randomization will be collected and adjusted for in the analysis. An independent statistician will perform the randomization.

#### Sample size

The sample size was calculated using the method of Hayes and Moulton<sup>1</sup>. All sample sizes will be recalculated based on the baseline data, which will be collected before the ceiling net installation.

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The following calculations were based on the historical data collected from the same Lake Victoria region in Kenya with a clinical malaria incidence rate of 0.5 per person-year for children under 14 years old by RDT (personal communication), 40% parasite prevalence for all age groups by PCR, and a betweencluster coefficient of variation (CV) of incidence rate = 0.24 in both arms. In the study site, RTS, S vaccination began in 2019, with an additional mass distribution of pyrethroid-PBO LLINs at the end of 2023. Therefore, the intervention effect is expected to be smaller than in previous studies and was conservatively assumed to be 25%. Assuming 38 individuals per cluster to be followed for up to 18 months with 20 % loss-to-follow up rate, we require 22 clusters per arm to achieve 80% power to detect a significant incidence rate ratio of 0.75 (25% protective efficacy) at a two-sided type 1 error of 5%. With 44 clusters and 50 individuals per cluster, for the outcome of *Plasmodium* prevalence by PCR, we would achieve 80% power to detect a 23.5 % relative reduction. We do not specify the sample size for identifying spillover effects because spillovers tend to have smaller effect sizes relative to total or overall effects, so typically larger sample sizes are required to detect them. Although our study may be underpowered to detect spillovers, we will report the results as an exploratory analysis.

#### Framework

Our null hypothesis for the primary outcome is that pyrethroid-PBO ceiling nets + standard malaria treatment and prevention measures do not reduce the clinical malaria incidence compared to standard malaria treatment and prevention measures in children 6 months to 14 years at 18 months post-intervention.

#### Statistical interim analyses and stopping guidance

Neither the ceiling nets nor synergist PBO are known to pose significant health and safety risks. This has also been demonstrated in our previous CRT on Mfangano Island<sup>2</sup>. Therefore, no interim analysis is planned.

#### Timing of final analysis

We will conduct the final analysis after 18 months of follow-up. Results will immediately be submitted for publication in peer-reviewed journals.

Timing of outcome assessments



Figure1: Timetable of trial activities

#### Statistical Principles

#### Confidence intervals and P values

We will use a two-sided significance level of  $\alpha = 0.05$  for hypothesis testing. All statistical tests will be conducted at this predetermined level of significance unless otherwise specified. For each estimated parameter, 95% confidence intervals will be calculated and reported.

#### Adherence and protocol deviations

Since the intervention (ceiling net) will be installed in trial participants' houses, participants not sleeping in their own houses will not benefit from the intervention. In the cohort, non-adherence to the intervention can be inferred from travel history during monthly interviews. Therefore, participants who regularly sleep outside their homes will be removed from the analyses. In addition, if a cohort participant is absent for three consecutive visits or for more than half of all visits, the child will be excluded from the analysis. Other protocol deviations will be carefully documented and categorized during the study.

#### Analysis populations

The intention to treat (ITT) analysis is the primary analysis approach for both the primary and secondary objectives. The per-protocol (PP) analysis is included as a supplementary analysis for the primary and secondary objectives.

# So So th

Trial population

#### Screening data

Screening data will be collected during the cohort enrollment and each cross-sectional survey to assess the eligibility of potential participants. This information will include demographic characteristics such as age, sex, SES, and other relevant parameters outlined in the study protocol.

#### Eligibility

The inclusion criteria for the installation of the pyrethroid-PBO ceiling net are (1) residential structures housing at least one permanent resident aged 18 years or older in the household, (2) informed consent provided by at least one adult in the household and (3) applicable house structure for the ceiling net in terms of size of the structure, presence of eave, ceiling board, and vertical beams, and material of the top part of the wall. The applicability of the ceiling net installation will be assessed by experienced field staff. The exclusion criteria are (1) vacant dwelling structure (confirmed by at least two visits by CHPs), (2) dwelling structure to be vacated or destroyed within the study period and (3) non-eligible house structure for the ceiling net installation.

The inclusion criteria for prospective cohorts of children aged 6 months to 14 years old are (1) living in the study area at the time of pyrethroid-PBO ceiling net installation, (2) having no plan to leave or stay outside the study area for an extended period (longer than 1 month) over the 18-month follow-up period, and (3) informed consent provided by the participant's parent or guardian. The exclusion criterion is having severe chronic illnesses.

The inclusion criteria for cross-sectional malaria surveys for all age groups are (1) living in the study area during the study period, and (2) informed consent being provided by the parent or legal guardian before each survey. The exclusion criterion is having severe chronic illnesses.

#### Recruitment

For the baseline survey, we will randomly choose 50 enumeration areas (comprising one or two villages) in Kanyamwa Kologi Ward, Ndhiwa Sub-County. The survey includes a questionnaire for all households, mRDT testing of all children aged 6 months to 14 years. We will not create buffer zones to minimize contamination since a buffer zone of 400–600 m from the boundary will greatly reduce the number of houses in the core area available for analysis in many clusters. Thirty-eight eligible children will be randomly recruited into our cohort in each cluster. Recruitment will be limited to children aged 12 or younger, to prevent children from aging out during the 18 months monitoring period. For the cross-sectional survey at each time point, we will randomly select 50 individuals of all age groups from each

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cluster. To reflect the age structure of the populations, the selection will be done with age category stratifications.

#### Withdrawal/follow-up

Those who migrate between the arms or emigrate from the study areas, or those who dismount the ceiling net from their house structure will be dropped from the intervention. For the cohort, those who are absent for three consecutive visits or for more than half of all visits will be excluded from the analysis as lost to follow-up. A summary of study participant selection is shown in Figure 2.





#### **Baseline characteristics**

We will report a list of baseline characteristics of the intervention and control arms. The list will include population, mean number of people per household, median age of population, number of selected children

for the cohort monitoring, number of selected individuals for each cross-sectional survey, malaria infection prevalence by RDT in children aged 0.5–14 years, LLIN usage, malaria vaccine coverage among children, SES, the proportion of suitable houses for the ceiling net installation, the mean indoor vectors per household per night.

#### Analysis

#### Endpoints

#### Primary endpoint:

• Overall malaria case incidence in children 6 months-14 years among intervention and control clusters during the 18-month follow-up period.

#### Secondary endpoints:

- 1. Malaria infection prevalence by PCR at 6, 12, and 18 months post-intervention in all age groups among intervention and control clusters.
- Malaria infection incidence by PCR in children 6 months-14 years among intervention and control clusters during the 18-month follow-up period.

#### Definition of malaria case incidence

Incidence of clinical malaria in the prospective cohort will be estimated by both active and passive case detections. For active case detection, we will visit the home of cohort participants every month. At each monthly visit, axillary temperature will be taken from each cohort participant. A clinical case is defined as positive mRDT accompanied by fever (>37.5°C) or any malaria-related symptoms during or within 48 hours of the home visit. All participants with positive mRDT will be treated with artemether-lumefantrine (artemisinin-based combination therapy [ACT]). For passive case detection, we ask all cohort participants to visit designated health facilities in case they suspect malaria between home visits. If two consecutive RDTs are positive, there are two patterns: active case detection or passive case detection for the detection of the second positive. If the second positive RDT is detected by active case detection, we will refer the child to a health facility and regard it as a new malaria infection if subsequent microscopy or PCR confirms parasites after 15 days or more passive case detection of a second RDT positive, we will regard it as a new malaria infection if as a new malaria the first RDT test. If not, it is considered a carryover from the previous infection. For the passive case detection of a second RDT positive, we will regard it as a new malaria infection if subsequent test.

For the overall incidence rate calculation, the time at the risk will be adjusted by subtracting the 14 days

of "protection period" of ACT. If a participant misses a particular visit or a second positive is considered a carryover from the previous infection, the period is not included in the at-risk period.

If the cohort children visit health care facility and get tested for malaria between each visit, both positive and negative results will be utilized for our analysis. Specifically, the 14 days prior to the test result will be incorporated into the denominator of the incidence calculation as the at-risk period. Specific patterns for incidence rate calculation are shown in Figure 3.

If a participant is absent for three consecutive visits or for more than half of all visits, the child will be excluded from the analysis.

#### Definition of malaria infection incidence

In addition, we will test all cohort children by PCR every month. For the secondary outcome, the infection incidence is defined as the total number of monthly PCR-positive tests per individual divided by the total number of tests conducted per individual per time period, as described in Bennett et al<sup>3</sup>. If two consecutive PCR results are positive, the second positive result will be removed only if no treatment was provided in the previous month. Furthermore, as a supplementary analysis, we will include passively detected cases in the infection incidence counts to capture any new infections after the passive case treatment by each health center. Passively detected positives will be assigned to the closest active visit–either the one immediately before or after the passive case detection–depending on which is closer in time.

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#### **BMJ** Open

#### Analysis methods

We will follow the CONSORT guidelines extended for CRT<sup>4</sup> for the statistical analysis and results reporting.

#### Clinical malaria incidence

We will determine the protective efficacy of pyrethroid-PBO ceiling nets against malaria case incidence by comparing clinical malaria incidence rates between arms. We will use mixed effects negative binomial regression accounting for within-cluster correlation of responses by following equations:

$$\mu_{k,i} = \exp \left(\beta_0 + \boldsymbol{x}_{k,i}^T \boldsymbol{\beta} + z_k\right),$$
$$z_k \sim N(0,\sigma^2),$$

where  $\mu_{k,i}$  is the mean incidence rate of individual *i* in cluster *k*,  $x_{k,i}$  is the covariate vector including individual and cluster level data,  $z_k$  is the Gaussian-type random effect at the cluster level. The protective efficacy will be estimated by  $(1 - \exp(\hat{\beta})) \times 100\%$ , where  $\hat{\beta}$  is the estimated regression coefficient of the treatment. Possible confounding factors such as age, sex, bed net usage, house structure, and SES will be adjusted as well as the covariates used in the covariate-constrained randomization. In addition, because we will not set a buffer zone, the distance to the nearest household in the other arm will be adjusted as a covariate to reduce the contamination between two arms. The variable was selected from the previous study<sup>5</sup>.

#### Prevalence of malaria infection

The secondary outcome, prevalence of malaria infection by PCR and microscopy measured at 6-, 12-, and 18-months after the ceiling net installation will be analyzed using mixed effects logistic regression adjusting for the above-mentioned confounding factors.

#### Exploratory analysis for spillover effects

Evidence for positive spillover effects of the ceiling net on malaria infection prevalence of all age group will be assessed by comparing individuals with no intervention conditioning 1) the distance to ceiling net installed household, and 2) the coverage of surrounding households with ceiling net within 400 m (Figure 4). The distance of 400 m was chosen as the spillover effect appears to attenuate at this distance based on previous reports<sup>6</sup>. As there may be a bias that households without a ceiling net in the intervention cluster have different characteristics (e.g. preventive behaviour against malaria), we will include only control clusters for the spillover analysis to ensure comparability.

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- 🚹 : Household with ceiling net
- : Household without ceiling net

*d*: the distance to the nearest discordant household *c*: the coverage of surrounding households with ceiling net within 400 m Household with ceiling net

Figure 4: The distance to the nearest discordant household and the coverage of treatment.

#### Missing data

We will make substantial effort to avoid having missing values on outcome (malaria infection status and visit dates) by encouraging individual participants and CHPs repeatedly. When missing values occur for an outcome for reasons not related to the outcome, reasons for missingness and the missing fraction by treatment arm and cluster will be reported. Per protocol, the subjects are screened actively on their malaria status (the outcome) every four weeks.

In both cases, all the available data from the subject will be included in the primary and secondary analysis, without employing any specific missing data analysis techniques, due to the ignorability of the missing mechanisms. Missing baseline covariates (individual-level, household-level, and cluster-level) that are a part of the regression models for the outcome of interest will be imputed using simple hot-deck imputation methods if the missing fraction for the covariate is <5%. If the missing fraction for a covariable is  $\geq5\%$ , appropriate multiple imputation approaches will be applied. If a non-ignorable portion of the subjects have missing values on a covariate (due to missing at random or missing completely at random), that covariate may be excluded in the model.

#### Additional analysis

We will perform the same analysis for three age subgroups ( $\leq$  59 months old; 5 years old to 14 years old; 15 years old or older) to examine if the effects of pyrethroid-PBO ceiling net differ by age groups. In addition, we will perform other machine learning based approach such as causal forest and super learner to estimate the conditional average treatment effect.

#### Harms

All unanticipated problems will be reported to the research team and Homa Bay County Ministry of Health (MOH) through CHPs. Medical officers from Homa Bay County will assess the relatedness of the reported events to the study and report to the research team, including the PI. In the event of a study-related serious adverse event, the study team will convene a meeting immediately with the MOH and Homa Bay County Teaching and Referral Hospital representatives to review the case and take necessary action. Also, the ceiling net is made of the same materials and chemicals as LLIN already on the market, and is therefore not expected to have significant environmental impact.

#### Statistical software

For all data handling and analysis, we will use R software version 4.3.2 (R Core Team (2021). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <u>https://www.R-project.org/.</u>)

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- Campbell, M. K., Piaggio, G., Elbourne, D. R. & Altman, D. G. Consort 2010 statement: extension to cluster randomised trials. *BMJ* 345, (2012).
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# 0. Consent form

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Thank you!	
Please make sure to show the consent form on the tablet.	
I have read the information about the study and have received answers to any questions I asked. I consent to take part in all the activities mentioned above.	<ul><li>○ Yes</li><li>○ No</li></ul>
Name of participant	
Signature of participant	
Name of witness	
Signature of witness	
Do you have a child to participate in the study?	<ul><li>○ Yes</li><li>○ No</li></ul>
Check the following box.	<ul> <li>I DO CONSENT: I do agree my child to take par in this study.</li> <li>I DO NOT CONSENT: I do not wish my child to rticipate in this study.</li> </ul>
Parent/Guardian's name	
Parent/Guardian's signature	
Witness: I hereby confirm that the study has been explained to the parent/ guardian. All questions (if any) have also been answered to his/ her satisfaction, and he/ she, of his/ her own free will, has consented for his/ her child to take part in the study.	
Name of witness	
Cine at the state of the second	

id1	
id2	
id3	
'[id1]-[id2]-[id3]"	
Please fix the structure ID above on the roof in front of the door.	
Date	

# Page 55 of 90 **1. Structure**

Please complete the survey below.	
Thank you!	
Longitude	
Latitude	
Is this structure the first registration in the household?	○ Yes ○ No
Record the structure ID of the first structure in this household	
(i.g. 12-1-7 )	
Name of the village	
What is the main source of drinking water for members of your household?	<ul> <li>PIPED INTO DWELLING</li> <li>PIPED TO YARD/PLOT</li> <li>PIPED TO NEIGHBOR</li> <li>PUBLIC TAP/STANDPIPE</li> <li>DUG PROTECTED WELL</li> <li>DUG UNPROTECTED WELL</li> <li>WATER FROM PROTECTED SPRING</li> <li>WATER FROM UNPROTECTED SPRING</li> <li>RAINWATER</li> <li>TANKER TRUCK</li> <li>CART WITH SMALL TANK</li> <li>SURFACE WATER (RIVER/DAM/LAKE/POND/STREA/ /IRRIGATION CHANNEL)</li> <li>BOTTLED WATER</li> <li>OTHER</li> </ul>
Specify it.	
What is the main source of water used by your household for other purposes such as cooking and handwashing?	<ul> <li>PIPED INTO DWELLING</li> <li>PIPED TO YARD/PLOT</li> <li>PIPED TO NEIGHBOR</li> <li>PUBLIC TAP/STANDPIPE</li> <li>DUG PROTECTED WELL</li> <li>DUG UNPROTECTED WELL</li> <li>WATER FROM PROTECTED SPRING</li> <li>WATER FROM UNPROTECTED SPRING</li> <li>RAINWATER</li> <li>TANKER TRUCK</li> <li>CART WITH SMALL TANK</li> <li>SURFACE WATER (RIVER/DAM/LAKE/POND/STREA/IRRIGATION CHANNEL)</li> <li>OTHER</li> </ul>

Where is that water source located?	<ul> <li>IN OWN DWELLING</li> <li>IN OWN YARD/PLOT</li> <li>ELSEWHERE</li> </ul>
How long does it take to go there, get water, and come back? (MINUTES)	
What kind of toilet facility do members of your household usually use? IF NOT POSSIBLE TO DETERMINE, ASK PERMISSION TO OBSERVE THE FACILITY.	<ul> <li>FLUSH TO PIPED SEWER SYSTEM</li> <li>FLUSH TO SEPTIC TANK</li> <li>FLUSH TO PIT LATRINE</li> <li>FLUSH TO SOMEWHERE ELSE</li> <li>FLUSH, DON'T KNOW WHERE</li> <li>VENTILATED IMPROVED PIT LATRINE</li> <li>PIT LATRINE WITH SLAB</li> <li>PIT LATRINE WITHOUT SLAB/OPEN PIT</li> <li>COMPOSTING TOILET</li> <li>BUCKET TOILET</li> <li>HANGING TOILET/HANGING LATRINE</li> <li>NO FACILITY/BUSH/FIELD</li> <li>OTHER</li> </ul>
Specify it.	
Do you share this toilet facility with other households?	<ul><li>○ Yes</li><li>○ No</li></ul>
Including your own compound, how many households use this toilet facility?	<ul> <li>LESS THAN 10 HOUSEHOLDS</li> <li>10 OR MORE HOUSEHOLDS</li> <li>DON'T KNOW</li> </ul>
Including your own household, how many households use this toilet facility (if less than 10)?	2
Where is this toilet facility located?	<ul> <li>○ IN OWN DWELLING</li> <li>○ IN OWN YARD/PLOT</li> <li>○ ELSEWHERE</li> </ul>
In your household, what type of cooking device (cookstove) is mainly used for cooking?	<ul> <li>ELECTRIC STOVE</li> <li>SOLAR COOKER</li> <li>LIQUEFIED PETROLEUM GAS (LPG)/COOKING GAS</li> <li>PIPED NATURAL GAS STOVE</li> <li>BIOGAS STOVE</li> <li>LIQUID FUEL STOVE</li> <li>MANUFACTURED SOLID FUEL STOVE (i.g. Jiko)</li> <li>THREE STONE STOVE/OPENFIRE</li> <li>NO FOOD COOKED IN THE HOUSEHOLD</li> <li>OTHER</li> </ul>
Specify it.	
What type of fuel or energy source is mainly used in this cookstove?	<ul> <li>ALCOHOL/ETHANOL</li> <li>GASOLINE/DIESEL</li> <li>KEROSENE/PARAFFIN</li> <li>COAL/LIGNITE</li> <li>CHARCOAL</li> <li>WOOD</li> <li>STRAW/SHRUBS/GRASS</li> <li>AGRICULTURAL CROP</li> <li>ANIMAL DUNG/WASTE</li> <li>PROCESSED BIOMASS (PELLETS) OR WOODCHIPS</li> <li>GARBAGE/PLASTIC</li> <li>SAWDUST</li> <li>OTHER</li> </ul>
---	--
Specify it.	
How many rooms in this household are used for sleeping?	
Does this household own any livestock, herds, other farm animals, or poultry?	○ Yes ○ No
How many of the following (animals) livestock does this household own?	
- Local cattle (indigenous)	
How many of the following (animals) livestock does this household own?	
- Exotic/grade cattle	
How many of the following (animals) livestock does this household own?	2
- Horses	
How many of the following (animals) livestock does this household own?	
- Donkeys	1
How many of the following (animals) livestock does this household own?	
- Mules	
How many of the following (animals) livestock does this household own?	
- Goats	
How many of the following (animals) livestock does this household own?	
- Sheep	

How many of the following (animals) livestock does this household own?		
- Chickens or other poultry		
How many of the following (animals) livestock does this household own?		
- Pigs		
Does any member of this household own any agricultural land?	<ul><li>○ Yes</li><li>○ No</li></ul>	
Do you know how many acres of agricultural land do members of this household own?	<ul><li>○ Yes</li><li>○ No</li></ul>	
How many acres of agricultural land do members of this household own?		
ACRES		/rignı,
Does your household have:	<ul> <li>Electricity?</li> <li>A radio?</li> <li>A television?</li> <li>A fixedlinetelephone?</li> <li>A computer?</li> <li>A computer?</li> <li>A refrigerator?</li> <li>A solarpanel?</li> <li>A table?</li> <li>A chair?</li> <li>A chair?</li> <li>A sofa?</li> <li>A bed?</li> <li>A clock?</li> <li>A microwave oven?</li> <li>A DVD player?</li> <li>A CD player?</li> </ul>	Including for uses related to text and data minin
Does any member of this compound own:	<ul> <li>A wrist watch?</li> <li>A mobile phone?</li> <li>A bicycle?</li> <li>A motorcycle or motor scooter?</li> <li>An animal-drawn cart?</li> <li>A car or truck?</li> <li>A boat with a motor?</li> </ul>	iy, Ai naminy, and si
Does any member of this household have an account in a bank or other financial institution?	<ul><li>○ Yes</li><li>○ No</li></ul>	
Does any member of this household use a mobile phone to make financial transactions such as sending or receiving money, paying bills, purchasing goods or services, or receiving wages?	<ul><li>○ Yes</li><li>○ No</li></ul>	
In the past year, has this household ever used mosquito repellent spray (e.g. Doom), ointments, vaporizers coils, herbs, or plants to protect against mosquitoes/malaria?	○ Yes ○ No	

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Does your household have any bed nets?	<ul><li>○ Yes</li><li>○ No</li></ul>
How many mosquito nets does your household have?	
Will you accept to install the ceiling net if you are offered?	<ul><li>○ Yes</li><li>○ No</li></ul>
What is the reason for not installing the ceiling net? Select all that apply.	<ul> <li>Air flow disturbance</li> <li>Heat</li> <li>Appearance</li> <li>Pets</li> <li>Fire</li> <li>Social culture and religious factor</li> <li>Others</li> </ul>
Specify it	
Do you have any concerns about the ceiling net? Select all that apply.	<ul> <li>Air flow disturbance</li> <li>Heat</li> <li>Appearance</li> <li>Pets</li> <li>Fire</li> <li>Social culture and religious factor</li> <li>No concern</li> <li>Others</li> </ul>
Specify it	2
OBSERVE MAIN MATERIAL OF THE FLOOR OF THE DWELLING/SLEEPING ROOM. RECORD OBSERVATION.	<ul> <li>EARTH/SAND</li> <li>DUNG</li> <li>WOOD PLANKS</li> <li>PALM/BAMBOO</li> <li>PARQUET OR POLISHED WOOD</li> <li>VINYL OR ASPHALT STRIPS</li> <li>CERAMIC TILES</li> <li>CEMENT</li> <li>CARPET</li> <li>OTHER</li> </ul>
Specify it.	

