BMJ Open

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

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2024-087832
Article Type:	Protocol
Date Submitted by the Author:	20-Apr-2024
Complete List of Authors:	Ko, Yura; Karolinska Institute, 1Department of Microbiology, Tumor and Cell Biology (MTC); Tohoku University Kagaya, Wataru; Nagasaki University Omondi, Protus; Osaka Metropolitan University Musyoka, Kelvin ; Osaka Metropolitan University Okai, Takatsugu; Osaka Metropolitan University Chan, Chim; Osaka Metropolitan University Kongere, James; Osaka Metropolitan University; Center for Research in Tropical Medicine and Community Development Opiyo, Victor; Center for Research in Tropical Medicine and Community Development Oginga, Jared; Center for Research in Tropical Medicine and Community Development Mungai, Samuel; Mount Kenya University; United States International University Africa Kanoi, Bernard; Mount Kenya University Kanamori, Mariko ; Stockholm University; Kyoto University Yoneoka, Daisuke; National Institute of Infectious Diseases (KNBS), Kenya National Bureau of Statistics; Kenya National Bureau of Statistics Keitany, Kibor; Kenya National Malaria Control Program Songok, Elijah; Kenya Medical Research Institute, Okomo, Gordon ; Ministry of Health Minakawa, Noboru; Nagasaki University Gitaka, Jesse; Mount Kenya University, Research and Innovation Kaneko, Akira; Karolinska Institute, 1Department of Microbiology, Tumor and Cell Biology (MTC); Osaka Metropolitan University
Keywords:	Malaria, Mosquito Vectors, Infection control < INFECTIOUS DISEASES

Title

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

Authors

Yura K Ko[1,2], Wataru Kagaya[3], Protus Omondi[4], Kelvin B. Musyoka[4], Takatsugu Okai[4], Chim W. Chan[4], James Kongere[4,5], Victor Opiyo[5], Jared Oginga[5], Samuel M. Mbugua[6,7,8], Bernard N. Kanoi[6,8], Mariko Kanamori[9,10], Daisuke Yoneoka[11], Kenya National Bureau of Statistics (KNBS)[12], Kibor Keitany[13], Elijah Songok[14], Gordon Okomo[15], Noboru Minakawa[16], Jesse Gitaka[6,8](*), Akira Kaneko[1,4,16](*)

[1]Department of Microbiology, Tumor and Cell Biology (MTC), Karolinska Institutet, Sweden

[2]Department of Virology, Tohoku University Graduate School of Medicine, Japan

[3]Department of Ecoepidemiology, Institute of Tropical Medicine (NEKKEN), Nagasaki University, Japan

[4]Department of Virology and Parasitology, Graduate School of Medicine, Osaka Metropolitan University, Japan

[5]Center for Research in Tropical Medicine and Community Development, Kenya

[6]Center for Research in Infectious Diseases, Directorate of Research and Innovation, Mount Kenya University, Kenya

[7]School of pharmacy and health sciences, United States International University Africa, Kenya

[8]Center for Malaria Elimination, Mount Kenya University, Kenya

[9]Department of Public Health Sciences, Stockholm University, Sweden

[10]Institute for the Future of Human Society, Kyoto University, Japan

[11]Center for Surveillance, Immunization, and Epidemiologic Research, National Institute of Infectious Diseases, Japan

[12]Kenya National Bureau of Statistics, Kenya

[13]National Malaria Control Programme, Ministry of Health, Kenya

[14]Kenya Medical Research Institute, Kenya

[15]Department of Health, Homa Bay County, Kenya

[16]Department of Vector Ecology and Environment, Institute of Tropical Medicine (NEKKEN), Nagasaki University, Japan

Correspondence to: Wataru Kagaya

*Senior joint authors

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

Title {1}	Evaluation of the protective efficacy of Olyset®Plus ceiling net on reducing malaria incidence in children in the Great Lake Region, Kenya: study protocol for a cluster-randomized controlled trial
Trial registration {2a and 2b}.	UMIN000053873
Protocol version {3}	Version 5.1
Funding {4}	This work is supported by the Japan International Cooperation Agency (JICA) and Japan Agency for Medical Research and Development (AMED) under the Science and Technology Research Partnership for Sustainable Development Goals (SATREPS) program.
Author details {5a}	Osaka Metropolitan University, Japan Nagasaki University, Japan Tohoku University, Japan National Institute of Infectious Diseases, Japan Mount Kenya University, Kenya National Malaria Control Program, Nairobi, Kenya Kenya National Bureau of Statistics, Nairobi, Kenya Kenya Medical Research Institute, Kenya Homa Bay County, Kenya Karolinska Institutet, Sweden Stockholm University, Sweden