OBSERVE MAIN MATERIAL OF THE ROOF OF THE DWELLING. RECORD OBSERVATION.	<ul> <li>NO ROOF</li> <li>THATCH/PALM LEAF</li> <li>RUSTIC MAT</li> <li>PALM/BAMBOO</li> <li>WOOD PLANKS</li> <li>CARDBOARD</li> <li>IRON SHEETS</li> <li>WOOD</li> <li>CALAMINE/CEMENT FIBER</li> <li>BRICK/CLAY TILES</li> </ul>
Specify it.	<ul> <li>CEMENT</li> <li>ROOFING SHINGLES</li> <li>OTHER</li> </ul>
OBSERVE MAIN MATERIAL OF THE EXTERIOR WALLS OF THE DWELLING. RECORD OBSERVATION.	<ul> <li>NO WALLS</li> <li>WOOD WITH MUD</li> <li>IRON SHEET</li> <li>BRICKS</li> <li>CANE/PALM/TRUNKS</li> <li>BAMBOO WITH MUD</li> <li>STONE WITH MUD</li> <li>UNCOVERED ADOBE</li> <li>PLYWOOD</li> <li>CARDBOARD</li> <li>REUSED WOOD</li> <li>CEMENT</li> <li>STONE WITH LIME/CEMENT</li> <li>CEMENT BLOCKS</li> <li>COVERED ADOBE</li> <li>WOOD PLANKS/SHINGLES</li> <li>OTHER</li> </ul>
Specify it.	2
OBSERVE EAVES OF THE DWELLING.	⊖ Open
RECORD OBSERVATION.	<ul> <li>Partly open</li> <li>Close</li> </ul>
OBSERVE BEAMS OF THE DWELLING.	O No vertical beam
RECORD OBSERVATION.	<ul> <li>One vertical beam</li> <li>More than one vertical beams</li> </ul>
Tick all that apply	<ul> <li>2 or more vertical beams in the same room</li> <li>Ceiling board/ Flat roof</li> <li>The roof is very low</li> <li>The room is used for kitchen</li> <li>None</li> </ul>
Has this structure been done with IRS (Indoor Residual Spraying) within three years?	○ Yes ○ No
When did you have IRS?	☐ 2021 ☐ 2022 ☐ 2023 ☐ Don't know

		$\bigcirc$ res	
"Living" means that the child usua household. If the child is usually s boarding school, but now he/she i house because of a school closure regarded as "living".	ally stay in the taying at a is staying in this a, that is not		
Once you complete, "Show More S	Save Options">"Save &	Go to Next Form"	

#### 2. Children

Please complete the survey below.

Thank you!

But RDT tests are for children from 6 month to 14 years old	d.
RECORD TWINS AND TRIPLETS SEPARATELY.	
What name was given to the child?	
First name	
What name was given to the child?	
Middle name	
What name was given to the child?	
_ast name	
s the child a boy or a girl?	O BOY O GIRL
Nas that a single or multiple pregnancy?	O SING O MULT
Do you know the birthday of the child?	⊖ Yes ⊖ No
On what day, month, and year was the child born?	
How old was the child at the last birthday?	
The birthday and your age are contradicting. Please check	the true age again.
s the child living with you?	
Living with" means that you and the child usually stay in the same household. If the child is usually staying at a boarding school, but now he/she is being with you because of a school closure, that is not regarded as "living with you".	U NO
Has the child been ill with a fever at any time in the ast 2 weeks?	<ul> <li>○ YES</li> <li>○ NO</li> <li>○ DON'T KNOW</li> </ul>

blood taken from a finger or heel for testing?	
Nere you told by a healthcare provider that the child nad malaria?	<ul> <li>YES</li> <li>NO</li> <li>ODON'T KNOW</li> </ul>
Did you seek advice or treatment for the illness from any source?	<ul><li>○ Yes</li><li>○ No</li></ul>
How many times did you seek advice or treatment for he illness from any source?	
Where did you first seek advice or treatment? Anywhere else? PROBE TO IDENTIFY THE TYPE OF SOURCE. F UNABLE TO DETERMINE IF PUBLIC, PRIVATE, OR NGO SECTOR, RECORD 'OTHER'	<ul> <li>GOVERNMENT HOSPITAL</li> <li>GOVERNMENT HEALTH CENTER</li> <li>GOVERNMENT DISPENSARY</li> <li>GOVERNMENT MOBILE CLINIC</li> <li>COMMUNITY HEALTH WORKER/FIELD WORKER</li> <li>PRIVATE HOSPITAL</li> <li>PRIVATE CLINIC</li> <li>PHARMACY</li> <li>PRIVATE MOBILE CLINIC</li> <li>COMMUNITY HEALTH WORKER</li> <li>SHOP</li> <li>TRADITIONAL PRACTITIONER</li> <li>MARKET</li> <li>ITINERANT DRUG SELLER</li> <li>OTHER</li> </ul>
Specify it.	
Where did you second seek advice or treatment? Anywhere else? PROBE TO IDENTIFY THE TYPE OF SOURCE. F UNABLE TO DETERMINE IF PUBLIC, PRIVATE, OR NGO SECTOR, RECORD 'OTHER'	<ul> <li>GOVERNMENT HOSPITAL</li> <li>GOVERNMENT HEALTH CENTER</li> <li>GOVERNMENT DISPENSARY</li> <li>GOVERNMENT MOBILE CLINIC</li> <li>COMMUNITY HEALTH WORKER/FIELD WORKER</li> <li>PRIVATE HOSPITAL</li> <li>PRIVATE CLINIC</li> <li>PHARMACY</li> <li>PRIVATE DOCTOR</li> <li>PRIVATE MOBILE CLINIC</li> <li>COMMUNITY HEALTH WORKER</li> <li>SHOP</li> <li>TRADITIONAL PRACTITIONER</li> <li>MARKET</li> <li>ITINERANT DRUG SELLER</li> <li>OTHER</li> </ul>
Specify it.	

Where did you third seek advice or treatment? Anywhere else? PROBE TO IDENTIFY THE TYPE OF SOURCE. IF UNABLE TO DETERMINE IF PUBLIC, PRIVATE, OR NGO SECTOR, RECORD 'OTHER'	<ul> <li>GOVERNMENT HOSPITAL</li> <li>GOVERNMENT HEALTH CENTER</li> <li>GOVERNMENT DISPENSARY</li> <li>GOVERNMENT MOBILE CLINIC</li> <li>COMMUNITY HEALTH WORKER/FIELD WORKER</li> <li>PRIVATE HOSPITAL</li> <li>PRIVATE CLINIC</li> <li>PHARMACY</li> <li>PRIVATE DOCTOR</li> <li>PRIVATE MOBILE CLINIC</li> <li>COMMUNITY HEALTH WORKER</li> <li>SHOP</li> <li>TRADITIONAL PRACTITIONER</li> <li>MARKET</li> <li>ITINERANT DRUG SELLER</li> <li>OTHER</li> </ul>
Specify it.	
How many days after the illness began did you first seek advice or treatment for the child?	
IF THE SAME DAY RECORD '0'.	
At any time during the illness, did the child take any medicine for the illness?	<ul><li>○ Yes</li><li>○ No</li></ul>
What medicine did the child take? Any other medicine? RECORD ALL MENTIONED. IF MEDICINE NOT KNOWN, ASK TO SEE THE PACKAGE OR PRESCRIPTION.	AL DHAP OTHER ACT (NOTALORDHAP) SP/FANSIDAR CHLOROQUINE AMODIAQUINE QUININE (PILLS) QUININE (INJECTION/IV) ARTESUNATE (RECTAL) ARTESUNATE (INJECTION/IV) OTHER ANTIMALARIAL AMOXICILLIN COTRIMOXAZOLE OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP) OTHER ANTIBIOTIC MEDICINE (INJECTION/IV) ASPIRIN PARACETAMOL/PANADOL/ACETAMINOPHEN IBUPROFEN OTHER DON'TKNOW
Specify it.	
How long after the fever started did the child first take an artemisinin-based combination therapy?	<ul> <li>SAME DAY</li> <li>NEXT DAY</li> <li>TWO DAYS AFTER FEVER</li> <li>THREE OR MORE DAYS AFTER FEVER</li> <li>DON'TKNOW</li> </ul>
Has [mis_wo213_1] received a malaria vaccine?	○ Yes ○ No

How many times has [mis_wo213_1] received malaria vaccine?	<ul> <li>1 dose</li> <li>2 doses</li> <li>3 doses</li> <li>4 doses</li> <li>Don't know</li> </ul>	
Where does [mis_wo213_1] usually sleep?	<ul> <li>Bed room</li> <li>Kitchen room</li> <li>Others</li> </ul>	
Specify it.		
Where Is [mis_wo213_1] usually living?	<ul> <li>This household</li> <li>Boarding school</li> <li>Relative's house outside the village</li> <li>Others</li> </ul>	
Specify it.		
Did [mis_wo213_1] spend any nights outside your house in the last 30 days?	<ul><li>○ Yes</li><li>○ No</li></ul>	
Where did [mis_wo213_1] spend those nights?	<ul> <li>Another house in Ndhiwa Sub-county</li> <li>Homa Bay county other than Ndhiwa</li> <li>Another county in Kenya</li> <li>Another country</li> </ul>	
How many nights did [mis_wo213_1] spend in another house in Ndhiwa?		
How many nights did [mis_wo213_1] spend in another house in Homa Bay County other than Ndhiwa?	2	
Specify the Sub-county name.	-0	
How many nights did [mis_wo213_1] spend in another house in another county in Kenya?	2	
Specify the county name.		
How many nights did [mis_wo213_1] spend in another house in another country?		
Specify the country name.		
Did the child sleep under a bed net last night?	<ul><li>○ Yes</li><li>○ No</li></ul>	
RDT result for P.f	O Negative	

RDT result for Pan	<ul> <li>Negative</li> <li>Positive</li> </ul>
If there is another child, press "Show More S	ave Options">"Save & Add New Instance
otherwise, press "Show More Save Options">	Go to Next Form".

### 3. Adults

1	
2	Please complete the survey below.

Thank you!	
Now, we would like to record the names of all adults who live Do not include a person who stays only a few days in a montl	e in this household on a permanent or weekly basis. h.
First name	
Middle name	
Last name	
Choose from the below. Sleep in this structure More than half of the week = Permanent Few days in a week regularly = Weekly Few days in a month regularly = Monthly Other type of resident	<ul> <li>Permanent Resident</li> <li>Weekly Resident</li> <li>Monthly Resident</li> <li>Others</li> </ul>
Answer his/her age with	<ul> <li>birthday</li> <li>age</li> <li>age group</li> </ul>
Birthday	
Age	(years old)
Age group	<ul> <li>High school</li> <li>After high school</li> <li>Was born before the independence of Kenya</li> </ul>
Sex	<ul> <li>Male</li> <li>Female</li> <li>Other</li> <li>Prefer not to say</li> </ul>

<ul> <li>Head</li> <li>Spouse (Husband or wife 1)</li> <li>Wife 2 or 3</li> <li>Parent</li> <li>Parent in law</li> <li>Child</li> </ul>	
<ul> <li>Spouse (Husband or wife 1)</li> <li>Wife 2 or 3</li> <li>Parent</li> <li>Parent in law</li> <li>Child</li> </ul>	
<ul> <li>Wife 2 or 3</li> <li>Parent</li> <li>Parent in law</li> <li>Child</li> </ul>	
<ul> <li>Parent</li> <li>Parent in law</li> <li>Child</li> </ul>	
○ Parent in law ○ Child	
$\stackrel{\frown}{\cap}$ Child in law	
O Brother/Sister	
$\bigcirc$ Brother/Sister in law	
$\bigcirc$ Grand Child	
O Uncle/Aunt	
⊖ Worker	
<ul> <li>Other relative</li> </ul>	
Other non-relative	
⊖ Head	
Spouse (Husband or wife 1)	
○ Wife 2 or 3	
Parent	
O Parent in law	
$\bigcirc$ Child	
$\bigcirc$ Child in law	
$\bigcirc$ Online in law $\bigcirc$ Brother/Sister	
O Brotner/Sister in law	
⊖ Grand Child	
O Nephew/Niece	
○ Uncle/Aunt	
Ŏ Worker	
$\check{\bigcirc}$ Other relative	
$\bigcirc$ Other non-relative	
	Grand Child Nephew/Niece Uncle/Aunt Other relative Other non-relative Head Spouse (Husband or wife 1) Wife 2 or 3 Parent Parent in law Child Child in law Brother/Sister Brother/Sister in law Grand Child Nephew/Niece Uncle/Aunt Worker Other relative Other non-relative

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1

2

ASK THE RESPONDENT TO SHOW YOU ALL THE NETS IN THE HOUSEHOLD. OBSERVE AND ANSWER THE QUESTIONS FOR EACH NET. ONE BY ONE.		
Please name this net for the sake of identification. i.e. boy's net, parent's net, net in the living room		
WAS THIS NET OBSERVED?	<ul><li>○ Yes</li><li>○ No</li></ul>	
How many months ago did your household get the mosquito net? IF LESS THAN ONE MONTH AGO, RECORD '00'.	0 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 23 24 25 26 27 28 29 30 31 32 33 34 35 36 MORE THAN 36 MONTHS AGO NOT SURE	

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OLYSET (SUPANET EXTRA)
<ul> <li>PERMANET (SUPANET EXTRA)</li> <li>VEERALIN</li> <li>NETPROTECT</li> <li>YORKOOL</li> <li>DAWAPLUS</li> <li>OTHER/DON'T KNOW BRAND (LLIN)</li> <li>OTHER TYPE (NOT LLIN)</li> <li>DON'T KNOW TYPE</li> </ul>
<ul> <li>YES, MASS DISTRIBUTION CAMPAIGN</li> <li>YES, ANTENATAL CARE VISIT</li> <li>YES, CHILD WELFARE VISIT</li> <li>NO</li> </ul>
<ul> <li>GOVERNMENT HEALTH FACILITY</li> <li>PRIVATE HEALTH FACILITY</li> <li>PHARMACY</li> <li>SHOP/MARKET</li> <li>CHP</li> <li>RELIGIOUS INSTITUTION</li> <li>SCHOOL</li> <li>OTHER</li> <li>DON'T KNOW</li> </ul>
<ul> <li>YES</li> <li>NO</li> <li>NOT SURE</li> </ul>
DNE,
<ul> <li>TOO HOT</li> <li>DON'T LIKE NET SHAPE/COLOR/SIZE</li> <li>DON'T LIKE SMELL</li> <li>UNABLE TO HANG NET</li> <li>SLEPT OUTDOORS</li> <li>USUAL USER DIDN'T SLEEP HERE LAST NIGH'</li> <li>NO MOSQUITOES/NO MALARIA</li> <li>EXTRA NET/SAVING FOR LATER</li> <li>NET TOO SMALL/SHORT</li> <li>NET BROUGHT BED BUGS</li> <li>OTHER</li> </ul>

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ruge	<i>'</i> '	01	20

#### Questionnaire

Please complete the survey below.	
Fhank you!	
Date and time of visit	
Cohort ID	
(i,e. "2_1")	
Cluster ID is incorrect.	
Structure ID	
(Typing the ID shown on the structure. i.e, 'malela-10-10")	
First name	
Middle name	
Last name	
This participant is available for the survey.	⊖ Yes ⊖ No
Please select the reason why the participant is not available.	<ul> <li>Moved out from the area (will never come back)</li> <li>Travel to another village in Ndhiwa</li> <li>Travel to Homa Bay County other than Ndhiwa</li> <li>Travel to Another county in Kenya</li> <li>Travel to Another country</li> <li>Refuse</li> <li>Do not know (Could not find)</li> <li>Others</li> </ul>
Please indicate when he/she will be back. (If you do not know, please write 0.)	
Specify the reason.	
Did [name_f] spend any nights outside [name_f]'s house in the last four weeks?	○ Yes ○ No
Where did [name_f] spend those nights?	<ul> <li>Another house in your village</li> <li>Another village in Ndhiwa</li> <li>Homa Bay County other than Ndhiwa</li> <li>Another county in Kenya</li> <li>Another country</li> </ul>

[name_f]'s village?	
Did you see the ceiling nets in the household you visited in another house in the village?	○ Yes ○ No
How many nights did [name_f] spend in another village in Ndhiwa?	
Did you see the ceiling nets in the household you visited in another village in Ndhiwa?	○ Yes ○ No
How many nights did [name_f] spend in Homa Bay County other than Mfangano and Mbita?	
How many nights did [name_f] spend in another county in Kenya?	
How many nights did [name_f] spend in another country?	
Did [name_f] visit any health facility in the last four weeks?	○ Yes ○ No
(Please refer to the booklet)	
Did [name_f] have the following symptoms at any point in the past four weeks?	<ul> <li>Fever</li> <li>Chills</li> <li>Profuse sweating</li> <li>Muscle/joint pain</li> <li>Abdominal pain</li> <li>Diarrhoea</li> <li>Nausea</li> <li>Vomiting</li> <li>Irritability</li> <li>Refusal to feed</li> <li>Prostration (difficulty to sit upright)</li> <li>Alteration in the level of consciousness</li> <li>Convulsions or coma</li> <li>Difficulty in breathing/respiratory distress</li> <li>Jaundice</li> <li>Others</li> <li>None</li> </ul>
Please list other symptoms [name_f] experienced in the past four weeks.	
How many times did the child visit health facilities?	<ul> <li>One time</li> <li>Two time</li> <li>Three time</li> <li>More than three</li> </ul>

Page	3
------	---

When did [name_f]visit the health facility?	
(Please refer to the booklet)	
Which health facility did [name_f] visit?	Malela level 4 hospital
(Please refer to the booklet)	<ul> <li>Kabongo HC</li> <li>Andiwo HC</li> <li>Wikomimo HC</li> <li>Abuoro HC</li> <li>Langi HC</li> <li>Kobodo HC</li> <li>Okok HC</li> <li>Other</li> </ul>
Please state the health facility [name_f] visited.	
(Please refer to the booklet)	<ul> <li>Fever</li> <li>Headache</li> <li>Muscle pain</li> <li>Abdominal pain</li> <li>Nausea</li> <li>Vomiting</li> <li>Diarrhea</li> <li>Convulsions or coma</li> <li>Jaundice</li> <li>Rapid breathing</li> <li>Difficulty in breathing/respiratory distress</li> <li>Pale conjunctivae/palms</li> <li>Loss of reactivity</li> <li>Others</li> </ul>
When did the symptom start?	
(Please refer to the booklet)	
Was [name_f] diagnosed with malaria?	
(Please refer to the booklet)	
What was the diagnosis?	
Did [name_f] take any treatment or medication?	⊖ Yes
(Please refer to the booklet)	() NO

What treatment or medication did [name_f] receive from	AL
the health facility?	
	OTHER ACT (NOT AL OR DHAP)
(Please refer to the booklet)	SP/FANSIDAR
	QUININE (PILLS)
	QUININE (INJECTION/IV)
	ARTESUNATE (RECTAL)
	ARTESUNATE (INJECTION/IV)
	OTHER ANTIMALARIAL
	OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP)
	OTHER ANTIBIOTIC MEDICINE (INJECTION/IV)
	PARACETAMOL/PANADOL/ACETAMINOPHEN
Please list other medications [name_f] received from	
the health facility.	
When did [name_f] FIRST visit the health facility?	
(Please refer to the booklet)	
Which health facility did [name_f] first visit?	Malela level 4 hospital
	/ 🗌 Kabongo HC
(Please refer to the booklet)	🗌 Andiwo HC
	🔲 Wikomimo HC
	🗌 Abuoro HC
	🔲 Langi HC
	🗌 Kobodo HC
	Okok HC
	☐ Other
Please state the health facility [name f] visited.	
Which symptoms did the child have at the first visit?	Fever
	Headache
(Please refer to the booklet)	Muscle pain
· · · · ·	Abdominal pain
	☐ Nausea
	Vomiting
	🗌 Diarrhea
	Convulsions or coma
	 Jaundice
	— Rapid breathing
	Difficulty in breathing/respiratory distress
	$\square$ Pale conjunctivae/palms
	$\Box$ Loss of reactivity
	$\Box$ Others

1 2 3	When did the symptoms for the first visit start?		
4 5 6	(Please refer to the booklet)		
7 8 9	Was [name_f] diagnosed with malaria for the first visit?	○ Yes ○ No	
10 11	(Please refer to the booklet)		
12 13 14	What was the diagnosis?		σ
15 16 17	Did [name_f] take any treatment or medication for the first visit?	⊖ Yes ⊖ No	rotected
18 19 20	(Please refer to the booklet)		by cop
21 22	What treatment or medication did [name_f] receive from the health facility?	□ AL □ DHAP	yright, i
23 24 25 26 27 28 29 30 31 32 33 34 35 36 37	(Please refer to the booklet)	<ul> <li>OTHER ACT (NOT AL OR DHAP)</li> <li>SP/FANSIDAR</li> <li>CHLOROQUINE</li> <li>AMODIAQUINE</li> <li>QUININE (PILLS)</li> <li>QUININE (INJECTION/IV)</li> <li>ARTESUNATE (RECTAL)</li> <li>ARTESUNATE (INJECTION/IV)</li> <li>OTHER ANTIMALARIAL</li> <li>AMOXICILLIN</li> <li>COTRIMOXAZOLE</li> <li>OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP)</li> <li>OTHER ANTIBIOTIC MEDICINE (INJECTION/IV)</li> <li>ASPIRIN</li> <li>PARACETAMOL/PANADOL/ACETAMINOPHEN</li> </ul>	Enseignement Superieur ( ncluding for uses related to text and dat
37 38 39 40		☐ IBUPROFEN ☐ OTHER ☐ DON'TKNOW	ABES) . a mining
41 42 43	Please list other medications [name_f] received from the health facility.		, Al trainin
44 45 46 47	When did [name_f] SECOND visit the health facility?		g, and sir
48 49	(Please refer to the booklet)		nilar tec
50 51 52	Which health facility did [name_f] second visit?	☐ Malela level 4 hospital ☐ Kabongo HC	hnolog
53 54 55 56 57 58 59 60	(Please refer to the booklet)	<ul> <li>Andiwo HC</li> <li>Wikomimo HC</li> <li>Abuoro HC</li> <li>Langi HC</li> <li>Kobodo HC</li> <li>Okok HC</li> <li>Other</li> </ul>	yies.

Please state the health facility [name_f] visited.	
Which symptoms did the child have at the second visit?	Fever     Headacha
(Please refer to the booklet)	<ul> <li>Headache</li> <li>Muscle pain</li> <li>Abdominal pain</li> <li>Nausea</li> <li>Vomiting</li> <li>Diarrhea</li> <li>Convulsions or coma</li> <li>Jaundice</li> </ul>
	<ul> <li>Rapid breating</li> <li>Difficulty in breathing/respiratory distress</li> <li>Pale conjunctivae/palms</li> <li>Loss of reactivity</li> <li>Others</li> </ul>
When did the symptoms for the second visit start?	
(Please refer to the booklet)	
Was [name_f] diagnosed with malaria for the second visit?	<ul><li>○ Yes</li><li>○ No</li></ul>
(Please refer to the booklet)	
What was the diagnosis?	
Did [name_f] take any treatment or medication for the second visit?	⊖ Yes ⊖ No
(Please refer to the booklet)	1
What treatment or medication did [name_f] receive from the health facility?	
(Please refer to the booklet)	<ul> <li>□ SP/FANSIDAR</li> <li>□ CHLOROQUINE</li> <li>□ AMODIAQUINE</li> <li>□ QUININE (PILLS)</li> <li>□ QUININE (INJECTION/IV)</li> <li>□ ARTESUNATE (RECTAL)</li> <li>□ ARTESUNATE (INJECTION/IV)</li> <li>□ OTHER ANTIMALARIAL</li> <li>□ AMOXICILLIN</li> <li>□ COTRIMOXAZOLE</li> <li>□ OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP)</li> <li>□ OTHER ANTIBIOTIC MEDICINE (INJECTION/IN</li> <li>□ ASPIRIN</li> <li>□ PARACETAMOL/PANADOL/ACETAMINOPHEN</li> <li>□ IBUPROFEN</li> <li>□ OTHER</li> <li>□ DON'TKNOW</li> </ul>

60 the health facility.

Diagon refer to the booklet)	
Vhich health facility did [name_f] third visit?	Malela level 4 hospital Kabanga HC
Please refer to the booklet)	<ul> <li>Andiwo HC</li> <li>Wikomimo HC</li> <li>Abuoro HC</li> <li>Langi HC</li> <li>Kobodo HC</li> <li>Okok HC</li> <li>Other</li> </ul>
Please state the health facility [name_f] visited.	
O	
Please refer to the booklet)	<ul> <li>Fever</li> <li>Headache</li> <li>Muscle pain</li> <li>Abdominal pain</li> <li>Nausea</li> <li>Vomiting</li> <li>Diarrhea</li> <li>Convulsions or coma</li> <li>Jaundice</li> <li>Rapid breathing</li> <li>Difficulty in breathing/respiratory distress</li> <li>Pale conjunctivae/palms</li> <li>Loss of reactivity</li> <li>Others</li> </ul>
When did the symptoms for the third visit start?	
Please refer to the booklet)	
Vas [name_f] diagnosed with malaria for the third risit?	<ul><li>○ Yes</li><li>○ No</li></ul>
Please refer to the booklet)	
Vhat was the diagnosis?	
Did [name_f] take any treatment or medication for the hird visit?	○ Yes ○ No
Please refer to the booklet)	

1	What treatment or medication did [name, f] receive from	
2	the health facility?	
3	the health facility?	
1	·	
4	(Please refer to the booklet)	SP/FANSIDAR
5		
6		
7		
, o		
0		
9		
10		ARTESUNATE (INJECTION/IV)
11		🗌 OTHER ANTIMALARIAL
12		
12		
13		
14		
15		
16		
17		PARACETAMOL/PANADOL/ACETAMINOPHEN
17		
18		
19		
20		
21		
22	Please list other medications [name_f] received from	
22	the health facility.	
23		
24		
25	Did [name_f] take treatment or medication from the	🗌 No
26	following in the past four weeks?	Friends
27		Relatives
20		$\square$ Pharmacy/chemist
20		
29		
30		
31	What medications did Iname fl take from the friends?	
32		
33		
31		
24		
35		
36		
37		
38		QUININE (INJECTION/IV)
30		ARTESUNATE (RECTAL)
10		ARTESUNATE (INJECTIÓN/IV)
40		
41		
42		
43		
ΔΛ		U OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP)
 4		OTHER ANTIBIOTIC MEDICINE (INJECTION/IV)
45		
46		PARACETAMOL/PANADOL/ACETAMINOPHEN
47		
48		
49		
50		
50		
51	Please list other medications [name f] took from the	
52	friends	
53		
54		
55		
55		
50		
57		
58		
59		
60		

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	What medications did [name_f] take from the relatives?	AL DHAP OTHER ACT (NOT AL OR DHAP) SP/FANSIDAR CHLOROQUINE AMODIAQUINE QUININE (PILLS) QUININE (INJECTION/IV) ARTESUNATE (RECTAL) ARTESUNATE (INJECTION/IV) ARTESUNATE (INJECTION/IV) OTHER ANTIMALARIAL AMOXICILLIN COTRIMOXAZOLE OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP) OTHER ANTIBIOTIC MEDICINE (INJECTION/IV) ASPIRIN PARACETAMOL/PANADOL/ACETAMINOPHEN
18 19 20		☐ IBUPROFEN ☐ OTHER ☐ DON'TKNOW
21 22 23	Please list other medications [name_f] took from the relatives.	
25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44	What medications did [name_f] take from the pharmacy/chemist?	AL DHAP OTHER ACT (NOT AL OR DHAP) SP/FANSIDAR CHLOROQUINE AMODIAQUINE QUININE (PILLS) QUININE (INJECTION/IV) ARTESUNATE (RECTAL) ARTESUNATE (RECTAL) ARTESUNATE (INJECTION/IV) OTHER ANTIMALARIAL AMOXICILLIN COTRIMOXAZOLE OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP) OTHER ANTIBIOTIC MEDICINE (INJECTION/IV) ASPIRIN PARACETAMOL/PANADOL/ACETAMINOPHEN BUPROFEN OTHER DON'TKNOW
45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60	Please list other medications [name_f] took from the pharmacy.	

What medications did [name f] take from the	
traditional healer?	
	OTHER ACT (NOT AL OR DHAP)
	QUININE (PILLS)
	QUININE (INJECTION/IV)
	🗍 ARTESUNÀTE (RECTAL)
	🗍 ARTESUNATE (INJECTIÓN/IV)
	🗍 OTHER ANTIMALARIAL
	OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP)
	OTHER ANTIBIOTIC MEDICINE (INJECTION/ÍV
	PARACETAMOL/PANADOL/ACETAMINOPHEN
	OTHER
Place list other medications Inome fl teck from the	
ricase nsi omer medications [name_i] took from the traditional healer	
Door Inome fil hours the following sumptome and ar in	
Does [name_i] have the following symptoms now of in	
the last 24 hours?	
	Profuse sweating
	Muscle/joint pain
	Diarrhoea
	Nausea
	Vomiting
	Refusal to feed
	Prostration (difficulty to sit upright)
	Alteration in the level of consciousness
	Convulsions or coma
	Difficulty in breathing/respiratory distress
	Jaundice
	☐ Others
Please list other symptoms [name_f] experience now or	
in the last 24 hours.	
Did [name_f] receive the malaria vaccine within four	⊖ Yes
weeks?	○ No
How many times has [name f] received the malaria	$\bigcirc$ 1 dose
vaccine, including the latest one?	$\check{\bigcirc}$ 2 doses
,	$\check{\bigcirc}$ 3 doses
	$\bigcirc$ 4 doses
	O Don't know
	-
Does the structure where Iname flusually sleeps have	⊖ Yes
ceiling nets?	$\bigcirc$ No

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rayc	- 01	UI.	20

#### Sample

1	
2	Please complete the survey below.

Thank you!	
Cohort ID	
First name	
Middle name	
_ast name	
Did you sleep under a bed net last night?	○ Yes ○ No
Axillary temperature (degrees Celsius)	
Perform finger prick	<ul><li>○ Yes</li><li>○ No</li></ul>
Blood spots on filter paper?	⊖ Yes ⊖ No
Fhick and thin blood films?	<ul><li>○ Yes</li><li>○ No</li></ul>
RDT results for P.f	<ul> <li>Negative</li> <li>Positive</li> </ul>
RDT results for Pan	<ul> <li>Negative</li> <li>Positive</li> </ul>

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#### Participant questionnaire

riease complete the survey below.		
Fhank you!		
Date and time of visit		
Date and time of visit		_
Survey ID		
i,e. "s2_1")		_
tructure ID		
Typing the ID shown on the structure. i.e, malela-10-10")		_
irst name		_
Aiddle name	\$	_
ast name		_
vge	(years old)	_
Does [name_f] know the birthday?	⊖ Yes ⊖ No	
Birthday	2/	_
he birthday and your age are contradicting. Please c	heck the true age again.	
ex	<ul> <li>Male</li> <li>Female</li> <li>Other</li> <li>Prefer not to say</li> </ul>	
ongitude		
atitude		
This participant is available for the survey.		

<ul> <li>Moved out from the area (will never come back</li> <li>Travel to another village in Ndhiwa</li> <li>Travel to Homa Bay County other than Ndhiwa</li> <li>Travel to Another county in Kenya</li> <li>Travel to Another country</li> <li>Refuse</li> <li>Do not know (Could not find)</li> <li>Others</li> </ul>
<ul><li>○ Yes</li><li>○ No</li></ul>
<ul> <li>Another house in your village</li> <li>Another village in Ndhiwa</li> <li>Homa Bay County other than Ndhiwa</li> <li>Another county in Kenya</li> <li>Another country</li> </ul>
○ Yes ○ No
⊖ Yes ⊖ No
4
0
<ul> <li>Yes</li> <li>No</li> <li>Don't know</li> </ul>

- 58 59
- 60

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What was the symptom? Tick all that apply.	<ul> <li>Fever</li> <li>Chills</li> <li>Profuse sweating</li> <li>Muscle/joint pain</li> <li>Abdominal pain</li> <li>Diarrhoea</li> <li>Nausea</li> <li>Vomiting</li> <li>Irritability</li> <li>Refusal to feed</li> <li>Prostration (difficulty to sit upright)</li> <li>Alteration in the level of consciousness</li> <li>Convulsions or coma</li> <li>Difficulty in breathing/respiratory distress</li> </ul>
Please list other symptoms [name f] experienced in the	
past four weeks.	
Did [name_f] visit any health facility in the last	
four weeks?	() No
Which health facility did [name_f] visit?	<ul> <li>Malela level 4 hospital</li> <li>Kabongo HC</li> <li>Andiwo HC</li> <li>Wikomimo HC</li> <li>Abuoro HC</li> <li>Langi HC</li> <li>Kobodo HC</li> <li>Okok HC</li> <li>Other</li> </ul>
Please state the health facility [name_f] visited.	2
Was [name_f] diagnosed with malaria?	○ Yes ○ No
What was the diagnosis?	1
Did [name_f] take any treatment or medication?	⊖ Yes
· · ····, · ····· ··· · · · · · · · · · · · · ·	◯ No
Do you know the name of the medication?	○ Yes ○ No

59 60

What treatment or medication did [name_f] receive from the health facility?	<ul> <li>AL</li> <li>DHAP</li> <li>OTHER ACT (NOT AL OR DHAP)</li> <li>SP/FANSIDAR</li> <li>CHLOROQUINE</li> <li>AMODIAQUINE</li> <li>QUININE (PILLS)</li> <li>QUININE (INJECTION/IV)</li> <li>ARTESUNATE (RECTAL)</li> <li>ARTESUNATE (INJECTION/IV)</li> <li>OTHER ANTIMALARIAL</li> <li>AMOXICILLIN</li> <li>COTRIMOXAZOLE</li> <li>OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP)</li> <li>OTHER ANTIBIOTIC MEDICINE (INJECTION/IV)</li> <li>ASPIRIN</li> <li>PARACETAMOL/PANADOL/ACETAMINOPHEN</li> <li>IBUPROFEN</li> <li>OTHER</li> </ul>
Please list other medications [name_f] received from the health facility.	
Did [name_f] take treatment or medication from friends, relatives, pharmacy/chemist, or traditional healers in the past four weeks?	<ul><li>○ Yes</li><li>○ No</li></ul>
Did [name_f] take treatment or medication from the following in the past four weeks?	<ul> <li>Friends</li> <li>Relatives</li> <li>Pharmacy/chemist</li> <li>Traditional healers</li> </ul>
Do you know the names of medications from your friends?	⊖ Yes ⊖ No
What medications did [name_f] take from the friends?	AL DHAP OTHER ACT (NOT AL OR DHAP) SP/FANSIDAR CHLOROQUINE AMODIAQUINE QUININE (PILLS) QUININE (INJECTION/IV) ARTESUNATE (RECTAL) ARTESUNATE (INJECTION/IV) ARTESUNATE (INJECTION/IV) OTHER ANTIMALARIAL AMOXICILLIN COTRIMOXAZOLE OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP) OTHER ANTIBIOTIC MEDICINE (INJECTION/IV) ASPIRIN PARACETAMOL/PANADOL/ACETAMINOPHEN IBUPROFEN OTHER
Please list other medications [name_f] took from the friends.	
Do you know the names of medications from your relatives?	○ Yes ○ No

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What medications did [name f] take from the relatives?	
mat modicatione and [name_i] take from the relatives:	
	$\Box$ OTHER ACT (NOT AL OR DHAP)
	$\square$ SP/FANSIDAR
	$\square \text{ ARTESUNATE (INJECTION/IV)}$
	OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP)
	PARACETAMOL/PANADOL/ACETAMINOPHEN
Please list other medications [name_f] took from the	
relatives.	
Do you know the names of medications from the	○ Yes
pharmacy/chemist?	$\bigcirc$ No
	0.10
What mediantions did Inome fl take from the	
what medications did [hame_i] take from the	
pnarmacy/cnemist?	
	$\Box OTHER ACT (NOT AL OR DHAP)$
	ARTESUNATE (INJECTION/IV)
	OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP)
	OTHER ANTIBIOTIC MEDICINE (INJECTION/IV
	PARACETAMOL/PANADOL/ACETAMINOPHEN
	🗌 OTHER
Please list other medications [name_f] took from the	
pharmacy.	
Do you know the names of medications from the	⊖ Yes
traditional healer?	○ No

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19	What medications did [name_f] take from the traditional healer?	<ul> <li>AL</li> <li>DHAP</li> <li>OTHER ACT (NOT AL OR DHAP)</li> <li>SP/FANSIDAR</li> <li>CHLOROQUINE</li> <li>AMODIAQUINE</li> <li>QUININE (PILLS)</li> <li>QUININE (INJECTION/IV)</li> <li>ARTESUNATE (RECTAL)</li> <li>ARTESUNATE (INJECTION/IV)</li> <li>OTHER ANTIMALARIAL</li> <li>AMOXICILLIN</li> <li>COTRIMOXAZOLE</li> <li>OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP)</li> <li>OTHER ANTIBIOTIC MEDICINE (INJECTION/IV)</li> <li>ASPIRIN</li> <li>PARACETAMOL/PANADOL/ACETAMINOPHEN</li> <li>IBUPROFEN</li> <li>OTHER</li> </ul>
20 21 22 23	Please list other medications [name_f] took from the traditional healer.	
23 24 25 26	Does [name_f] have any symptoms now or in the last 24 hours?	○ Yes ○ No
27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45	Does [name_f] have the following symptoms now or in the last 24 hours?	<ul> <li>Fever</li> <li>Chills</li> <li>Profuse sweating</li> <li>Muscle/joint pain</li> <li>Abdominal pain</li> <li>Diarrhoea</li> <li>Nausea</li> <li>Vomiting</li> <li>Irritability</li> <li>Refusal to feed</li> <li>Prostration (difficulty to sit upright)</li> <li>Alteration in the level of consciousness</li> <li>Convulsions or coma</li> <li>Difficulty in breathing/respiratory distress</li> <li>Jaundice</li> <li>Cough</li> <li>Rash</li> <li>Itches</li> <li>Others</li> </ul>
46 47 48 49	Please list other symptoms [name_f] experience now or in the last 24 hours.	
50 51	Has [name_f] received a malaria vaccine?	○ Yes ○ No
52 53	Please refer to the mother-child book.	
54 55 56 57	How many times has [name_f] received the malaria vaccine?	<ul> <li>1 dose</li> <li>2 doses</li> <li>3 doses</li> </ul>
58 59		O Don't know
60	Does the structure where [name_f] usually sleeps have ceiling nets?	○ Yes ○ No

## Sample

Please complete the survey below.

# Thank you!

Survey ID	
First name	
Middle name	
Last name	
Did you sleep under a bed net last night?	○ Yes ○ No
Axillary temperature (degrees Celsius)	
Perform finger prick	○ Yes ○ No
Blood spots on filter paper?	<ul><li>○ Yes</li><li>○ No</li></ul>
Thick and thin blood films?	<ul><li>○ Yes</li><li>○ No</li></ul>
RDT results for P.f	<ul> <li>Negative</li> <li>Positive</li> </ul>
RDT results for Pan	O Negative

e 89 of 90 Head questionnaire	BMJ Open F
Flease complete the survey below.	
Thank you!	
Who is the respondent?	<ul> <li>Head</li> <li>Primary care taker</li> <li>Participant</li> </ul>
*If the respondent are not sure about the answer(s), he/she can be helped by the other members.	○ Others
What is the respondent's relation to the participant?	Head
	$\bigcirc$ spouse (Husband or wife 1) $\bigcirc$ Wife 2 or 3
	$\bigcirc$ Parent
	$\bigcirc$ Parent in law
	$\bigcirc$ Child
	$\bigcirc$ Child in law
	O Brother/Sister
	Ŏ Brother/Sister in law
	🔿 Grand Child
	O Nephew/Niece
	C Uncle/Aunt
	O Worker
	Other relative
	O Other non-relative
What is the condition of the ceiling net?	O No damage
	O Damaged but repaired
	O Not installed
How many hole(s) does/did it have?	
(regardless of the size)	
	21
Where are the hole(s) located?	Around the edge (lower part, near the wall) Around the top
	☐ In the middle
What is/was the size of largest hole?	Smaller than the tip of index finger
	<ul> <li>Smaller than the fist</li> <li>larger than the fist</li> </ul>
What is/was the reason of the damage?	Accident during the cleaning
	<ul><li>○ Others</li></ul>
Please specify the reason of the damage	

why did they remove?	
What is the condition of the wooden battens securing the ceiling net to the wall?	<ul><li>○ Good</li><li>○ Damaged</li></ul>
Presence of gaps between battens and the wall	<ul><li>○ Yes</li><li>○ No</li></ul>
Do you agree with the following potential positive sides of the ceiling net?	<ul> <li>Stop mosquito entering the house</li> <li>Stop other insects/animals entering the house</li> <li>Durability of the ceiling nets</li> <li>To beautify the house</li> <li>Household coverage</li> <li>Keep the room cool</li> <li>Others</li> </ul>
Please specify.	
Do you agree with the following potential negative sides of the ceiling net?	<ul> <li>It makes room too hot</li> <li>It reduces the storage space a the top of the w all</li> <li>Fixing looks untidy</li> <li>It is hard to clean</li> <li>Dirt/debris trapped by the ceiling net</li> <li>Rewiring of power lines</li> <li>Others</li> </ul>
Please specify.	
Other features in the ceiling net (if any).	2
Will you pay for the ceiling nets if you need to buy them in the future?	○ Yes ○ No
How much will you pay the maximum for ceiling nets for your household?	<ul> <li>100 KSH</li> <li>300 KSH</li> <li>500 KSH</li> <li>1000 KSH</li> <li>2000 KSH</li> <li>5000 KSH</li> <li>More than 10,000 KSH</li> </ul>
How many mosquito nets does your household have?	
How many new (unopened) mosquito nets does your household have?	
Does anyone in your household wash the mosquito nets?	<ul><li>○ Yes</li><li>○ No</li></ul>

How often does your household wash the mosquito nets?	<ul> <li>Every day</li> <li>Every week</li> <li>Every month</li> <li>less frequently than every month</li> </ul>
How does your household wash the mosquito nets?	<ul> <li>With water</li> <li>With hot water</li> <li>With soap or detergent</li> <li>Others</li> </ul>
How does your household dry the mosquito nets after washing it?	<ul> <li>Indoor</li> <li>Under the sunlight</li> <li>Under the shade</li> <li>Others</li> </ul>
Have you ever gotten any instruction on how to use and treat the mosquito net?	<ul><li>○ Yes</li><li>○ No</li></ul>
From who did you get the instruction?	
In general, how long can you use the bed net effectively?	<ul> <li>One year even without damages</li> <li>Three years even without damages</li> <li>Ten years even without damages</li> <li>Until it gets damaged</li> </ul>
against mosquitoes?	⊖ No

#### Evaluation of the protective efficacy of Olyset®Plus ceiling nets for reduction of malaria incidence in children in Homa Bay County, Kenya: a cluster-randomized controlled study protocol

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2 3 ⊿	1	Title
5		
6 7	2	Evaluation of the protective efficacy of Olyset®Plus ceiling nets for reduction of malaria incidence in
8 9	3	children in Homa Bay County, Kenya: a cluster-randomized controlled study protocol
10 11	4	
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59 60	30	

#### **BMJ** Open

31	Abstract
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Introduction: Malaria is still a major health problem in sub-Saharan Africa, where 98% of global malaria mortality occurs. In addition, the spread of *Plasmodium falciparum* with partial artemisinin resistance in East Africa and beyond is a great concern. The establishment of more effective vector control, in addition to the current long-lasting insecticide-treated net (LLIN) distribution program, is an urgent task in these areas. One novel vector control candidate is the pyrethroid-PBO ceiling nets (Olyset®Plus ceiling nets) which can overcome the problems of variations in net use behaviors and metabolic resistance to insecticide in vectors. Our preliminary study suggests the protective efficacy and high acceptability of this tool. With this proposed second trial, we aim to evaluate the impact of this tool in a different eco-epidemiological setting in the lake endemic region of Kenya.

41 Methods: A cluster randomized controlled trial is designed to evaluate the impact of pyrethroid-PBO ceiling 42 nets in Ndhiwa Sub-County, Homa Bay County, Kenya. A total of 44 clusters will be randomly assigned in a 43 1:1 ratio to the intervention group (pyrethroid-PBO ceiling nets) and the control group. The assignment will 44 be accomplished through covariate-constrained randomization of clusters. For the primary outcome of 45 clinical malaria incidence, 38 children from each cluster will be enrolled in a cohort and followed for 18 46 months. We will also evaluate the effects of the intervention on entomological indicators as well as its 47 acceptance by communities and cost-effectiveness.

Ethics and dissemination: Ethics approvals were provided by the Mount Kenya University Institutional Scientific Ethics Review Committee and the Ethics Committee Osaka Metropolitan University. Study results will be shared with study participants and communities, the Homa Bay County Government and the Kenya National Malaria Control Programme. Results will also be disseminated through publications, conferences and workshops to help the development of novel malaria control strategies in other malaria-endemic countries.

54 Trial registration: UMIN000053873

#### 56 Keywords

Malaria, *Anopheles* mosquito, vector control, Pyrethroid resistance, Ceiling net, Kenya, Cluster-randomized
 controlled trial

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Role of sponsor {5c}	OMU will support project management oversight, trial managem
	data management, statistical analysis, and research governance. N
:	also holds overall authority together with project management an
;	analysis.
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2 3 4	72	
5 6	73	
7 8	74	Strength and limitations of this study
9 10	75	
11 12	76	• This is a second cluster-randomized controlled trial of a novel vector control tool, pyrethroid-PBO
13 14 15	77	ceiling net, to evaluate its efficacy in reducing malaria incidence among children.
16 17	78	
18 19	79	• The implementation of monthly active screening within the prospective cohort population
20 21 22	80	established in each cluster facilitates the assessment of infection incidence.
22 23	81	
24 25	82	• The incorporation of multidisciplinary outcomes, encompassing social aspects and cost-effectiveness
26 27 28	83	analyses, provides valuable insights for the potential future deployment of this intervention within
20 29 30	84	integrated malaria control strategies.
31 32	85	
33 34	86	• One of the anticipated limitations is the possible contamination between intervention and control
35 36	87	clusters because we will not set a buffer zone due to the geographical proximity among clusters.
37 38	88	
39 40	89	
41 42 42	90	
44 45	91	
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1 2	
3 100 4	
5 6 101	Introduction
8 102	Background and rationale {6a}
10 103	Malaria is still a major health problem, particularly in sub-Saharan Africa, where 98% of global malaria
<sup>12</sup> 104	mortality occurs [1]. Although the morbidity and mortality of malaria declined from the 2000s to 2015
<sup>14</sup> 105 15	owing to many investments and interventions, such as long-lasting insecticide-treated nets (LLINs), malaria
16 17 106	rapid diagnostic tests (RDTs), and artemisinin-based combination therapies (ACTs), progress has stalled
18 19 107	since 2015. Moreover, the spread of <i>Plasmodium falciparum</i> partially resistant to ACT in Africa is an
20 21 108	enormous concern. Currently five African countries, Rwanda [2], Uganda [3], Eritrea [4], Ethiopia [5], and
22 23 109	the United Republic of Tanzania [6] have reported delayed clearance of <i>P. falciparum</i> after treatment with
24 25 110 26	ACTs. Kenya's proximity to these countries highlights the urgent need to establish effective vector control,
27 111 28	in addition to maintaining antimalarial drug efficacy and strengthening resistance surveillance.
29 112 30	
<sup>31</sup> 113 32	Among several vector control measures, LLIN is the most widely adopted tool to prevent mosquito bites and
<sup>33</sup> 114 34	interrupt malaria transmission. However, suboptimal uses of LLIN are one of the key factors in reducing the
<sup>35</sup> 36 115	impact of LLIN on the malaria burden, together with insufficient provision in the mass net distribution
<sup>37</sup> 38 116	program or shortening durability of nets [7]. In the Lake Victoria basin, alternative uses of LLIN for fishing
39 40 117	and protecting crops and chicks are well-known local behaviors [8,9] as reported in other endemic areas [10].
41 42 118	In fact, in many areas including our study sites in Homa Bay County, Kenya, malaria prevalence remains
43 44 119 45	high despite widespread distribution of LLINs and their periodic replacements for more than a decade. This
46 120 47	suggests that LLIN alone is insufficient to interrupt malaria transmission in this region.
48 121 49	
<sup>50</sup> 122 51	Recently, we have proposed a novel vector control tool that covers the ceiling and the gap between the
<sup>52</sup> 123 53	ceiling and the walls of residential structures with co-formulated pyrethroid and piperonyl butoxide (PBO)
54 55 124	bed net material, called the Olyset®Plus (Sumitomo Chemical) ceiling net. The benefit of installing the
56 57 125	pyrethroid-PBO ceiling net in addition to conventional LLINs is detailed elsewhere [11]. Briefly, the
58 59 126 60	pyrethroid-PBO ceiling net provides a combination of physical and chemical protection against mosquitoes

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which seek human bloodmeal in the house. Recent reports have demonstrated that a substantial proportion of residual biting exposure occurs between the hours of entering indoor spaces and retiring to bed [12], pyrethroid-PBO ceiling nets may have a significant impact. Furthermore, the ceiling net is semi-permanently installed and requires no further action from end users, thus its protective efficacy is consistently extended to all who stay in the house and less affected by factors such as discomfort or sleeping arrangement that contribute to variations in conventional LLIN use [13]. The concept of ceiling net was previously investigated [14], and in this study, by integrating it with pyrethroid-PBO bed net material, this tool is anticipated to be effective even against pyrethroid-resistant mosquitoes, which are widely reported across Africa.

The aim of this study is to evaluate the efficacy, acceptability, and cost-effectiveness of pyrethroid-PBO 138 ceiling nets on malaria morbidity and transmission in the Lake Victoria basin of Kenya. Preliminary data 139 from our previous study on Mfangano Island in Lake Victoria [11] suggest a substantial reduction in malaria prevalence among school children and high community acceptance of this tool (unpublished data). With this proposed second trial, we aim to evaluate the impact of this tool in a different eco-epidemiological setting with relatively higher malaria transmission, more frequent human and vector movement, and synergistic impact from other interventions such as indoor residual spraying (IRS) and the RTS, S malaria vaccine. Since effective malaria controls need to be tailored to the local context, evidence of the effectiveness of pyrethroid-PBO ceiling nets from various transmission settings will increase the appeal of this intervention. Furthermore, considering the recent increase in choices of malaria control tools and the necessity of 147 combining various tools to maximize the impact of the malaria control program, it is important to understand 148 the acceptability and cost-effectiveness of each intervention to guide its future deployment.

To achieve these objectives, our collaboration with local institutions including the Kenya National Bureau of Statistics (KNBS), the National Malaria Control Programme (NMCP), the Kenya Medical Research Institute (KEMRI), and Homa Bay County, started from the research planning stage. This collaboration is crucial to the seamless transition from field trial to expanded implementation and policy development.

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## 55 **Objectives** {7}

6 The study has four research domains: epidemiology, entomology, social aspects, and cost-effectiveness.

For the epidemiology domain, the primary objective is to determine the protective efficacy of pyrethroid-PBO ceiling net in reducing malaria clinical incidence in children 6 months to 14 years old over 18 months post-intervention. This age range was selected to include both children under five years who are at high risk of malaria-related morbidity and mortality, and the school-age children who have the highest prevalence of *Plasmodium* infections[15]. The secondary objectives are (1) to determine the protective efficacy of pyrethroid-PBO ceiling nets in reducing *Plasmodium* infection prevalence by PCR in all age groups at 6-, 12-, and 18- months post-intervention; (2) to determine the spillover effects of pyrethroid-PBO ceiling nets in reducing *Plasmodium* infection prevalence in all age groups at 6-, 12-, and 18-months post-intervention; and (3) to determine the protective efficacy of pyrethroid-PBO ceiling net in reducing *Plasmodium* infection incidence in children 6 months to 14 years old over 18 months post-intervention.

For the entomology domain, the primary objective is to evaluate the impact of pyrethroid-PBO ceiling nets on the indoor mosquito density of the primary malaria vector species captured by CDC light traps. The secondary objectives are (1) to determine the impact of pyrethroid-PBO ceiling nets on the entomological inoculation rate (EIR) and (2) to determine the prevalence of voltage gated sodium channel (VGSC) mutations in vectors.

For the social aspects domain, the primary objective is to assess the determinants of social acceptability of the pyrethroid-PBO ceiling net in both the intervention and control arms. The secondary objectives are (1) to determine the feasibility of installing the pyrethroid-PBO ceiling nets and (2) to measure attitudes,

emotions, knowledge, and beliefs relating to the ceiling net in Ndhiwa Sub-County.

For the cost-effectiveness domain, the primary objective is to determine the incremental cost effectiveness
ratios (ICERs) of adding the pyrethroid-PBO ceiling net to existing malaria control interventions under field

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trial conditions. The secondary objectives are (1) to establish the relative contribution to costs of the distinct programmatic elements and identify the inputs that contribute the most to overall costs, and (2) to estimate the potential cost of providing pyrethroid-PBO ceiling net at a larger scale over 3 and 5 years under operational scenarios.

#### 87 Trial design {8}

The study is an open-label, cluster-randomized controlled trial (CRCT) with 44 clusters evenly divided between the intervention and the control arms. Each cluster will include one or two villages and consist of at least 50 households. A baseline survey will be conducted to determine the pre-intervention *Plasmodium* prevalence and *Anopheles* density, and to collect demographic and socioeconomic data for covariateconstrained randomization of clusters. The baseline survey will be conducted one month before cluster randomization. The post-intervention follow-up period will be 18 months. For the evaluation of the primary objective, 38 children aged 6 months to 14 years from each cluster will be recruited and followed for 18 months as a cohort. Cross-sectional surveys will be conducted after 6, 12, and 18 months of the intervention targeting 50 individuals of all ages from each cluster to estimate the overall *Plasmodium* prevalence.

## 98 Methods: Participants, interventions and outcomes

## 199 Study setting {9}

200 Location and administrative structure

Ndhiwa (713.5 km<sup>2</sup>) is one of nine sub-counties in Homa Bay County in Kenya. The sub-county has seven administrative wards: Kanyamwa Kologi, Kanyamwa Kosewa, Kabuoch North, Kwabwai, Kanyadoto, Kanikela, and Kabuoch South/Pala. Based on the number of malaria cases reported in the Kenya Health Information System (KHIS), the accessibility of the site, and population size, we selected Kanyamwa Kologi Ward as the target area (Figure 1). Agriculture is the primary economic activity, with sugarcane as a main commercial crop. County residents also keep animals such as dairy cattle, beef cattle, sheep, goats, and popultry [16]. The ward experiences a long rainy season from March to June and a short rainy season from October to December. As of 2019, the average monthly precipitation is 228.64 mm and the mean annual temperature is 26.7°C. The relative humidity remains elevated year-round, fluctuating between 75% to 85%

1	
<sup>2</sup> <sup>3</sup> 210 4	[17].
<sup>5</sup> 211	
<sup>7</sup> 212	Demographics
9 10 <sup>213</sup>	The population of Kanyamwa Kologi Ward is approximately 33,000 according to the 2019 national census
$^{11}_{12}214$	[18]. The dominant ethnic group in the region is Luo and the primary languages are DhoLuo, Kiswahili, and
13 14 215	English. There are 172 primary and 36 secondary schools in Ndhiwa Sub-County [19]. Within Kanyamwa
16 216 17	Kologi Ward, there are 28 primary and 7 secondary schools.
18 217 19	
20 218 21	Malaria epidemiology and control measures
<sup>22</sup> 219 23	Based on the KHIS, there were 429.1 and 457.2 confirmed malaria cases per 1,000 population in Ndhiwa
<sup>24</sup> 220 25	Sub-County and Kanyamwa Kologi Ward, respectively, in 2023. The primary malaria vector in the sub-
<sup>26</sup> 221 27	county is Anopheles funestus, which prefers feeding on humans. Although An. arabiensis exhibits
<sup>28</sup> <sub>29</sub> 222	predominantly zoophilic behavior, it is also a significant malaria vector in our study area [20]. In Homa Bay
<sup>30</sup> 31 223	County, LLINs have been distributed every three years since the early 2000s, and IRS and the RTS, S malaria
32 33 224	vaccine have been piloted in several areas since 2018 and 2019, respectively [21]. Notably PBO-
35 225 36	incorporated LLINs (Veeralin®LN, manufactured by VKA Polymers, Tamil Nadu, India) were distributed in
37 226 38	late 2023. In Kanyamwa Kologi Ward, there is one level four hospital and seven health centers.
39 <u>22</u> 7	
41 228 42	Eligibility criteria {10}
43 229 44	As the ceiling nets are installed per structure, we set the inclusion criteria on a structural basis. The inclusion
45 46 230	criteria for the installation of the ceiling nets are (1) residential structures with at least one permanent
47 48 231	resident aged 18 years or older in the household, (2) informed consent provided by a resident in the
<sup>49</sup> <sub>50</sub> 232	household, and (3) house structure amenable to ceiling net installation in terms of size of the structure,
51 52 233	presence of eave, ceiling board, and vertical beams, and material of the top part of the wall. The applicability
54 234	of the ceiling net installation will be assessed by experienced field staff. The exclusion criteria are (1) vacant
56 235 57	structure, confirmed by at least two visits by community health promoters (CHPs), (2) dwelling structure to
58 236 59	be vacated or destroyed within the study period, (3) non-eligible house structure for the ceiling net
60 237	installation, and (4) non-residential structures (school, shop, kitchen, storage, and toilet). The inclusion

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criteria for the prospective cohort are (1) children aged 6 months to 12 years old at the time of enrolment, (2) living in the study area at the time of pyrethroid-PBO ceiling net installation, (3) having no plan to leave or stay outside the study area for an extended period (longer than one month) over the 18-month follow-up period, and (4) informed consent provided by the participants or the parent or legal guardian. The exclusion criterion is having severe chronic illnesses. The inclusion criteria for cross-sectional malaria surveys for all age groups are (1) living in the study area during the study period, and (2) informed consent being provided by the participants or the parent or legal guardian before each survey. The exclusion criteria are (1) having severe chronic illnesses and (2) pregnancy known at the time of the surveys.

47 Who will take informed consent? {26a}

Written informed consent will be obtained by the study team members who fully understand the study protocol. After eligibility is confirmed, the study team members will present to the potential participant a document containing all relevant information about the study in Luo and English. If the participant cannot read, study information will be conveyed verbally in Luo, Kiswahili, and/or English by the study team members. The potential participant will have opportunities to ask any questions. Agreement to participate will be sought only after the participant indicates complete understanding of the study.

Additional consent provisions for collection and use of participant data and biological specimens {26b} The study information document for ceiling net installation contains the study overview. In addition, the documents for cross-sectional and cohort surveys contain details on collecting, storing, and using personal data and biological specimens during the study.

- 260 Interventions
- **Explanation for the choice of comparators {6b}**

In Kenya, LLIN is the most widely used malaria preventive measure. The Division of National Malaria
Programme coordinates free LLIN distribution, and the county governments deliver LLINs to residents in all
endemic counties every three years. In Homa Bay County, the RTS,S malaria vaccine has been implemented
since 2019. The primary purpose of this trial is to demonstrate the superiority in malaria prevention of

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adding pyrethroid-PBO ceiling nets to the standard malaria control program. Thus, in the control arm, no pyrethroid-PBO ceiling nets will be installed, but LLIN use and RTS,S immunization will be allowed in the control and intervention arms as the current best practice. There is no plan for new LLIN distribution during the study period.

## 271 Intervention description {11a}

In the intervention arm, pyrethroid-PBO ceiling nets will be installed in all dwelling units where residents sleep, free of charge to the households. All participants will be encouraged to continue to use LLINs, distributed by the Homa Bay County government. In each intervention cluster, 1 CHP and 2 community volunteers will be recruited from the intervention cluster and another 1 CHP from the control cluster will join the team to enable future knowledge dissemination. The net installation team will be trained to install ceiling nets by skilled local research assistants who participated in previous trials. The head (or another adult) of the household eligible to a ceiling net will be notified at least 24 hours before the scheduled installation time. The cost of the ceiling nets and their installation will be covered by the research team. Details of the installation procedure are described in the previous study protocol [11]. Briefly, the ceiling net is a rectangular sheet of pyrethroid-PBO net with loops sewn along the diagonal seams. The loops are roped to the support beams under the roof and the edges of the net are stapled to the wall.

## 284 Criteria for discontinuing or modifying allocated interventions {11b}

As the ceiling net is semi-permanently installed, the intervention will only be discontinued if the participant specifically requests the removal of the ceiling net by the study team. There will be no crossover from the control arm to the intervention arm during the follow-up period. Those who migrate between the arms or emigrate from the study areas will be dropped from the study follow-up.

290 Strategies to improve adherence to interventions {11c}

Adherence to the intervention cohort in this study is defined as sleeping in houses with pyrethroid-PBO
 ceiling nets. Adherence is monitored indirectly by assessing the number of nights each participant spends
 outside their house during the monthly interview. During each house visit, CHPs will visually inspect the

2	
3 294 4	condition of the ceiling nets. Any visible tear and damage to the ceiling net will be reported to the research
5 295 6	team, who will assess the size and location of the damage and perform repair or replace the ceiling net if
7 8 296	necessary.
9 10 297	
11 12 298	Relevant concomitant care permitted or prohibited during the trial {11d}
13 14 299	There is no specific concomitant care prohibited during the trial. All participants in both arms will continue
15 16 300	to receive and use free LLIN and have access to standard medical care, including malaria testing by RDT,
17 18 301	treatment with ACT and RTS,S malaria vaccination.
20 302	
<sup>21</sup> <sup>22</sup> 303	Provisions for post-trial care {30}
$\frac{23}{24}$ 304	All participants will be under the normal healthcare system in the study setting. No perceived health risks for
$\frac{26}{27}$ 305	the intended population are expected with the intervention. To monitor the long-term impact of the
<sup>28</sup> 29 306	intervention, the research team may conduct additional cross-sectional surveys 2 and 3 years post-
30 31 307	intervention to monitor further parasite transmission in the population.
32 33 308	
34 35 309	Outcomes {12}
36 37 310	Epidemiological domain: The primary outcome will be symptomatic malaria case incidence, defined as
38 39 311	axillary temperature of $\geq$ 37.5°C or a history of fever in the preceding 48 hours, and positive RDT, in
40 41 312	children aged 6 months to 14 years enrolled in the cohort, monitored with a monthly visit and passive case
<sup>42</sup> <sup>43</sup> 313	detection in the health facilities during an 18-month follow-up. The secondary outcomes will be (1) the
$\frac{45}{46}$ 314	prevalence of <i>Plasmodium</i> infections by PCR in all age groups at 6, 12, and 18 months post-intervention and
47 48 315	(2) infection incidence by PCR in the prospective cohort of children aged 6 months to 14 years over 18
49 50 316	months.
51 52 317	
53 54 318	Entomological domain: The primary outcome will be the density of the primary malaria vectors, species
55 56 319	composition and sporozoite infection rates. Indoor malaria vector density will be determined using CDC
57 58 320	light trap, and species composition and sporozoite infection rates will be determined by microscopy and
59 60 321	PCR. The secondary outcomes of the entomology domains will be (1) changes in EIR as a measure of

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malaria transmission and (2) prevalence of VGSC mutations associated with insecticide resistance in
 *Anopheles* mosquitoes captured by light trap.

Social aspect domain: The primary outcome will be the percentage of households consenting to pyrethroid-PBO ceiling net installation when offered. In addition, we will include observations and discussions about individual attitudes toward the ceiling net. The secondary outcomes of the social aspect domain will be the percentage of the intact ceiling net, description of damaged net, and the impact on the living environment such as perceived temperature in the house, dirt/debris trapped by the ceiling net, loss of storage space at the top of the wall, and rewiring of power lines. They will be evaluated by questionnaires at 6, 12, and 18 months post-intervention.

Cost-effectiveness domain: The primary outcome will be the incremental cost-effectiveness of adding pyrethroid-PBO ceiling net to existing malaria control interventions under field trial conditions from the societal and provider perspectives. The secondary outcomes of the cost-effectiveness domains will be (1) the costs of the distinct programmatic elements and the inputs that contribute the most to overall costs, and (2) the cost of providing pyrethroid-PBO ceiling net at a larger scale over three and five years under operational scenarios.

340 Participant timeline {13}

The schedule of trial activities is presented in Figure 2. The detail of each survey is described in Figure 3.

Sample size {14}

344 The sample size was calculated using the method of Hayes and Moulton [22]. All sample sizes will be 345 recalculated based on the baseline data, which will be collected about one month before the ceiling net 346 installation.

8 348 Epidemiological survey

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The following calculations were based on the historical data collected from the Lake Victoria region in Kenya with a clinical malaria incidence rate of 0.5 per person-year in children under 14 years old by RDT (unpublished data on Mfangano island), 40% parasite prevalence for all age groups by PCR and a betweencluster coefficient of variation (CV) in incidence rate of 0.24 in both groups. In the study site, RTS,S malaria vaccination began in 2019, with a mass distribution of PBO-incorporated LLINs at the end of 2023. Therefore, the intervention effect is expected to be smaller than those in previous studies and is conservatively assumed to be 25%. Assuming 38 individuals per cluster to be followed for up to 18 months with 20 % loss-to-follow up rate, we require 22 clusters per arm, a total of 1,672 children, to achieve 80% power to detect a significant incidence rate ratio of 0.75 (25% protective efficacy) at a two-sided type 1 error of 5%. With 50 individuals per cluster (2,200 total individuals) for the secondary outcome of *Plasmodium* prevalence by PCR in all age groups, we would achieve 5% type 1 error and 80% power to detect 23.5 % relative reduction. We do not specify the sample size for identifying spillover effects because spillovers tend to have smaller effect sizes relative to total or overall effects, so typically larger sample sizes are required to detect them. Although our study may be underpowered to detect spillovers, we will report the results as an exploratory analysis.

365 Entomological survey

Based on the previous entomological study conducted in Homa Bay County, we assume a mean vector density (number of mosquitoes per CDC light traps) of 3.3, a standard deviation (SD) of 0.634, and CV of 0.192 [14]. For 80% power to detect a 50% decrease in mean mosquito densities at 5% type 1 error level, we need to capture mosquitoes from five houses in each of 44 clusters.

## 371 Recruitment {15}

Thirty-eight eligible children in each cluster will be randomly recruited into our cohort. Recruitment will be limited to children aged 12 or younger, to avoid children aging out during the 18-month monitoring period. Study team staff will obtain informed consent from the parents or caregivers of the children before enrolling the children in the cohort. For the cross-sectional survey at each time point, we will randomly select from each cluster 50 individuals of all age groups. To guarantee the representativeness for all age groups, the

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3 377 4	selection will be done with following age category stratifications; 0-4, 5-9, 10-14, 15-19, and 20 and above.
<sup>5</sup> 378 6	
7 8 379	Assignment of interventions: allocation
9 10 380	Sequence generation {16a}
12 381 13	Random numbers will be generated using the sample function in R software.
14 382 15	
16 383 17	Concealment mechanism {16b}
18 19 384 20	The individual, household, and villages (clusters) are all given unique IDs at the beginning of the baseline.
21 385 22	Any following steps handle only these anonymized IDs.
23 386 24	
<sup>25</sup> 387 26	Implementation {16c}
<sup>27</sup> 388	After the baseline survey, covariate-constrained randomization will be used to allocate the 44 clusters across
<sup>29</sup> 389	the two study arms. The following factors will be constrained: baseline malaria infection prevalence by RDT
<sup>31</sup> 32 390	in children aged 0.5-14 years, LLIN usage, malaria vaccine coverage, socioeconomic status (SES),
34 391	population size, the proportion of eligible houses for the ceiling net installation, and vector densities. An
36 392 37	independent statistician will perform the randomization. Local study assistants will perform participant
38 393 39	enrollment.
40 41 394	
42 43 395	Assignment of interventions: Blinding
44 45 396	Who will be blinded {17a}
46 47 397	Due to the visibility of the pyrethroid-PBO ceiling net, neither the trial participants nor the members of the
48 49 398 50	study team who take part in field activities can be blinded. However, laboratory- and office-based personnel
51 399 52	(e.g., microscopists, laboratory technicians, and data analysts) will be blinded to the identity and intervention
<sup>53</sup> 400 54	status of the trial participants since all biological specimens will be identified by a unique numeric study
<sup>55</sup> 401 56	identifier, and personal information will be removed before analyses.
57 58 402	
59 60 403	Procedure for unblinding if needed {17b}

This is an open-label trial, and only the data measurers are blinded. Therefore, there is no circumstance that

4 5 405

6 7 they need to be unblinded.

406 8 9 10<sup>407</sup> **Data collection and management** 11 12 408 Questionnaires for the baseline survey, cohort surveys, and post-intervention cross-sectional surveys are 13 14 409 provided in the supplementary file. 15 16410 17 18411 Plans for assessment and collection of outcomes {18a} 19 20 4 1 2 Census and baseline cross-sectional survey 21 22 413 In Kanyamwa Kologi Ward, 85 census enumeration areas (EAs) are defined by the 2019 Kenya Population 23 <sup>24</sup> 414 and Housing Census. Births, deaths, and migrations in each EA are regularly updated by CHPs using the 25 <sup>26</sup> 415 integrated community health system maintained by the Ministry of Health. Fifty EAs are randomly selected 28 416 for our baseline survey, during which demographic information of all individuals is updated. To ensure 29 30 417 balanced cluster allocation, the baseline survey includes a questionnaire for all households, RDT testing of 31 32 <sub>33</sub> 418 all children aged 6 months to 14 years, and an entomological survey of randomly sampled households. We 34 35 419 modified the questionnaire used in the 2020 Kenya Malaria Indicator Survey (KMIS) mainly to quantify the 36 37 4 20 SES of each household and bed net usage. In addition, we add questions to quantify the favorability of 38 39 4 2 1 ceiling nets before the intervention. 40 41 422 42 <sup>43</sup> 423 Cohort monitoring 44 <sup>45</sup>.424 Incidence of clinical malaria in the prospective cohort will be estimated by both active and passive case 46 47 425 detections. For active case detection, we will conduct home visits every four weeks. From all cohort 48 49 .) 50 426 participants, axillary temperature will be measured using a digital thermometer, and Plasmodium infection 51 <sub>52</sub> 427 status will be determined by RDT and PCR. Participants with fever (>37.5°C) or other malaria-related 53 54 428 symptoms listed in the Kenya National Malaria Treatment Guideline at the time of home visit or within the 55 56 4 29 previous 48 hours will be tested for malaria by RDT. History of travel, confirmed malaria episode, and visit 57 58 4 3 0 to local health facilities since the previous visit is recorded. For passive case detection, we ask all cohort 59 60 4 3 1 participants to visit designated health facilities in case they suspect malaria between home visits. The

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designated facilities are asked to record all malaria tests performed regardless of their results together with the cohort ID. The cost of RDT and anti-malarial treatment will be covered by the research team to encourage cohort participants to use only designated facilities.

## Cross-sectional malariometric surveys

Malaria prevalence in children and adults will be estimated using cross-sectional malariometric surveys in communities. These surveys will be conducted at 6, 12, and 18 months post-installation. Community surveys will be conducted by house visits.

*Plasmodium* infection status will be determined using three methods: RDT, microscopy, and PCR. A fingerprick blood sample will be collected for on-site diagnosis using the Bioline Malaria Ag P.f/Pan RDT (Abbott Diagnostics Korea Inc., Republic of Korea). Survey participants with positive test results will be provided with a treatment course of artemether-lumefantrine with dosing instructions in accordance with guidelines from the Ministry of Health in Kenya after checking their recent treatment history. Blood smears will be prepared on site and transported to the main laboratory in Homa Bay where thin smears are fixed with methanol and all smears are stained with 3% Giemsa solution for 30 minutes, then examined by experienced microscopists. Two blood samples (70 µl each) will be collected with a 75-mm heparinized micro-hematocrit capillary tube (Thermo Fisher Scientific, MA, USA) and spotted on Whatman ET31 Chr filter paper (Whatman International. Maidstone, UK). The blood samples will be allowed to dry at ambient temperature and stored in individual zipped plastic bags at -20°C. The dried blood spots will be used for the determination of malaria status by PCR [23].

Entomological surveys

Indoor mosquitoes will be collected from five randomly selected houses within each cluster using the CDC light trap method. Samples will be preserved in 96% ethanol and placed in a cool box with ice. Specimens will be examined for sex determination by microscopy and species identification by microscopy and PCR. Indoor mosquitoes will be collected at baseline, 6, 12 and 18 months post ceiling net installation.

Social aspects

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We will conduct an exploratory sequential research design using integrated mixed methods (qualitative and quantitative). Qualitative assessment of community perceptions on the pyrethroid-PBO ceiling nets, community facilitators, and concerns of pyrethroid-PBO ceiling net use will be implemented, followed by quantitative assessments every 6 months and routine monitoring to evaluate the durability of pyrethroid-PBO ceiling nets using observation checklists in randomly sampled houses. At the end of the study, other qualitative case studies, such as focus group discussions and key informant interviews, will be conducted to document any remarks related to the study and inform the sustainability and scalability of the intervention.

Cost-effectiveness analysis

Incremental financial and economic cost data of pyrethroid-PBO ceiling net will be collected alongside the intervention. In cases where resources, such as staff, are shared among multiple elements, the allocation of costs will be carried out using an appropriate proxy. Costs related to research activities will be excluded from this allocation. Financial costs will be derived from project expenditure records, while economic costs, which encompass financial expenditures and donated resources, will be identified through project records and social aspects activities. The value of donated resources will be credited based on prevailing market rates. Furthermore, capital costs will be annualized over their useful life for financial costing and annualized at a discount rate of 3% for economic costing.

Plans to promote participant retention and complete follow-up {18b}

All surveys planned for the epidemiological and entomological domains will be conducted by house visits. CHPs will make an appointment with eligible participants before each visit to confirm the participants' available date and time. Small remunerations will be provided to survey participants to compensate for their time. CHPs will receive detailed instructions and participatory training for all field procedures and will be actively supervised by the research team throughout the duration of the study. Feedback will be regularly sought from CHPs regarding any issues raised by study participants, and discussions will be held to resolve issues from the field.

- 59
- Data management {19}

All data from the baseline, cohort, and cross-sectional surveys will be captured using the Research Electronic Data Capture (REDCap) software on electronic tablets. Data will be uploaded daily to a highly secure server hosted by Mount Kenya University (MKU). All data from the quantitative surveys will also be stored securely and backed up regularly to prevent data loss. Data access and management of databases will be limited to authorized study investigators and collaborators. After validation of data uploaded to the MKU server, data stored locally on the tablet computers will be permanently deleted to minimize unauthorized access.

**Confidentiality {27}** 

To maintain confidentiality, each participant in cross-sectional surveys, the longitudinal cohort, and the quantitative surveys is assigned a unique identifier. The data collected will be labelled using the unique identifier and stored separately from the key linking personal information (name, date of birth, GPS of each household, and phone number). The data will be kept on a secure server that is only accessible to the research staff. Publications will contain only aggregated data, and no personal information will be included.

# Plans for collection, laboratory evaluation and storage of biological specimens for genetic or molecular analysis in this trial/future use {33}

Anonymized blood samples from study participants will be stored and analyzed for Plasmodium infections by microscopy and PCR in our laboratory in Homa Bay. Microscopic examinations of adult mosquito specimens will be conducted in our field laboratory in Mbita, while PCR analyses will be conducted in our 508 laboratories in Homa Bay and MKU. Laboratory data outputs will be entered in Microsoft Excel and imported into the database. No human genetic analysis is planned for this study. However, remaining biological materials will be stored indefinitely for future studies unless the participants opt out during the informed consent process. Participants are provided with contact information of the research team and can remove themselves from this study or any future studies at any time without penalty or prejudice.

- 58 514 Statistical methods

#### 60 5 1 5 Statistical methods for primary and secondary outcomes {20a}

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We will follow the CONSORT guidelines extended for CRCT for statistical analysis and result reporting. The intention-to-treat (ITT) analysis is the primary analysis approach for both the primary and secondary objectives for the epidemiological and entomological studies. The per-protocol (PP) analysis is included as a supplementary analysis for the primary and secondary objectives for the epidemiological and entomological studies. Detailed methodologies for the epidemiological part are described in the supplementary file of statistical analysis plan.

#### Clinical malaria incidence

We will determine the protective efficacy of pyrethroid-PBO ceiling nets against malaria case incidence by comparing clinical malaria incidence rates between arms. We will use mixed effects negative binomial regression accounting for within-cluster correlation of outcomes. Possible confounding factors such as age, sex, bed net usage, house structure, malaria vaccination history, and SES will be adjusted as well as covariates used in the covariate-constrained randomization. In addition, because we will not set a buffer zone, the distance to the nearest household in the other arm will be adjusted in the following analysis to reduce the contamination between two arms. The variable was selected from the previous study [24].

#### Prevalence of malaria infection

The secondary outcome, the prevalence of malaria infection by PCR and microscopy measured at 6, 12, and 18 months after the ceiling net installation will be analyzed using mixed effects logistic regression adjusting for the above-mentioned confounding factors.

#### Exploratory analysis for spillover effects

Evidence for positive spillover effects of the ceiling net on malaria infection prevalence in all age groups will be assessed by comparing individuals with no intervention conditioning 1) the distance to the nearest ceiling net installed household, and 2) the coverage of surrounding households with ceiling net within 400 m. The distance of 400 m was chosen as the spillover effect appears to attenuate at this distance based on previous reports [25].

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## Entomology

Differences in vector density and EIR between arms will be evaluated by random effects negative binomial regression taking into account the intracluster correlation.

## Social aspects

We will employ the Framework for Reporting Adaptations and Modifications to Evidence-based Implementation Strategies (FRAME-IS) [26] to document the implementation processes of the ceiling nets, and the evidence integration triangle framework [27] to align the evidence generated to policy and vector control strategies from the health systems aspect. The theoretical framework in qualitative research will be grounded theory [28]. Data from ethnographic, focus group discussions, key informant interview will be summarized using content thematic analysis. Pre- and post-intervention acceptability to install pyrethroid-PBO ceiling net intervention will be compared to actual consent using logistic regressions.

## Cost-effectiveness

The economic and financial costs associated with the pyrethroid-PBO ceiling net intervention will be presented in total and disaggregated forms, highlighting the relative contribution of each program element to the overall program costs. To facilitate comparisons with other malaria vector control interventions, the costs will be converted into cost per household and per person receiving the intervention annually. Various program scenarios, such as different scales and durations, will be presented to estimate operational implementation costs. Compared to the control group, we will utilize the number of malaria cases averted in the pyrethroid-PBO ceiling net arm to calculate the DALYs averted using standard methods.

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## Interim analyses {21b}

No interim analysis is planned because neither the insecticide permethrin nor the synergist PBO as formulated in pyrethroid-PBO LLINs is known to pose significant health and safety risks [11,14].

## Methods for additional analyses (e.g. subgroup analyses) {20b}

We will perform the same analysis for three age subgroups ( $\leq$  59 months old; 5 years old to 14 years old; 15

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years old or older) to examine if the effects of pyrethroid-PBO ceiling net differ by age groups. In addition, we plan to use other machine learning methods to estimate the conditional average treatment effect (CATE), such as causal forests—which extend random forest algorithms for causal inference [29] —and the super learner algorithm, an ensemble method that combines multiple predictive models to improve accuracy [30].

# Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing

data {20c}

In the cohort, non-adherence to the intervention can be identified by monthly interviews. Participants who regularly sleep outside their homes will be removed from the analyses. The extent and patterns of missing data will be assessed once all data collection has been completed. If necessary, we will apply simple hotdeck imputation methods if the missing fraction for the covariate is <5% or appropriate multiple imputation approaches if the missing fraction for a covariable are  $\geq 5\%$ . If a non-ignorable portion of the subjects have missing values on a covariate (due to missing at random or missing completely at random), that covariate may be excluded in the model.

## Plans to give access to the full protocol, participant level-data and statistical code {31c}

This manuscript is the full protocol. The corresponding author will make the de-identified datasets or any future statistical code available upon reasonable request.

**Oversight and monitoring** 

## Composition of the coordinating centre and trial steering committee {5d}

The sampling team, composed of CHPs and laboratory technicians, set up a day-to-day communication group and exchanged their experiences. A local management team of study investigators from Kenya and Japan also joined this, leading and advising the activities and monitoring the sample and data integrity. A monthly meeting will be held by the steering committee composed of all key researchers from Kenya and Japan, including the principal investigator (PI) and co-PI, to monitor the progress of the trial.

Composition of the data monitoring committee, its role and reporting structure {21a}

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Our intervention is considered to be of a low-risk nature. The data safety monitoring committee will consist of two medical doctors who are independent from the project organizations and sponsor and have no competing interests. The primary responsibilities of this committee will be to periodically review selfreported adverse events derived from the monthly questionnaire in the cohort. All severe adverse events observed or reported during the study will be reported to the committee in a timely manner, and the committee will determine the relationship between the severe adverse events and the intervention. For additional credibility about study quality, the researchers will consult a third statistician, if necessary.

Adverse event reporting and harms {22}

In addition to the safety monitoring committee, researchers will compare self-reported non-serious adverse events such as coughs, rashes, and itches between the intervention and the control arms in the cohort and cross-sectional surveys. In the event of a study-related serious adverse event, the study team will convene a meeting immediately with the MOH and Homa Bay County Teaching and Referral Hospital representatives to review the case and take necessary action.

## Frequency and plans for auditing trial conduct {23}

A monthly meeting will be held during the follow-up period to ensure that all surveys and investigations are conducted according to the study protocol. The study is required to submit annual reports and renewal to ethical review boards of Osaka Metropolitan University, Japan, and Mount Kenya University, Kenya.

Plans for communicating important protocol amendments to relevant parties (e.g. trial participants, 46 47 ethical committees) {25}

Decisions on important trial amendments must be made through a formal procedure and will be approved by

institutional review boards (IRB) at Mount Kenya University and Osaka Metropolitan University. The

protocol in the clinical trials registry will also be updated accordingly.

#### 58 6 2 6 **Dissemination plans {31a}**

60 627 Study results will be shared with the study participants and communities, the Homa Bay County Government

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and the Kenya National Malaria Control Programme. Results will also be disseminated through publications, conferences and workshops to help the development of novel malaria control strategies in other malariaendemic countries. Suggestions from the participants will also help shape the future improvement of the intervention.

Discussion

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Global malaria progress has flatlined in recent years: targets of reductions in malaria morbidity and mortality and required funding by 2030 are all off track as of 2023[6]. In addition, *P. falciparum* with partial artemisinin resistance, which has been a problem in the Great Mekong Subregion (GMS) for more than a decade, is emerging independently in sub-Saharan Africa [2–6,31]. Novel interventions that are costeffective and widely accepted by local communities are urgently needed to contain the spread of artemisininresistant *P. falciparum* in sub-Saharan Africa.

Early results from our cluster randomized controlled trial of pyrethroid-PBO ceiling nets on Mfangano Island in Lake Victoria, Kenya suggest that ceiling nets can reduce *Plasmodium* prevalence and are positively received by the local communities. Nevertheless, there are regional differences in housing design, vector abundance and composition, and availability of malaria control interventions. As such the feasibility and acceptability of the ceiling net intervention are likely to depend on local eco-epidemiological context [32]. Furthermore, one of the secondary objectives in this study is to measure the spillover effects, i.e. how much a household that does not have a ceiling net benefits from living near a house with a ceiling net. This enables a broader understanding of the impact of the ceiling nets at the community level.

This trial has several limitations. First, although the study is designed as a cluster-randomized controlled 51 <sub>52</sub> 651 trial, contamination between intervention and control clusters cannot be excluded, as buffer zones between 53 54 652 intervention and control clusters cannot be created due to geographic proximity of houses and villages in the 55 56 653 ward. A recent study, however, has shown that the spillover effect of interventions on malaria can extend to 57 58 6 5 4 3 km [33], so buffer zones of a few hundred meters, as set out in many studies, may not be sufficient. We 59 60 655 will try to eliminate such contamination effects by integrating spatial data into our statistical model. Second,

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because of the visible nature of the ceiling net, we cannot exclude open-label and observer biases. It is conceivable that participants receiving ceiling nets may reduce their usage of conventional LLIN, as both interventions are made of the same materials and may be perceived to protect against malaria in the same manner. We aim to reduce such bias as much as possible through repeated reminders by CHPs that ceiling nets serve as an addition to and not a replacement of conventional LLINs. We will conduct surveys and indepth interviews to elicit participants' perceptions of the ceiling net, which can guide future messaging and implementation. To reduce observer bias, laboratory investigators and data analysts will be blinded. Third, in the study area, pyrethroid+PBO-incorporated LLINs were distributed in 2023. It may reduce the effect of our ceiling net intervention because pyrethroid+PBO-incorporated LLINs are more effective than non-PBOincorporated LLINs by targeting both Anopheles vectors with and without metabolic resistance to pyrethroids. Pyrethroid+PBO incorporated LLINs received a conditional endorsement from the World Health Organization (WHO) in 2017, and approximately half of the LLINs distributed in sub-Saharan Africa in 2022 were of this type [6]. Given the abundance of PBO-incorporated LLINs in the region, it is important to assess the effectiveness of the pyrethroid-PBO ceiling net as an addition to these LLINs to inform policy recommendations. Recently LLINs combining two different classes of insecticides have been shown to be superior to pyrethroid-based LLINs [34]. When these new LLINs become widely available, the effectiveness of pyrethroid-PBO ceiling nets needs to be re-investigated.

## 674 Trial status

The Baseline survey was started on April 8, 2024. The recruitment of the intervention participants and the
ceiling net installation were conducted in June 2024. The current protocol is version 6.0 as of November 11,
2024.

## 2 679 Abbreviations

4 680 ACT: artemisinin-based combination therapy

-6681 CHP: community health promoter

682 CRCT: cluster-randomized controlled trial

2	
<sup>3</sup> 683 4	CV: coefficient of variation
5 684 6	KHIS: Kenya Health Information System
<sup>7</sup> 685	ITN: insecticide treated nets
9 10 686	IRS: indoor residual spraying
$^{11}_{12}687$	LLIN: long-lasting insecticidal nets
13 14 688 15	MKU: Mount Kenya University
16 689 17	PBO: piperonyl butoxide
18 690 19	RDT: rapid diagnosis tests
20 691 21	VGSC: Voltage gated sodium channel
22 22 692	
23 09 <b>-</b> 24	
25 693 26	Declarations
27 694 28	Acknowledgements
29 695 30	We would like to express our sincere gratitude to this study's participants, field, and laboratory staff. In
31 696 32 33 697	addition, we acknowledge the collaboration and support of health offices in Homa Bay County, Kenya.
<sup>34</sup> <sup>35</sup> 698	Authors' contributions {31b}
<sup>37</sup> 38 699	AK and JG are co-principal investigators. AK is the guarantor. YKK, WK, and AK developed the original
<sup>39</sup> 40 700	concept. All authors discussed and contributed to the study protocol. YKK, WK, PO, KBM, JK, VO, JO,
41 42 701	SMM, KNBS, KK, ES, GO, and AK contributed the preparation of the baseline survey. YKK, WK, PO, BM,
43 44 702	TO, CWC, JK, SM, and MK drafted the manuscript. YKK, WK, CWC, MK, GO, and JG contributed to the
45 46 703	revisions of the draft of the manuscript. DY participated as a senior statistician. YKK and MK drafted the
48 704 49	statistical analysis plan (SAP) and WK, CWC, and DY revised. The authors read and approved the final
50 705	manuscript and SAP.
52 706	
<sup>54</sup> 707 55	Funding {4}
<sup>56</sup> 708 57	AK and JG received support from JICA/AMED joint research project (SATREPS) (Grant no.
<sup>58</sup> 709 59 709 60	20JM0110020H0002), Hitachi Fund Support for Research Related to Infectious Diseases, and Sumitomo

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2	
3 710 4	Chemical Corporation. The funding bodies play no role in the study design, data collection, analysis,
5 711 6	interpretation, and publication.
7 712 8 712	
9 10 <sup>713</sup>	Availability of data and materials {29}
11 12 12	The study regimes, consent forms, assent forms, and study-related materials are accessible from the
14 715	corresponding author. The final trial dataset will be available to all investigators. The corresponding author
16 716 17	will make the de-identified datasets and source codes for all analysis available upon reasonable request.
18 717 19	
20 718 21	Patient and public involvement
22 719 23	Although the study design was developed through discussions among the researchers, consultations with the
<sup>24</sup> 720 25	local population were conducted prior to initiating the baseline survey, and their input was incorporated into
<sup>26</sup> 721	the study. Community involvement will also be ongoing during the implementation of interventions and
<sup>28</sup> 29 30	research activities.
31 723	
33 724 34	Ethics approval and consent to participate {24}
35 725 36	Ethics approvals were received from Mount Kenya University Institutional Scientific Ethics Review
37 726 38	Committee (MKU-ISERC) (approval number: 2565) and the Ethics Committee in Osaka Metropolitan
39 727 40	University (approval number: 2024-068).
41 728 42	Written informed consents will be sought from study participants before the baseline survey, installation of
<sup>43</sup> 729 44	ceiling nets, each cross-sectional survey, and the start of prospective cohort surveys. In cross-sectional and
<sup>45</sup> 730 46	cohort surveys, informed assent will be obtained from children under the age of 15 who can understand the
47 48 49	study at a level appropriate for their development, in addition to the consent of a parent or legal guardian.
50 732	Participants have the right to withdraw from the study at any time, and the option to withhold previously
52 733	collected samples from any future analyses and studies.
54 734 55	The samples collected in this study may potentially be used for other research purposes. This is clearly stated
56 735 57	in the informed consent form. In such cases, we will obtain the necessary ethical approval and provide
58 736 59	participants with the chance to opt-out from this. All experiments will be carried out in adherence to WHO
60 737	requirements and the Declaration of Helsinki.

1			
2 3 738 4			
5 739 6	Con	esent for publication {32}	
7 740 8 740	We	will not present identifying images or other personal or clinical details of participants. The participant	
9 10 <sup>741</sup>	info	rmation materials and informed consent form are available from the corresponding author on request.	
11 12 742			
<sup>14</sup> 743 15	Competing interests {28}		
16 744 17	AK and JG were partially supported by a research grant from Sumitomo Chemical Corporation. Other		
<sup>18</sup> 745 19	authors had no competing interests.		
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Evaluation of the protective efficacy of Olyset®Plus ceiling nets for reduction of malaria incidence children in Homa Bay County, Kenya: statistical analysis plan for clinical and epidemiological outcomes

#### Version 6.0

Nov 1, 2024 prepared by Yura K Ko (yongra.ko@ki.se)

#### **SAP** revisions

Version	Date	Summary of Changes
1.0	Jan 23, 2024	First draft
2.0	Feb 5, 2024	Added more details based on collaborators' feedback
3.0	Mar 4, 2024	Revised by the senior statistician (Dr. Daisuke Yoneoka)
4.0	April 9, 2024	Revised based on collaborators' feedback
5.0	Jun 4, 2024	Changed the cohort monitoring interval to one month due to
		feasibility after discussion with CHPs and local research staff.
6.0	Nov 1, 2024	1) Removed the secondary objective of time-to-first infection
		because it is impossible to ascertain the outcome without initial
		parasite clearance at enrollment.
		2) Modified the definition of infection incidence based on the
		journal reviewer's comments.
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#### Introduction

Objectives

#### Primary objective:

• To determine the protective efficacy of pyrethroid-PBO (Olyset®Plus) ceiling nets in reducing malaria case incidence in children 6 months-14 years for 18 months post-intervention

#### Secondary objectives:

- 1. To determine the protective efficacy of pyrethroid-PBO ceiling nets in reducing malaria infection prevalence in all age groups at 6-, 12-, and 18-months post-intervention
- 2. To determine the spillover effects of pyrethroid-PBO ceiling nets in reducing malaria infection prevalence in all age groups at 6-, 12-, and 18-months post-intervention
- 3. To determine the protective efficacy of pyrethroid-PBO ceiling net in reducing malaria infection incidence in children 6 months to 14 years old over 18 months post-intervention.

#### Study Methods

#### Trial design

The study is a cluster-randomized controlled trial (CRCT) with 44 clusters evenly divided between the intervention and the control arms. Each cluster will be one or two villages consisting of at least 50 households. A baseline survey will be conducted to determine pre-intervention *Plasmodium* prevalence and to collect demographic and socioeconomic data for covariate-constrained randomization of clusters. The baseline survey will be conducted approximately one month before randomization. The post-intervention follow-up period will be 18 months. Thirty-eight children aged 6 months to 14 years from each cluster will be recruited and followed for 18 months as a cohort to determine the protective efficacy of the pyrethroid-PBO ceiling net on clinical malaria incidence (primary objective) and *Plasmodium* infection incidence (secondary objectives). Cross-sectional surveys will be conducted at 6, 12, and 18 months post-intervention targeting 50 individuals of all ages from each cluster to determine the overall *Plasmodium* prevalence and to estimate the spillover effect (secondary objectives).

#### Randomization

After the baseline survey, covariate-constrained randomization will be used to allocate the 44 clusters across the two study arms. Covariate-constrained allocation ensures that the arms are balanced overall by excluding allocations where predetermined factors are not balanced within set margins. The following factors will be constrained: baseline malaria infection prevalence by RDT in children aged 0.5–14 years, LLIN usage, malaria vaccine coverage, socioeconomic status (SES), population size, the proportion of eligible houses for the ceiling net installation, and vector densities.

For the proportions of interest, we require the average difference between the arms of no more than 10% for the means of interest, and we require the difference in means to be no more than a quarter of the standard deviation of the variable among individuals in the population. After enumerating the allocations that fulfil the criteria, we may relax or tighten up the balance criteria when the allocated number is too small or very large. One allocation will be selected randomly among all possible allocations meeting the balancing constraints. Data on any additional potentially confounding ecological factors not included in the covariate-constrained randomization will be collected and adjusted for in the analysis. An independent statistician will perform the randomization.

#### Sample size

The sample size was calculated using the method of Hayes and Moulton<sup>1</sup>. All sample sizes will be recalculated based on the baseline data, which will be collected before the ceiling net installation.

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The following calculations were based on the historical data collected from the same Lake Victoria region in Kenya with a clinical malaria incidence rate of 0.5 per person-year for children under 14 years old by RDT (personal communication), 40% parasite prevalence for all age groups by PCR, and a betweencluster coefficient of variation (CV) of incidence rate = 0.24 in both arms. In the study site, RTS, S vaccination began in 2019, with an additional mass distribution of pyrethroid-PBO LLINs at the end of 2023. Therefore, the intervention effect is expected to be smaller than in previous studies and was conservatively assumed to be 25%. Assuming 38 individuals per cluster to be followed for up to 18 months with 20 % loss-to-follow up rate, we require 22 clusters per arm to achieve 80% power to detect a significant incidence rate ratio of 0.75 (25% protective efficacy) at a two-sided type 1 error of 5%. With 44 clusters and 50 individuals per cluster, for the outcome of *Plasmodium* prevalence by PCR, we would achieve 80% power to detect a 23.5 % relative reduction. We do not specify the sample size for identifying spillover effects because spillovers tend to have smaller effect sizes relative to total or overall effects, so typically larger sample sizes are required to detect them. Although our study may be underpowered to detect spillovers, we will report the results as an exploratory analysis.

#### Framework

Our null hypothesis for the primary outcome is that pyrethroid-PBO ceiling nets + standard malaria treatment and prevention measures do not reduce the clinical malaria incidence compared to standard malaria treatment and prevention measures in children 6 months to 14 years at 18 months post-intervention.

#### Statistical interim analyses and stopping guidance

Neither the ceiling nets nor synergist PBO are known to pose significant health and safety risks. This has also been demonstrated in our previous CRT on Mfangano Island<sup>2</sup>. Therefore, no interim analysis is planned.

#### Timing of final analysis

We will conduct the final analysis after 18 months of follow-up. Results will immediately be submitted for publication in peer-reviewed journals.

Timing of outcome assessments



Figure1: Timetable of trial activities

#### Statistical Principles

#### Confidence intervals and P values

We will use a two-sided significance level of  $\alpha = 0.05$  for hypothesis testing. All statistical tests will be conducted at this predetermined level of significance unless otherwise specified. For each estimated parameter, 95% confidence intervals will be calculated and reported.

#### Adherence and protocol deviations

Since the intervention (ceiling net) will be installed in trial participants' houses, participants not sleeping in their own houses will not benefit from the intervention. In the cohort, non-adherence to the intervention can be inferred from travel history during monthly interviews. Therefore, participants who regularly sleep outside their homes will be removed from the analyses. In addition, if a cohort participant is absent for three consecutive visits or for more than half of all visits, the child will be excluded from the analysis. Other protocol deviations will be carefully documented and categorized during the study.

#### Analysis populations

The intention to treat (ITT) analysis is the primary analysis approach for both the primary and secondary objectives. The per-protocol (PP) analysis is included as a supplementary analysis for the primary and secondary objectives.

## So So th

Trial population

#### Screening data

Screening data will be collected during the cohort enrollment and each cross-sectional survey to assess the eligibility of potential participants. This information will include demographic characteristics such as age, sex, SES, and other relevant parameters outlined in the study protocol.

#### Eligibility

The inclusion criteria for the installation of the pyrethroid-PBO ceiling net are (1) residential structures housing at least one permanent resident aged 18 years or older in the household, (2) informed consent provided by at least one adult in the household and (3) applicable house structure for the ceiling net in terms of size of the structure, presence of eave, ceiling board, and vertical beams, and material of the top part of the wall. The applicability of the ceiling net installation will be assessed by experienced field staff. The exclusion criteria are (1) vacant dwelling structure (confirmed by at least two visits by CHPs), (2) dwelling structure to be vacated or destroyed within the study period and (3) non-eligible house structure for the ceiling net installation.

The inclusion criteria for prospective cohorts of children aged 6 months to 14 years old are (1) living in the study area at the time of pyrethroid-PBO ceiling net installation, (2) having no plan to leave or stay outside the study area for an extended period (longer than 1 month) over the 18-month follow-up period, and (3) informed consent provided by the participant's parent or guardian. The exclusion criterion is having severe chronic illnesses.

The inclusion criteria for cross-sectional malaria surveys for all age groups are (1) living in the study area during the study period, and (2) informed consent being provided by the parent or legal guardian before each survey. The exclusion criterion is having severe chronic illnesses.

#### Recruitment

For the baseline survey, we will randomly choose 50 enumeration areas (comprising one or two villages) in Kanyamwa Kologi Ward, Ndhiwa Sub-County. The survey includes a questionnaire for all households, mRDT testing of all children aged 6 months to 14 years. We will not create buffer zones to minimize contamination since a buffer zone of 400–600 m from the boundary will greatly reduce the number of houses in the core area available for analysis in many clusters. Thirty-eight eligible children will be randomly recruited into our cohort in each cluster. Recruitment will be limited to children aged 12 or younger, to prevent children from aging out during the 18 months monitoring period. For the cross-sectional survey at each time point, we will randomly select 50 individuals of all age groups from each

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cluster. To reflect the age structure of the populations, the selection will be done with age category stratifications.

#### Withdrawal/follow-up

Those who migrate between the arms or emigrate from the study areas, or those who dismount the ceiling net from their house structure will be dropped from the intervention. For the cohort, those who are absent for three consecutive visits or for more than half of all visits will be excluded from the analysis as lost to follow-up. A summary of study participant selection is shown in Figure 2.





#### **Baseline characteristics**

We will report a list of baseline characteristics of the intervention and control arms. The list will include population, mean number of people per household, median age of population, number of selected children

for the cohort monitoring, number of selected individuals for each cross-sectional survey, malaria infection prevalence by RDT in children aged 0.5–14 years, LLIN usage, malaria vaccine coverage among children, SES, the proportion of suitable houses for the ceiling net installation, the mean indoor vectors per household per night.

#### Analysis

#### Endpoints

#### Primary endpoint:

• Overall malaria case incidence in children 6 months-14 years among intervention and control clusters during the 18-month follow-up period.

#### Secondary endpoints:

- 1. Malaria infection prevalence by PCR at 6, 12, and 18 months post-intervention in all age groups among intervention and control clusters.
- Malaria infection incidence by PCR in children 6 months-14 years among intervention and control clusters during the 18-month follow-up period.

#### Definition of malaria case incidence

Incidence of clinical malaria in the prospective cohort will be estimated by both active and passive case detections. For active case detection, we will visit the home of cohort participants every month. At each monthly visit, axillary temperature will be taken from each cohort participant. A clinical case is defined as positive mRDT accompanied by fever (>37.5°C) or any malaria-related symptoms during or within 48 hours of the home visit. All participants with positive mRDT will be treated with artemether-lumefantrine (artemisinin-based combination therapy [ACT]). For passive case detection, we ask all cohort participants to visit designated health facilities in case they suspect malaria between home visits. If two consecutive RDTs are positive, there are two patterns: active case detection or passive case detection for the detection of the second positive. If the second positive RDT is detected by active case detection, we will refer the child to a health facility and regard it as a new malaria infection if subsequent microscopy or PCR confirms parasites after 15 days or more passive case detection of a second RDT positive, we will regard it as a new malaria infection if as a new malaria the first RDT test. If not, it is considered a carryover from the previous infection. For the passive case detection of a second RDT positive, we will regard it as a new malaria infection if subsequent test.

For the overall incidence rate calculation, the time at the risk will be adjusted by subtracting the 14 days

of "protection period" of ACT. If a participant misses a particular visit or a second positive is considered a carryover from the previous infection, the period is not included in the at-risk period.

If the cohort children visit health care facility and get tested for malaria between each visit, both positive and negative results will be utilized for our analysis. Specifically, the 14 days prior to the test result will be incorporated into the denominator of the incidence calculation as the at-risk period. Specific patterns for incidence rate calculation are shown in Figure 3.

If a participant is absent for three consecutive visits or for more than half of all visits, the child will be excluded from the analysis.

#### Definition of malaria infection incidence

In addition, we will test all cohort children by PCR every month. For the secondary outcome, the infection incidence is defined as the total number of monthly PCR-positive tests per individual divided by the total number of tests conducted per individual per time period, as described in Bennett et al<sup>3</sup>. If two consecutive PCR results are positive, the second positive result will be removed only if no treatment was provided in the previous month. Furthermore, as a supplementary analysis, we will include passively detected cases in the infection incidence counts to capture any new infections after the passive case treatment by each health center. Passively detected positives will be assigned to the closest active visit–either the one immediately before or after the passive case detection–depending on which is closer in time.

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#### Analysis methods

We will follow the CONSORT guidelines extended for CRT<sup>4</sup> for the statistical analysis and results reporting.

#### Clinical malaria incidence

We will determine the protective efficacy of pyrethroid-PBO ceiling nets against malaria case incidence by comparing clinical malaria incidence rates between arms. We will use mixed effects negative binomial regression accounting for within-cluster correlation of responses by following equations:

$$\mu_{k,i} = \exp \left(\beta_0 + \boldsymbol{x}_{k,i}^T \boldsymbol{\beta} + z_k\right),$$
$$z_k \sim N(0,\sigma^2),$$

where  $\mu_{k,i}$  is the mean incidence rate of individual *i* in cluster *k*,  $x_{k,i}$  is the covariate vector including individual and cluster level data,  $z_k$  is the Gaussian-type random effect at the cluster level. The protective efficacy will be estimated by  $(1 - \exp(\hat{\beta})) \times 100\%$ , where  $\hat{\beta}$  is the estimated regression coefficient of the treatment. Possible confounding factors such as age, sex, bed net usage, house structure, and SES will be adjusted as well as the covariates used in the covariate-constrained randomization. In addition, because we will not set a buffer zone, the distance to the nearest household in the other arm will be adjusted as a covariate to reduce the contamination between two arms. The variable was selected from the previous study<sup>5</sup>.

#### Prevalence of malaria infection

The secondary outcome, prevalence of malaria infection by PCR and microscopy measured at 6-, 12-, and 18-months after the ceiling net installation will be analyzed using mixed effects logistic regression adjusting for the above-mentioned confounding factors.

#### Exploratory analysis for spillover effects

Evidence for positive spillover effects of the ceiling net on malaria infection prevalence of all age group will be assessed by comparing individuals with no intervention conditioning 1) the distance to ceiling net installed household, and 2) the coverage of surrounding households with ceiling net within 400 m (Figure 4). The distance of 400 m was chosen as the spillover effect appears to attenuate at this distance based on previous reports<sup>6</sup>. As there may be a bias that households without a ceiling net in the intervention cluster have different characteristics (e.g. preventive behaviour against malaria), we will include only control clusters for the spillover analysis to ensure comparability.

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- 🚹 : Household with ceiling net
- : Household without ceiling net

*d*: the distance to the nearest discordant household *c*: the coverage of surrounding households with ceiling net within 400 m Household with ceiling net

Figure 4: The distance to the nearest discordant household and the coverage of treatment.

#### Missing data

We will make substantial effort to avoid having missing values on outcome (malaria infection status and visit dates) by encouraging individual participants and CHPs repeatedly. When missing values occur for an outcome for reasons not related to the outcome, reasons for missingness and the missing fraction by treatment arm and cluster will be reported. Per protocol, the subjects are screened actively on their malaria status (the outcome) every four weeks.

In both cases, all the available data from the subject will be included in the primary and secondary analysis, without employing any specific missing data analysis techniques, due to the ignorability of the missing mechanisms. Missing baseline covariates (individual-level, household-level, and cluster-level) that are a part of the regression models for the outcome of interest will be imputed using simple hot-deck imputation methods if the missing fraction for the covariate is <5%. If the missing fraction for a covariable is  $\geq5\%$ , appropriate multiple imputation approaches will be applied. If a non-ignorable portion of the subjects have missing values on a covariate (due to missing at random or missing completely at random), that covariate may be excluded in the model.

#### Additional analysis

We will perform the same analysis for three age subgroups ( $\leq$  59 months old; 5 years old to 14 years old; 15 years old or older) to examine if the effects of pyrethroid-PBO ceiling net differ by age groups. In addition, we will perform other machine learning based approach such as causal forest and super learner to estimate the conditional average treatment effect.

#### Harms

All unanticipated problems will be reported to the research team and Homa Bay County Ministry of Health (MOH) through CHPs. Medical officers from Homa Bay County will assess the relatedness of the reported events to the study and report to the research team, including the PI. In the event of a study-related serious adverse event, the study team will convene a meeting immediately with the MOH and Homa Bay County Teaching and Referral Hospital representatives to review the case and take necessary action. Also, the ceiling net is made of the same materials and chemicals as LLIN already on the market, and is therefore not expected to have significant environmental impact.

#### Statistical software

For all data handling and analysis, we will use R software version 4.3.2 (R Core Team (2021). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <u>https://www.R-project.org/.</u>)

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### 0. Consent form

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Thank you!	
Please make sure to show the consent form on the tablet.	
I have read the information about the study and have received answers to any questions I asked. I consent to take part in all the activities mentioned above.	<ul><li>○ Yes</li><li>○ No</li></ul>
Name of participant	
Signature of participant	
Name of witness	
Signature of witness	
Do you have a child to participate in the study?	<ul><li>○ Yes</li><li>○ No</li></ul>
Check the following box.	<ul> <li>I DO CONSENT: I do agree my child to take par in this study.</li> <li>I DO NOT CONSENT: I do not wish my child to rticipate in this study.</li> </ul>
Parent/Guardian's name	
Parent/Guardian's signature	
Witness: I hereby confirm that the study has been explained to the parent/ guardian. All questions (if any) have also been answered to his/ her satisfaction, and he/ she, of his/ her own free will, has consented for his/ her child to take part in the study.	
Name of witness	
Cine at the state of the second	

id1	
id2	
id3	
'[id1]-[id2]-[id3]"	
Please fix the structure ID above on the roof in front of the door.	
Date	

# Page 55 of 90 **1. Structure**

Please complete the survey below.	
Thank you!	
Longitude	
Latitude	
Is this structure the first registration in the household?	○ Yes ○ No
Record the structure ID of the first structure in this household	
(i.g. 12-1-7 )	
Name of the village	
What is the main source of drinking water for members of your household?	<ul> <li>PIPED INTO DWELLING</li> <li>PIPED TO YARD/PLOT</li> <li>PIPED TO NEIGHBOR</li> <li>PUBLIC TAP/STANDPIPE</li> <li>DUG PROTECTED WELL</li> <li>DUG UNPROTECTED WELL</li> <li>WATER FROM PROTECTED SPRING</li> <li>WATER FROM UNPROTECTED SPRING</li> <li>RAINWATER</li> <li>TANKER TRUCK</li> <li>CART WITH SMALL TANK</li> <li>SURFACE WATER (RIVER/DAM/LAKE/POND/STREA/ /IRRIGATION CHANNEL)</li> <li>BOTTLED WATER</li> <li>OTHER</li> </ul>
Specify it.	
What is the main source of water used by your household for other purposes such as cooking and handwashing?	<ul> <li>PIPED INTO DWELLING</li> <li>PIPED TO YARD/PLOT</li> <li>PIPED TO NEIGHBOR</li> <li>PUBLIC TAP/STANDPIPE</li> <li>DUG PROTECTED WELL</li> <li>DUG UNPROTECTED WELL</li> <li>WATER FROM PROTECTED SPRING</li> <li>WATER FROM UNPROTECTED SPRING</li> <li>RAINWATER</li> <li>TANKER TRUCK</li> <li>CART WITH SMALL TANK</li> <li>SURFACE WATER (RIVER/DAM/LAKE/POND/STREA/IRRIGATION CHANNEL)</li> <li>OTHER</li> </ul>

Where is that water source located?	<ul> <li>IN OWN DWELLING</li> <li>IN OWN YARD/PLOT</li> <li>ELSEWHERE</li> </ul>
How long does it take to go there, get water, and come back? (MINUTES)	
What kind of toilet facility do members of your household usually use? IF NOT POSSIBLE TO DETERMINE, ASK PERMISSION TO OBSERVE THE FACILITY.	<ul> <li>FLUSH TO PIPED SEWER SYSTEM</li> <li>FLUSH TO SEPTIC TANK</li> <li>FLUSH TO PIT LATRINE</li> <li>FLUSH TO SOMEWHERE ELSE</li> <li>FLUSH, DON'T KNOW WHERE</li> <li>VENTILATED IMPROVED PIT LATRINE</li> <li>PIT LATRINE WITH SLAB</li> <li>PIT LATRINE WITHOUT SLAB/OPEN PIT</li> <li>COMPOSTING TOILET</li> <li>BUCKET TOILET</li> <li>HANGING TOILET/HANGING LATRINE</li> <li>NO FACILITY/BUSH/FIELD</li> <li>OTHER</li> </ul>
Specify it.	
Do you share this toilet facility with other households?	<ul><li>○ Yes</li><li>○ No</li></ul>
Including your own compound, how many households use this toilet facility?	O LESS THAN 10 HOUSEHOLDS O 10 OR MORE HOUSEHOLDS O DON'T KNOW
Including your own household, how many households use this toilet facility (if less than 10)?	2
Where is this toilet facility located?	<ul> <li>○ IN OWN DWELLING</li> <li>○ IN OWN YARD/PLOT</li> <li>○ ELSEWHERE</li> </ul>
In your household, what type of cooking device (cookstove) is mainly used for cooking?	<ul> <li>ELECTRIC STOVE</li> <li>SOLAR COOKER</li> <li>LIQUEFIED PETROLEUM GAS (LPG)/COOKING GAS</li> <li>PIPED NATURAL GAS STOVE</li> <li>BIOGAS STOVE</li> <li>LIQUID FUEL STOVE</li> <li>MANUFACTURED SOLID FUEL STOVE (i.g. Jiko)</li> <li>THREE STONE STOVE/OPENFIRE</li> <li>NO FOOD COOKED IN THE HOUSEHOLD</li> <li>OTHER</li> </ul>
Specify it.	

What type of fuel or energy source is mainly used in this cookstove?	<ul> <li>ALCOHOL/ETHANOL</li> <li>GASOLINE/DIESEL</li> <li>KEROSENE/PARAFFIN</li> <li>COAL/LIGNITE</li> <li>CHARCOAL</li> <li>WOOD</li> <li>STRAW/SHRUBS/GRASS</li> <li>AGRICULTURAL CROP</li> <li>ANIMAL DUNG/WASTE</li> <li>PROCESSED BIOMASS (PELLETS) OR WOODCHIPS</li> <li>GARBAGE/PLASTIC</li> <li>SAWDUST</li> <li>OTHER</li> </ul>
Specify it.	
How many rooms in this household are used for sleeping?	
Does this household own any livestock, herds, other farm animals, or poultry?	○ Yes ○ No
How many of the following (animals) livestock does this household own?	
- Local cattle (indigenous)	
How many of the following (animals) livestock does this household own?	
- Exotic/grade cattle	
How many of the following (animals) livestock does this household own?	2
- Horses	
How many of the following (animals) livestock does this household own?	
- Donkeys	1
How many of the following (animals) livestock does this household own?	
- Mules	
How many of the following (animals) livestock does this household own?	
- Goats	
How many of the following (animals) livestock does this household own?	
- Sheep	

How many of the following (animals) livestock does this household own?		
- Chickens or other poultry		
How many of the following (animals) livestock does this household own?		
- Pigs		
Does any member of this household own any agricultural land?	<ul><li>○ Yes</li><li>○ No</li></ul>	
Do you know how many acres of agricultural land do members of this household own?	<ul><li>○ Yes</li><li>○ No</li></ul>	
How many acres of agricultural land do members of this household own?		
ACRES		/rignı,
Does your household have:	<ul> <li>Electricity?</li> <li>A radio?</li> <li>A television?</li> <li>A fixedlinetelephone?</li> <li>A computer?</li> <li>A computer?</li> <li>A refrigerator?</li> <li>A solarpanel?</li> <li>A table?</li> <li>A chair?</li> <li>A chair?</li> <li>A sofa?</li> <li>A bed?</li> <li>A clock?</li> <li>A microwave oven?</li> <li>A DVD player?</li> <li>A CD player?</li> </ul>	Including for uses related to text and data minin
Does any member of this compound own:	<ul> <li>A wrist watch?</li> <li>A mobile phone?</li> <li>A bicycle?</li> <li>A motorcycle or motor scooter?</li> <li>An animal-drawn cart?</li> <li>A car or truck?</li> <li>A boat with a motor?</li> </ul>	iy, Ai naminy, and si
Does any member of this household have an account in a bank or other financial institution?	<ul><li>○ Yes</li><li>○ No</li></ul>	
Does any member of this household use a mobile phone to make financial transactions such as sending or receiving money, paying bills, purchasing goods or services, or receiving wages?	<ul><li>○ Yes</li><li>○ No</li></ul>	
In the past year, has this household ever used mosquito repellent spray (e.g. Doom), ointments, vaporizers coils, herbs, or plants to protect against mosquitoes/malaria?	○ Yes ○ No	

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Does your household have any bed nets?	<ul><li>○ Yes</li><li>○ No</li></ul>
How many mosquito nets does your household have?	
Will you accept to install the ceiling net if you are offered?	○ Yes ○ No
What is the reason for not installing the ceiling net? Select all that apply.	<ul> <li>Air flow disturbance</li> <li>Heat</li> <li>Appearance</li> <li>Pets</li> <li>Fire</li> <li>Social culture and religious factor</li> <li>Others</li> </ul>
Specify it	
Do you have any concerns about the ceiling net? Select all that apply.	<ul> <li>Air flow disturbance</li> <li>Heat</li> <li>Appearance</li> <li>Pets</li> <li>Fire</li> <li>Social culture and religious factor</li> <li>No concern</li> <li>Others</li> </ul>
Specify it	2
OBSERVE MAIN MATERIAL OF THE FLOOR OF THE DWELLING/SLEEPING ROOM. RECORD OBSERVATION.	<ul> <li>EARTH/SAND</li> <li>DUNG</li> <li>WOOD PLANKS</li> <li>PALM/BAMBOO</li> <li>PARQUET OR POLISHED WOOD</li> <li>VINYL OR ASPHALT STRIPS</li> <li>CERAMIC TILES</li> <li>CEMENT</li> <li>CARPET</li> <li>OTHER</li> </ul>
Specify it.	

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OBSERVE MAIN MATERIAL OF THE ROOF OF THE DWELLING. RECORD OBSERVATION.	<ul> <li>NO ROOF</li> <li>THATCH/PALM LEAF</li> <li>RUSTIC MAT</li> <li>PALM/BAMBOO</li> <li>WOOD PLANKS</li> <li>CARDBOARD</li> <li>IRON SHEETS</li> <li>WOOD</li> <li>CALAMINE/CEMENT FIBER</li> <li>BRICK/CLAY TILES</li> </ul>
Specify it.	<ul> <li>CEMENT</li> <li>ROOFING SHINGLES</li> <li>OTHER</li> </ul>
OBSERVE MAIN MATERIAL OF THE EXTERIOR WALLS OF THE DWELLING. RECORD OBSERVATION.	<ul> <li>NO WALLS</li> <li>WOOD WITH MUD</li> <li>IRON SHEET</li> <li>BRICKS</li> <li>CANE/PALM/TRUNKS</li> <li>BAMBOO WITH MUD</li> <li>STONE WITH MUD</li> <li>UNCOVERED ADOBE</li> <li>PLYWOOD</li> <li>CARDBOARD</li> <li>REUSED WOOD</li> <li>CEMENT</li> <li>STONE WITH LIME/CEMENT</li> <li>CEMENT BLOCKS</li> <li>COVERED ADOBE</li> <li>WOOD PLANKS/SHINGLES</li> <li>OTHER</li> </ul>
Specify it.	2
OBSERVE EAVES OF THE DWELLING.	⊖ Open
RECORD OBSERVATION.	<ul> <li>Partly open</li> <li>Close</li> </ul>
OBSERVE BEAMS OF THE DWELLING.	O No vertical beam
RECORD OBSERVATION.	<ul> <li>One vertical beam</li> <li>More than one vertical beams</li> </ul>
Tick all that apply	<ul> <li>2 or more vertical beams in the same room</li> <li>Ceiling board/ Flat roof</li> <li>The roof is very low</li> <li>The room is used for kitchen</li> <li>None</li> </ul>
Has this structure been done with IRS (Indoor Residual Spraying) within three years?	○ Yes ○ No
When did you have IRS?	☐ 2021 ☐ 2022 ☐ 2023 ☐ Don't know

		$\bigcirc$ res	
"Living" means that the child usua household. If the child is usually s boarding school, but now he/she i house because of a school closure regarded as "living".	ally stay in the taying at a is staying in this a, that is not		
Once you complete, "Show More S	Save Options">"Save &	Go to Next Form"	

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### 2. Children

Please complete the survey below.

Thank you!

But RDT tests are for children from 6 month to 14 years old	d.
RECORD TWINS AND TRIPLETS SEPARATELY.	
What name was given to the child?	
First name	
What name was given to the child?	
Middle name	
What name was given to the child?	
_ast name	
s the child a boy or a girl?	O BOY O GIRL
Nas that a single or multiple pregnancy?	O SING O MULT
Do you know the birthday of the child?	⊖ Yes ⊖ No
On what day, month, and year was the child born?	
How old was the child at the last birthday?	
The birthday and your age are contradicting. Please check	the true age again.
s the child living with you?	
Living with" means that you and the child usually stay in the same household. If the child is usually staying at a boarding school, but now he/she is being with you because of a school closure, that is not regarded as "living with you".	U NO
Has the child been ill with a fever at any time in the ast 2 weeks?	<ul> <li>○ YES</li> <li>○ NO</li> <li>○ DON'T KNOW</li> </ul>

blood taken from a finger or heel for testing?	
Nere you told by a healthcare provider that the child nad malaria?	<ul> <li>YES</li> <li>NO</li> <li>ODON'T KNOW</li> </ul>
Did you seek advice or treatment for the illness from any source?	<ul><li>○ Yes</li><li>○ No</li></ul>
How many times did you seek advice or treatment for he illness from any source?	
Where did you first seek advice or treatment? Anywhere else? PROBE TO IDENTIFY THE TYPE OF SOURCE. F UNABLE TO DETERMINE IF PUBLIC, PRIVATE, OR NGO SECTOR, RECORD 'OTHER'	<ul> <li>GOVERNMENT HOSPITAL</li> <li>GOVERNMENT HEALTH CENTER</li> <li>GOVERNMENT DISPENSARY</li> <li>GOVERNMENT MOBILE CLINIC</li> <li>COMMUNITY HEALTH WORKER/FIELD WORKER</li> <li>PRIVATE HOSPITAL</li> <li>PRIVATE CLINIC</li> <li>PHARMACY</li> <li>PRIVATE MOBILE CLINIC</li> <li>COMMUNITY HEALTH WORKER</li> <li>SHOP</li> <li>TRADITIONAL PRACTITIONER</li> <li>MARKET</li> <li>ITINERANT DRUG SELLER</li> <li>OTHER</li> </ul>
Specify it.	
Where did you second seek advice or treatment? Anywhere else? PROBE TO IDENTIFY THE TYPE OF SOURCE. F UNABLE TO DETERMINE IF PUBLIC, PRIVATE, OR NGO SECTOR, RECORD 'OTHER'	<ul> <li>GOVERNMENT HOSPITAL</li> <li>GOVERNMENT HEALTH CENTER</li> <li>GOVERNMENT DISPENSARY</li> <li>GOVERNMENT MOBILE CLINIC</li> <li>COMMUNITY HEALTH WORKER/FIELD WORKER</li> <li>PRIVATE HOSPITAL</li> <li>PRIVATE CLINIC</li> <li>PHARMACY</li> <li>PRIVATE DOCTOR</li> <li>PRIVATE MOBILE CLINIC</li> <li>COMMUNITY HEALTH WORKER</li> <li>SHOP</li> <li>TRADITIONAL PRACTITIONER</li> <li>MARKET</li> <li>ITINERANT DRUG SELLER</li> <li>OTHER</li> </ul>
Specify it.	

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Where did you third seek advice or treatment? Anywhere else? PROBE TO IDENTIFY THE TYPE OF SOURCE. IF UNABLE TO DETERMINE IF PUBLIC, PRIVATE, OR NGO SECTOR, RECORD 'OTHER'	<ul> <li>GOVERNMENT HOSPITAL</li> <li>GOVERNMENT HEALTH CENTER</li> <li>GOVERNMENT DISPENSARY</li> <li>GOVERNMENT MOBILE CLINIC</li> <li>COMMUNITY HEALTH WORKER/FIELD WORKER</li> <li>PRIVATE HOSPITAL</li> <li>PRIVATE CLINIC</li> <li>PHARMACY</li> <li>PRIVATE DOCTOR</li> <li>PRIVATE MOBILE CLINIC</li> <li>COMMUNITY HEALTH WORKER</li> <li>SHOP</li> <li>TRADITIONAL PRACTITIONER</li> <li>MARKET</li> <li>ITINERANT DRUG SELLER</li> <li>OTHER</li> </ul>
Specify it.	
How many days after the illness began did you first seek advice or treatment for the child?	
IF THE SAME DAY RECORD '0'.	
At any time during the illness, did the child take any medicine for the illness?	<ul><li>○ Yes</li><li>○ No</li></ul>
What medicine did the child take? Any other medicine? RECORD ALL MENTIONED. IF MEDICINE NOT KNOWN, ASK TO SEE THE PACKAGE OR PRESCRIPTION.	AL DHAP OTHER ACT (NOTALORDHAP) SP/FANSIDAR CHLOROQUINE AMODIAQUINE QUININE (PILLS) QUININE (INJECTION/IV) ARTESUNATE (RECTAL) ARTESUNATE (INJECTION/IV) OTHER ANTIMALARIAL AMOXICILLIN COTRIMOXAZOLE OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP) OTHER ANTIBIOTIC MEDICINE (INJECTION/IV) ASPIRIN PARACETAMOL/PANADOL/ACETAMINOPHEN IBUPROFEN OTHER DON'TKNOW
Specify it.	
How long after the fever started did the child first take an artemisinin-based combination therapy?	<ul> <li>SAME DAY</li> <li>NEXT DAY</li> <li>TWO DAYS AFTER FEVER</li> <li>THREE OR MORE DAYS AFTER FEVER</li> <li>DON'TKNOW</li> </ul>
Has [mis_wo213_1] received a malaria vaccine?	○ Yes ○ No

How many times has [mis_wo213_1] received malaria vaccine?	<ul> <li>1 dose</li> <li>2 doses</li> <li>3 doses</li> <li>4 doses</li> <li>Don't know</li> </ul>	
Where does [mis_wo213_1] usually sleep?	<ul> <li>Bed room</li> <li>Kitchen room</li> <li>Others</li> </ul>	
Specify it.		
Where Is [mis_wo213_1] usually living?	<ul> <li>This household</li> <li>Boarding school</li> <li>Relative's house outside the village</li> <li>Others</li> </ul>	
Specify it.		
Did [mis_wo213_1] spend any nights outside your house in the last 30 days?	<ul><li>○ Yes</li><li>○ No</li></ul>	
Where did [mis_wo213_1] spend those nights?	<ul> <li>Another house in Ndhiwa Sub-county</li> <li>Homa Bay county other than Ndhiwa</li> <li>Another county in Kenya</li> <li>Another country</li> </ul>	
How many nights did [mis_wo213_1] spend in another house in Ndhiwa?		
How many nights did [mis_wo213_1] spend in another house in Homa Bay County other than Ndhiwa?	2	
Specify the Sub-county name.	-0	
How many nights did [mis_wo213_1] spend in another house in another county in Kenya?	2	
Specify the county name.		
How many nights did [mis_wo213_1] spend in another house in another country?		
Specify the country name.		
Did the child sleep under a bed net last night?	<ul><li>○ Yes</li><li>○ No</li></ul>	
RDT result for P.f	O Negative	

RDT result for Pan	<ul> <li>Negative</li> <li>Positive</li> </ul>
If there is another child, press "Show More S	ave Options">"Save & Add New Instance
otherwise, press "Show More Save Options">	Go to Next Form".

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### 3. Adults

1	
2	Please complete the survey below.

Thank you!	
Now, we would like to record the names of all adults who live Do not include a person who stays only a few days in a montl	e in this household on a permanent or weekly basis. h.
First name	
Middle name	
Last name	
Choose from the below. Sleep in this structure More than half of the week = Permanent Few days in a week regularly = Weekly Few days in a month regularly = Monthly Other type of resident	<ul> <li>Permanent Resident</li> <li>Weekly Resident</li> <li>Monthly Resident</li> <li>Others</li> </ul>
Answer his/her age with	<ul> <li>birthday</li> <li>age</li> <li>age group</li> </ul>
Birthday	
Age	(years old)
Age group	<ul> <li>High school</li> <li>After high school</li> <li>Was born before the independence of Kenya</li> </ul>
Sex	<ul> <li>Male</li> <li>Female</li> <li>Other</li> <li>Prefer not to say</li> </ul>

<ul> <li>Head</li> <li>Spouse (Husband or wife 1)</li> <li>Wife 2 or 3</li> <li>Parent</li> <li>Parent in law</li> <li>Child</li> </ul>	
<ul> <li>Spouse (Husband or wife 1)</li> <li>Wife 2 or 3</li> <li>Parent</li> <li>Parent in law</li> <li>Child</li> </ul>	
<ul> <li>Wife 2 or 3</li> <li>Parent</li> <li>Parent in law</li> <li>Child</li> </ul>	
<ul> <li>Parent</li> <li>Parent in law</li> <li>Child</li> </ul>	
○ Parent in law ○ Child	
$\stackrel{\frown}{\cap}$ Child in law	
O Brother/Sister	
$\bigcirc$ Brother/Sister in law	
$\bigcirc$ Grand Child	
O Uncle/Aunt	
⊖ Worker	
<ul> <li>Other relative</li> </ul>	
Other non-relative	
⊖ Head	
Spouse (Husband or wife 1)	
○ Wife 2 or 3	
Parent	
O Parent in law	
$\bigcirc$ Child	
$\bigcirc$ Child in law	
$\bigcirc$ Online in law $\bigcirc$ Brother/Sister	
O Brotner/Sister in law	
⊖ Grand Child	
O Nephew/Niece	
○ Uncle/Aunt	
Ŏ Worker	
$\check{\bigcirc}$ Other relative	
$\bigcirc$ Other non-relative	
	Grand Child Nephew/Niece Uncle/Aunt Other relative Other non-relative Head Spouse (Husband or wife 1) Wife 2 or 3 Parent Parent in law Child Child in law Brother/Sister Brother/Sister in law Grand Child Nephew/Niece Uncle/Aunt Worker Other relative Other non-relative

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2

ASK THE RESPONDENT TO SHOW YOU ALL THE NETS IN THE HOUSEHOLD. OBSERVE AND ANSWER THE QUESTIONS FOR EACH NET, ONE BY ONE.  Please name this net for the sake of identification. i.e. boy's net, parent's net, net in the living room		
How many months ago did your household get the mosquito net? IF LESS THAN ONE MONTH AGO, RECORD '00'.	0 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 23 24 25 26 27 28 29 30 31 32 33 34 35 36 MORE THAN 36 MONTHS AGO NOT SURE	

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OLYSET (SUPANET EXTRA)
<ul> <li>PERMANET (SUPANET EXTRA)</li> <li>VEERALIN</li> <li>NETPROTECT</li> <li>YORKOOL</li> <li>DAWAPLUS</li> <li>OTHER/DON'T KNOW BRAND (LLIN)</li> <li>OTHER TYPE (NOT LLIN)</li> <li>DON'T KNOW TYPE</li> </ul>
<ul> <li>YES, MASS DISTRIBUTION CAMPAIGN</li> <li>YES, ANTENATAL CARE VISIT</li> <li>YES, CHILD WELFARE VISIT</li> <li>NO</li> </ul>
<ul> <li>GOVERNMENT HEALTH FACILITY</li> <li>PRIVATE HEALTH FACILITY</li> <li>PHARMACY</li> <li>SHOP/MARKET</li> <li>CHP</li> <li>RELIGIOUS INSTITUTION</li> <li>SCHOOL</li> <li>OTHER</li> <li>DON'T KNOW</li> </ul>
<ul> <li>YES</li> <li>NO</li> <li>NOT SURE</li> </ul>
DNE,
<ul> <li>TOO HOT</li> <li>DON'T LIKE NET SHAPE/COLOR/SIZE</li> <li>DON'T LIKE SMELL</li> <li>UNABLE TO HANG NET</li> <li>SLEPT OUTDOORS</li> <li>USUAL USER DIDN'T SLEEP HERE LAST NIGH'</li> <li>NO MOSQUITOES/NO MALARIA</li> <li>EXTRA NET/SAVING FOR LATER</li> <li>NET TOO SMALL/SHORT</li> <li>NET BROUGHT BED BUGS</li> <li>OTHER</li> </ul>

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ruge	<i>'</i> '	01	20

### Questionnaire

Please complete the survey below.		
Fhank you!		
Date and time of visit		
Cohort ID		
(i,e. "2_1")		
Cluster ID is incorrect.		
Structure ID		
(Typing the ID shown on the structure. i.e, "malela-10-10")		
First name		
Middle name		
_ast name		
This participant is available for the survey.	⊖ Yes ⊖ No	
Please select the reason why the participant is not available.	<ul> <li>Moved out from the area (will never come back)</li> <li>Travel to another village in Ndhiwa</li> <li>Travel to Homa Bay County other than Ndhiwa</li> <li>Travel to Another county in Kenya</li> <li>Travel to Another country</li> <li>Refuse</li> <li>Do not know (Could not find)</li> <li>Others</li> </ul>	
Please indicate when he/she will be back. (If you do not know, please write 0.)		
Specify the reason.		
Did [name_f] spend any nights outside [name_f]'s house in the last four weeks?	○ Yes ○ No	
Where did [name_f] spend those nights?	<ul> <li>Another house in your village</li> <li>Another village in Ndhiwa</li> <li>Homa Bay County other than Ndhiwa</li> <li>Another county in Kenya</li> <li>Another country</li> </ul>	

[name_f]'s village?	
Did you see the ceiling nets in the household you visited in another house in the village?	○ Yes ○ No
How many nights did [name_f] spend in another village in Ndhiwa?	
Did you see the ceiling nets in the household you visited in another village in Ndhiwa?	○ Yes ○ No
How many nights did [name_f] spend in Homa Bay County other than Mfangano and Mbita?	
How many nights did [name_f] spend in another county in Kenya?	
How many nights did [name_f] spend in another country?	
Did [name_f] visit any health facility in the last four weeks?	<ul><li>○ Yes</li><li>○ No</li></ul>
(Please refer to the booklet)	
Did [name_f] have the following symptoms at any point in the past four weeks?	<ul> <li>Fever</li> <li>Chills</li> <li>Profuse sweating</li> <li>Muscle/joint pain</li> <li>Abdominal pain</li> <li>Diarrhoea</li> <li>Nausea</li> <li>Vomiting</li> <li>Irritability</li> <li>Refusal to feed</li> <li>Prostration (difficulty to sit upright)</li> <li>Alteration in the level of consciousness</li> <li>Convulsions or coma</li> <li>Difficulty in breathing/respiratory distress</li> <li>Jaundice</li> <li>Others</li> <li>None</li> </ul>
Please list other symptoms [name_f] experienced in the past four weeks.	
How many times did the child visit health facilities?	<ul> <li>One time</li> <li>Two time</li> <li>Three time</li> <li>More than three</li> </ul>
Page	3
------	---
------	---

When did [name_f]visit the health facility?	
(Please refer to the booklet)	
Which health facility did [name_f] visit?	Malela level 4 hospital
(Please refer to the booklet)	<ul> <li>Kabongo HC</li> <li>Andiwo HC</li> <li>Wikomimo HC</li> <li>Abuoro HC</li> <li>Langi HC</li> <li>Kobodo HC</li> <li>Okok HC</li> <li>Other</li> </ul>
Please state the health facility [name_f] visited.	
(Please refer to the booklet)	<ul> <li>Fever</li> <li>Headache</li> <li>Muscle pain</li> <li>Abdominal pain</li> <li>Nausea</li> <li>Vomiting</li> <li>Diarrhea</li> <li>Convulsions or coma</li> <li>Jaundice</li> <li>Rapid breathing</li> <li>Difficulty in breathing/respiratory distress</li> <li>Pale conjunctivae/palms</li> <li>Loss of reactivity</li> <li>Others</li> </ul>
When did the symptom start?	
(Please refer to the booklet)	
Was [name_f] diagnosed with malaria?	
(Please refer to the booklet)	
What was the diagnosis?	
Did [name_f] take any treatment or medication?	⊖ Yes
(Please refer to the booklet)	() NO

What treatment or medication did [name_f] receive from	AL
the health facility?	
	OTHER ACT (NOT AL OR DHAP)
(Please refer to the booklet)	SP/FANSIDAR
	QUININE (PILLS)
	QUININE (INJECTION/IV)
	ARTESUNATE (RECTAL)
	ARTESUNATE (INJECTION/IV)
	OTHER ANTIMALARIAL
	OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP)
	OTHER ANTIBIOTIC MEDICINE (INJECTION/IV)
	PARACETAMOL/PANADOL/ACETAMINOPHEN
Please list other medications [name_f] received from	
the health facility.	
When did [name_f] FIRST visit the health facility?	
(Please refer to the booklet)	
Which health facility did [name_f] first visit?	Malela level 4 hospital
	/ 🗌 Kabongo HC
(Please refer to the booklet)	🗌 Andiwo HC
	🔲 Wikomimo HC
	🗌 Abuoro HC
	🔲 Langi HC
	🗌 Kobodo HC
	Okok HC
	☐ Other
Please state the health facility [name f] visited.	
Which symptoms did the child have at the first visit?	Fever
	Headache
(Please refer to the booklet)	Muscle pain
· · · · ·	Abdominal pain
	☐ Nausea
	Vomiting
	🗌 Diarrhea
	Convulsions or coma
	 Jaundice
	— Rapid breathing
	Difficulty in breathing/respiratory distress
	$\square$ Pale conjunctivae/palms
	$\Box$ Loss of reactivity
	$\Box$ Others

1 2 3	When did the symptoms for the first visit start?		
4 5 6	(Please refer to the booklet)		
7 8 9	Was [name_f] diagnosed with malaria for the first visit?	○ Yes ○ No	
10 11	(Please refer to the booklet)		
12 13 14	What was the diagnosis?		Ψ
15 16 17	Did [name_f] take any treatment or medication for the first visit?	⊖ Yes ⊖ No	rotected
18 19 20	(Please refer to the booklet)		by cop
21 22	What treatment or medication did [name_f] receive from the health facility?	□ AL □ DHAP	yright, i
23 24 25 26 27 28 29 30 31 32 33 34 35 36 37	(Please refer to the booklet)	<ul> <li>OTHER ACT (NOT AL OR DHAP)</li> <li>SP/FANSIDAR</li> <li>CHLOROQUINE</li> <li>AMODIAQUINE</li> <li>QUININE (PILLS)</li> <li>QUININE (INJECTION/IV)</li> <li>ARTESUNATE (RECTAL)</li> <li>ARTESUNATE (INJECTION/IV)</li> <li>OTHER ANTIMALARIAL</li> <li>AMOXICILLIN</li> <li>COTRIMOXAZOLE</li> <li>OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP)</li> <li>OTHER ANTIBIOTIC MEDICINE (INJECTION/IV)</li> <li>ASPIRIN</li> <li>PARACETAMOL/PANADOL/ACETAMINOPHEN</li> </ul>	Enseignement Superieur ( ncluding for uses related to text and dat
37 38 39 40		☐ IBUPROFEN ☐ OTHER ☐ DON'TKNOW	ABES) . a mining
41 42 43	Please list other medications [name_f] received from the health facility.		, Al trainin
44 45 46 47	When did [name_f] SECOND visit the health facility?		g, and sir
48 49	(Please refer to the booklet)		nilar tec
50 51 52	Which health facility did [name_f] second visit?	☐ Malela level 4 hospital ☐ Kabongo HC	hnolog
53 54 55 56 57 58 59 60	(Please refer to the booklet)	<ul> <li>Andiwo HC</li> <li>Wikomimo HC</li> <li>Abuoro HC</li> <li>Langi HC</li> <li>Kobodo HC</li> <li>Okok HC</li> <li>Other</li> </ul>	yies.

Please state the health facility [name_f] visited.	
Which symptoms did the child have at the second visit?	Fever     Headacha
(Please refer to the booklet)	<ul> <li>Headache</li> <li>Muscle pain</li> <li>Abdominal pain</li> <li>Nausea</li> <li>Vomiting</li> <li>Diarrhea</li> <li>Convulsions or coma</li> <li>Jaundice</li> </ul>
	<ul> <li>Rapid breating</li> <li>Difficulty in breathing/respiratory distress</li> <li>Pale conjunctivae/palms</li> <li>Loss of reactivity</li> <li>Others</li> </ul>
When did the symptoms for the second visit start?	
(Please refer to the booklet)	
Was [name_f] diagnosed with malaria for the second visit?	<ul><li>○ Yes</li><li>○ No</li></ul>
(Please refer to the booklet)	
What was the diagnosis?	
Did [name_f] take any treatment or medication for the second visit?	⊖ Yes ⊖ No
(Please refer to the booklet)	1
What treatment or medication did [name_f] receive from the health facility?	
(Please refer to the booklet)	<ul> <li>□ SP/FANSIDAR</li> <li>□ CHLOROQUINE</li> <li>□ AMODIAQUINE</li> <li>□ QUININE (PILLS)</li> <li>□ QUININE (INJECTION/IV)</li> <li>□ ARTESUNATE (RECTAL)</li> <li>□ ARTESUNATE (INJECTION/IV)</li> <li>□ OTHER ANTIMALARIAL</li> <li>□ AMOXICILLIN</li> <li>□ COTRIMOXAZOLE</li> <li>□ OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP)</li> <li>□ OTHER ANTIBIOTIC MEDICINE (INJECTION/IN</li> <li>□ ASPIRIN</li> <li>□ PARACETAMOL/PANADOL/ACETAMINOPHEN</li> <li>□ IBUPROFEN</li> <li>□ OTHER</li> <li>□ DON'TKNOW</li> </ul>

60 the health facility.

Diagon refer to the booklet)	
Vhich health facility did [name_f] third visit?	Malela level 4 hospital Kabanga HC
Please refer to the booklet)	<ul> <li>Andiwo HC</li> <li>Wikomimo HC</li> <li>Abuoro HC</li> <li>Langi HC</li> <li>Kobodo HC</li> <li>Okok HC</li> <li>Other</li> </ul>
Please state the health facility [name_f] visited.	
O	
Please refer to the booklet)	<ul> <li>Fever</li> <li>Headache</li> <li>Muscle pain</li> <li>Abdominal pain</li> <li>Nausea</li> <li>Vomiting</li> <li>Diarrhea</li> <li>Convulsions or coma</li> <li>Jaundice</li> <li>Rapid breathing</li> <li>Difficulty in breathing/respiratory distress</li> <li>Pale conjunctivae/palms</li> <li>Loss of reactivity</li> <li>Others</li> </ul>
When did the symptoms for the third visit start?	
Please refer to the booklet)	
Vas [name_f] diagnosed with malaria for the third risit?	<ul><li>○ Yes</li><li>○ No</li></ul>
Please refer to the booklet)	
Vhat was the diagnosis?	
Did [name_f] take any treatment or medication for the hird visit?	○ Yes ○ No
Please refer to the booklet)	

1	What treatment or medication did [name, f] receive from	
2	the health facility?	
3	the health facility?	
1	·	
4	(Please refer to the booklet)	SP/FANSIDAR
5		
6		
7		
, o		
0		
9		
10		ARTESUNATE (INJECTION/IV)
11		🗌 OTHER ANTIMALARIAL
12		
12		
13		
14		
15		
16		
17		PARACETAMOL/PANADOL/ACETAMINOPHEN
17		
18		
19		
20		
21		
22	Please list other medications [name_f] received from	
22	the health facility.	
23		
24		
25	Did [name_f] take treatment or medication from the	🗌 No
26	following in the past four weeks?	Friends
27		Relatives
20		$\square$ Pharmacy/chemist
20		
29		
30		
31	What medications did Iname fl take from the friends?	
32		
33		
31		
24		
35		
36		
37		
38		QUININE (INJECTION/IV)
30		ARTESUNATE (RECTAL)
10		ARTESUNATE (INJECTIÓN/IV)
40		
41		
42		
43		
ΔΛ		U OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP)
45		OTHER ANTIBIOTIC MEDICINE (INJECTION/IV)
45		
46		PARACETAMOL/PANADOL/ACETAMINOPHEN
47		
48		
49		
50		
50		
51	Please list other medications [name f] took from the	
52	friends	
53		
54		
55		
55		
50		
57		
58		
59		
60		

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16	What medications did [name_f] take from the relatives?	AL DHAP OTHER ACT (NOT AL OR DHAP) SP/FANSIDAR CHLOROQUINE AMODIAQUINE QUININE (PILLS) QUININE (INJECTION/IV) ARTESUNATE (RECTAL) ARTESUNATE (INJECTION/IV) ARTESUNATE (INJECTION/IV) OTHER ANTIMALARIAL AMOXICILLIN COTRIMOXAZOLE OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP) OTHER ANTIBIOTIC MEDICINE (INJECTION/IV) ASPIRIN PARACETAMOL/PANADOL/ACETAMINOPHEN
18 19 20		☐ IBUPROFEN ☐ OTHER ☐ DON'TKNOW
21 22 23	Please list other medications [name_f] took from the relatives.	
25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44	What medications did [name_f] take from the pharmacy/chemist?	AL DHAP OTHER ACT (NOT AL OR DHAP) SP/FANSIDAR CHLOROQUINE AMODIAQUINE QUININE (PILLS) QUININE (INJECTION/IV) ARTESUNATE (RECTAL) ARTESUNATE (RECTAL) ARTESUNATE (INJECTION/IV) OTHER ANTIMALARIAL AMOXICILLIN COTRIMOXAZOLE OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP) OTHER ANTIBIOTIC MEDICINE (INJECTION/IV) ASPIRIN PARACETAMOL/PANADOL/ACETAMINOPHEN BUPROFEN OTHER DON'TKNOW
45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60	Please list other medications [name_f] took from the pharmacy.	

What medications did [name f] take from the	
traditional healer?	
	OTHER ACT (NOT AL OR DHAP)
	QUININE (PILLS)
	QUININE (INJECTION/IV)
	🗍 ARTESUNÀTE (RECTAL)
	🗍 ARTESUNATE (INJECTIÓN/IV)
	🗍 OTHER ANTIMALARIAL
	OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP)
	OTHER ANTIBIOTIC MEDICINE (INJECTION/ÍV
	PARACETAMOL/PANADOL/ACETAMINOPHEN
	OTHER
Place list other medications Inome fl teck from the	
ricase nsi omer medications [name_i] took from the traditional healer	
Door Inome fil hours the following sumptome and ar in	
Does [name_i] have the following symptoms now of in	
the last 24 hours?	
	Profuse sweating
	Muscle/joint pain
	Diarrhoea
	Nausea
	Vomiting
	Refusal to feed
	Prostration (difficulty to sit upright)
	Alteration in the level of consciousness
	Convulsions or coma
	Difficulty in breathing/respiratory distress
	Jaundice
	☐ Others
Please list other symptoms [name_f] experience now or	
in the last 24 hours.	
Did [name_f] receive the malaria vaccine within four	⊖ Yes
weeks?	○ No
How many times has [name f] received the malaria	$\bigcirc$ 1 dose
vaccine, including the latest one?	$\check{\bigcirc}$ 2 doses
,	$\check{\bigcirc}$ 3 doses
	$\bigcirc$ 4 doses
	O Don't know
	-
Does the structure where Iname flusually sleeps have	⊖ Yes
ceiling nets?	$\bigcirc$ No

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rayc	- 01	UI.	20

## Sample

1	
2	Please complete the survey below.

Thank you!	
Cohort ID	
First name	
Middle name	
_ast name	
Did you sleep under a bed net last night?	○ Yes ○ No
Axillary temperature (degrees Celsius)	
Perform finger prick	<ul><li>○ Yes</li><li>○ No</li></ul>
Blood spots on filter paper?	⊖ Yes ⊖ No
Fhick and thin blood films?	<ul><li>○ Yes</li><li>○ No</li></ul>
RDT results for P.f	<ul> <li>Negative</li> <li>Positive</li> </ul>
RDT results for Pan	<ul> <li>Negative</li> <li>Positive</li> </ul>

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## Participant questionnaire

riease complete the survey below.		
Fhank you!		
Date and time of visit		
Date and time of visit		_
Survey ID		
i,e. "s2_1")		_
structure ID		
Typing the ID shown on the structure. i.e, malela-10-10")		_
irst name		_
Aiddle name	\$	_
ast name	0	_
vge	(years old)	_
Does [name_f] know the birthday?	⊖ Yes ⊖ No	
Birthday	2/	_
he birthday and your age are contradicting. Please c	heck the true age again.	
ex	<ul> <li>Male</li> <li>Female</li> <li>Other</li> <li>Prefer not to say</li> </ul>	
ongitude		
atitude		
This participant is available for the survey.		

Please select the reason why the participant is not available.	<ul> <li>Moved out from the area (will never come back</li> <li>Travel to another village in Ndhiwa</li> <li>Travel to Homa Bay County other than Ndhiwa</li> <li>Travel to Another county in Kenya</li> <li>Travel to Another country</li> <li>Refuse</li> <li>Do not know (Could not find)</li> <li>Others</li> </ul>
Specify the reason.	
Did [name_f] spend any nights outside [name_f]'s house in the last four weeks?	○ Yes ○ No
Where did [name_f] spend those nights?	<ul> <li>Another house in your village</li> <li>Another village in Ndhiwa</li> <li>Homa Bay County other than Ndhiwa</li> <li>Another county in Kenya</li> <li>Another country</li> </ul>
How many nights did [name_f] spend in another house in [name_f]'s village?	
Did you see the ceiling nets in the household you visited in another house in the village?	○ Yes ○ No
How many nights did [name_f] spend in another village	
Did you see the ceiling nets in the household you visited in another village in Ndhiwa?	O Yes O No
How many nights did [name_f] spend in Homa Bay County other than Ndhiwa?	4
How many nights did [name_f] spend in another county in Kenya?	0
How many nights did [name_f] spend in another country?	
Did [name_f] have any symptoms at any point in the past four weeks?	<ul> <li>○ Yes</li> <li>○ No</li> <li>○ Don't know</li> </ul>

- 58 59
- 60

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What was the symptom? Tick all that apply.	<ul> <li>Fever</li> <li>Chills</li> <li>Profuse sweating</li> <li>Muscle/joint pain</li> <li>Abdominal pain</li> <li>Diarrhoea</li> <li>Nausea</li> <li>Vomiting</li> <li>Irritability</li> <li>Refusal to feed</li> <li>Prostration (difficulty to sit upright)</li> <li>Alteration in the level of consciousness</li> <li>Convulsions or coma</li> <li>Difficulty in breathing/respiratory distress</li> </ul>
Please list other symptoms [name f] experienced in the	
past four weeks.	
Did [name_f] visit any health facility in the last	
four weeks?	() No
Which health facility did [name_f] visit?	<ul> <li>Malela level 4 hospital</li> <li>Kabongo HC</li> <li>Andiwo HC</li> <li>Wikomimo HC</li> <li>Abuoro HC</li> <li>Langi HC</li> <li>Kobodo HC</li> <li>Okok HC</li> <li>Other</li> </ul>
Please state the health facility [name_f] visited.	2
Was [name_f] diagnosed with malaria?	<ul><li>○ Yes</li><li>○ No</li></ul>
What was the diagnosis?	1
Did [name_f] take any treatment or medication?	⊖ Yes
· · ····, · ····· ··· · · · · · · · · · · · · ·	◯ No
Do you know the name of the medication?	○ Yes ○ No

59 60

What treatment or medication did [name_f] receive from the health facility?	<ul> <li>AL</li> <li>DHAP</li> <li>OTHER ACT (NOT AL OR DHAP)</li> <li>SP/FANSIDAR</li> <li>CHLOROQUINE</li> <li>AMODIAQUINE</li> <li>QUININE (PILLS)</li> <li>QUININE (INJECTION/IV)</li> <li>ARTESUNATE (RECTAL)</li> <li>ARTESUNATE (INJECTION/IV)</li> <li>OTHER ANTIMALARIAL</li> <li>AMOXICILLIN</li> <li>COTRIMOXAZOLE</li> <li>OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP)</li> <li>OTHER ANTIBIOTIC MEDICINE (INJECTION/IV)</li> <li>ASPIRIN</li> <li>PARACETAMOL/PANADOL/ACETAMINOPHEN</li> <li>IBUPROFEN</li> <li>OTHER</li> </ul>
Please list other medications [name_f] received from the health facility.	
Did [name_f] take treatment or medication from friends, relatives, pharmacy/chemist, or traditional healers in the past four weeks?	<ul><li>○ Yes</li><li>○ No</li></ul>
Did [name_f] take treatment or medication from the following in the past four weeks?	<ul> <li>Friends</li> <li>Relatives</li> <li>Pharmacy/chemist</li> <li>Traditional healers</li> </ul>
Do you know the names of medications from your friends?	⊖ Yes ⊖ No
What medications did [name_f] take from the friends?	AL DHAP OTHER ACT (NOT AL OR DHAP) SP/FANSIDAR CHLOROQUINE AMODIAQUINE QUININE (PILLS) QUININE (INJECTION/IV) ARTESUNATE (RECTAL) ARTESUNATE (INJECTION/IV) ARTESUNATE (INJECTION/IV) OTHER ANTIMALARIAL AMOXICILLIN COTRIMOXAZOLE OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP) OTHER ANTIBIOTIC MEDICINE (INJECTION/IV) ASPIRIN PARACETAMOL/PANADOL/ACETAMINOPHEN BUPROFEN OTHER
Please list other medications [name_f] took from the friends.	
Do you know the names of medications from your relatives?	○ Yes ○ No

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What medications did [name f] take from the relatives?	
mat modicatione and [name_i] take from the relatives:	
	$\Box$ OTHER ACT (NOT AL OR DHAP)
	$\square$ SP/FANSIDAR
	$\square \text{ ARTESUNATE (INJECTION/IV)}$
	OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP)
	PARACETAMOL/PANADOL/ACETAMINOPHEN
Please list other medications [name_f] took from the	
relatives.	
Do you know the names of medications from the	$\bigcirc$ Yes
nharmacy/chemist?	$\bigcirc$ No
	$\bigcirc$ i.e
What mediantions did Inome fl take from the	
what medications did [name_i] take from the	
pnarmacy/cnemist?	
	ARTESUNATE (INJECTION/IV)
	OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP)
	OTHER ANTIBIOTIC MEDICINE (INJECTION/IV
	PARACETAMOL/PANADOL/ACETAMINOPHEN
Please list other medications [name_f] took from the	
pharmacy.	
Do you know the names of medications from the	⊖ Yes
traditional healer?	() No

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19	What medications did [name_f] take from the traditional healer?	<ul> <li>AL</li> <li>DHAP</li> <li>OTHER ACT (NOT AL OR DHAP)</li> <li>SP/FANSIDAR</li> <li>CHLOROQUINE</li> <li>AMODIAQUINE</li> <li>QUININE (PILLS)</li> <li>QUININE (INJECTION/IV)</li> <li>ARTESUNATE (RECTAL)</li> <li>ARTESUNATE (INJECTION/IV)</li> <li>OTHER ANTIMALARIAL</li> <li>AMOXICILLIN</li> <li>COTRIMOXAZOLE</li> <li>OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP)</li> <li>OTHER ANTIBIOTIC MEDICINE (INJECTION/IV)</li> <li>ASPIRIN</li> <li>PARACETAMOL/PANADOL/ACETAMINOPHEN</li> <li>IBUPROFEN</li> <li>OTHER</li> </ul>
20 21 22 23	Please list other medications [name_f] took from the traditional healer.	
23 24 25 26	Does [name_f] have any symptoms now or in the last 24 hours?	○ Yes ○ No
27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46	Does [name_f] have the following symptoms now or in the last 24 hours?	<ul> <li>Fever</li> <li>Chills</li> <li>Profuse sweating</li> <li>Muscle/joint pain</li> <li>Abdominal pain</li> <li>Diarrhoea</li> <li>Nausea</li> <li>Vomiting</li> <li>Irritability</li> <li>Refusal to feed</li> <li>Prostration (difficulty to sit upright)</li> <li>Alteration in the level of consciousness</li> <li>Convulsions or coma</li> <li>Difficulty in breathing/respiratory distress</li> <li>Jaundice</li> <li>Cough</li> <li>Rash</li> <li>Itches</li> <li>Others</li> </ul>
46 47 48 49	Please list other symptoms [name_f] experience now or in the last 24 hours.	
50 51	Has [name_f] received a malaria vaccine?	○ Yes ○ No
52 53	Please refer to the mother-child book.	
54 55 56 57	How many times has [name_f] received the malaria vaccine?	<ul> <li>1 dose</li> <li>2 doses</li> <li>3 doses</li> </ul>
58 59		O Don't know
60	Does the structure where [name_f] usually sleeps have ceiling nets?	○ Yes ○ No

## Sample

Please complete the survey below.

## Thank you!

		-
Survey ID		-
First name		
Middle name		- 
Last name		-
Did you sleep under a bed net last night?	<ul><li>○ Yes</li><li>○ No</li></ul>	-
Axillary temperature (degrees Celsius)		
Perform finger prick	⊖ Yes ⊖ No	
Blood spots on filter paper?	⊖ Yes ⊖ No	
Thick and thin blood films?	⊖ Yes ⊖ No	
RDT results for P.f	<ul> <li>Negative</li> <li>Positive</li> </ul>	
RDT results for Pan	<ul> <li>Negative</li> <li>Positive</li> </ul>	

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Flease complete the survey below.	
Thank you!	
Who is the respondent?	<ul> <li>Head</li> <li>Primary care taker</li> <li>Participant</li> </ul>
*If the respondent are not sure about the answer(s), he/she can be helped by the other members.	○ Others
What is the respondent's relation to the participant?	Head
	$\bigcirc$ spouse (Husband or wife 1) $\bigcirc$ Wife 2 or 3
	$\bigcirc$ Parent
	$\bigcirc$ Parent in law
	$\bigcirc$ Child
	$\bigcirc$ Child in law
	O Brother/Sister
	Ŏ Brother/Sister in law
	🔿 Grand Child
	O Nephew/Niece
	C Uncle/Aunt
	O Worker
	Other relative
	O Other non-relative
What is the condition of the ceiling net?	O No damage
	O Damaged but repaired
	O Not installed
How many hole(s) does/did it have?	
(regardless of the size)	
	21
Where are the hole(s) located?	Around the edge (lower part, near the wall) Around the top
	☐ In the middle
What is/was the size of largest hole?	Smaller than the tip of index finger
	<ul> <li>Smaller than the fist</li> <li>larger than the fist</li> </ul>
What is/was the reason of the damage?	Accident during the cleaning
	<ul><li>○ Others</li></ul>
Please specify the reason of the damage	

why did they remove?	
What is the condition of the wooden battens securing the ceiling net to the wall?	<ul><li>○ Good</li><li>○ Damaged</li></ul>
Presence of gaps between battens and the wall	<ul><li>○ Yes</li><li>○ No</li></ul>
Do you agree with the following potential positive sides of the ceiling net?	<ul> <li>Stop mosquito entering the house</li> <li>Stop other insects/animals entering the house</li> <li>Durability of the ceiling nets</li> <li>To beautify the house</li> <li>Household coverage</li> <li>Keep the room cool</li> <li>Others</li> </ul>
Please specify.	
Do you agree with the following potential negative sides of the ceiling net?	<ul> <li>It makes room too hot</li> <li>It reduces the storage space a the top of the w all</li> <li>Fixing looks untidy</li> <li>It is hard to clean</li> <li>Dirt/debris trapped by the ceiling net</li> <li>Rewiring of power lines</li> <li>Others</li> </ul>
Please specify.	
Other features in the ceiling net (if any).	2
Will you pay for the ceiling nets if you need to buy them in the future?	○ Yes ○ No
How much will you pay the maximum for ceiling nets for your household?	<ul> <li>100 KSH</li> <li>300 KSH</li> <li>500 KSH</li> <li>1000 KSH</li> <li>2000 KSH</li> <li>5000 KSH</li> <li>More than 10,000 KSH</li> </ul>
How many mosquito nets does your household have?	
How many new (unopened) mosquito nets does your household have?	
Does anyone in your household wash the mosquito nets?	<ul><li>○ Yes</li><li>○ No</li></ul>

How often does your household wash the mosquito nets?	<ul> <li>Every day</li> <li>Every week</li> <li>Every month</li> <li>less frequently than every month</li> </ul>
How does your household wash the mosquito nets?	<ul> <li>With water</li> <li>With hot water</li> <li>With soap or detergent</li> <li>Others</li> </ul>
How does your household dry the mosquito nets after washing it?	<ul> <li>Indoor</li> <li>Under the sunlight</li> <li>Under the shade</li> <li>Others</li> </ul>
Have you ever gotten any instruction on how to use and treat the mosquito net?	<ul><li>○ Yes</li><li>○ No</li></ul>
From who did you get the instruction?	
In general, how long can you use the bed net effectively?	<ul> <li>One year even without damages</li> <li>Three years even without damages</li> <li>Ten years even without damages</li> <li>Until it gets damaged</li> </ul>
against mosquitoes?	○ No