Name and contact information for the trial sponsor {5b}	Department of Virology and Parasitology/Research Center for Infectious Diseases, Graduate School of Medicine, Osaka Metropolitan University (OMU), Japan 1–4-3, Asahimachi, Abeno, Osaka, Osaka, Japan, 545–8585 TEL: + 81–6-6645–3760 Website: https://ocuparasitology.com/en/ Directorate of Research and Innovation, Mount Kenya University (MKU), Kenya General Kago Road, Thika, Kiambu, Kenya Website: https://www.mku.ac.ke
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.

Strength and limitations of this study

- This study is a cluster-randomized controlled trial (CRCT) to evaluate the efficacy of the Olyset®Plus ceiling net as a novel vector control tool and a complement to current malaria control tools in sub-Saharan Africa.

- This marks the second CRCT of the Olyset®Plus ceiling net intervention in the lake endemic region of Kenya, expanding the evidence base to a different eco-epidemiological setting from the previous CRCT, where promising results were observed on Mfangano Island.

- Collaboration with local Kenyan institutions such as the Kenya National Bureau of Statistics (KNBS), the National Malaria Control Programme (NMCP), the Kenya Medical Research Institute (KEMRI), and Homa Bay County from the research planning stage is one of the strengths of this trial, allowing for a seamless transition from research implementation in the field to policy development.

- One of the anticipated limitations is the possible contamination between intervention and control clusters because we will not set a buffer zone due to the geographical proximity of each cluster. We will try to account for such contamination effects by integrating spatial data into our statistical model.

Introduction

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.

The aim of this study is to evaluate the efficacy, acceptability, and cost-effectiveness of Olyset®Plus ceiling nets on malaria morbidity and transmission in the Lake Victoria basin of Kenya. Preliminary data from our previous study on Mfangano Island in Lake Victoria [9] 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 Olyset®Plus 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 combining various tools to maximize the impact of the malaria control program, it is important to understand 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.

Objectives {7}

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 Olyset®Plus ceiling net in reducing malaria clinical incidence in children 6 months to 14 years old over 18 months post-intervention. The secondary objectives are (1) to determine the protective efficacy of Olyset®Plus 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 protective efficacy of Olyset®Plus ceiling nets against the time-to-first *Plasmodium* infection**;** (3) to determine the spillover effects of Olyset®Plus ceiling nets in reducing

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.

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 covariate-constrained 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.

Methods: Participants, interventions and outcomes

Study setting {9}

Location and administrative structure

Ndhiwa (713.5 km²) 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 poultry [10]. The ward experiences a long rainy season from March to June and a short rainy season from October to December. As of 2019, the mean annual precipitation is 228.64 mm and the mean annual temperature is 26.7℃. The relative humidity remains elevated year-round, fluctuating between 75% to 85% [11].

Demographics

The population of Kanyamwa Kologi Ward is approximately 33,000 according to the 2019 national census [12]. The dominant ethnic group in the region is Luo and the primary languages are DhoLuo, Kiswahili, and English. There are 172 primary and 36 secondary schools in Ndhiwa Sub-County [13]. Within Kanyamwa Kologi Ward, there are 28 primary and 7 secondary schools.

Malaria epidemiology and control measures

Based on the KHIS, there were 429.1 and 457.2 confirmed malaria cases per 1,000 population in Ndhiwa Sub-County and Kanyamwa Kologi Ward , respectively, in 2023. The primary malaria vector in the sub-county is *Anopheles funestus*, which prefers feeding on humans. *An. arabiensis* is also an important malaria

vector [14]. In Homa Bay County, LLINs have been distributed every three years since the early 2000s, and IRS and the RTS,S malaria vaccine have been piloted in several areas since 2018 and 2019, respectively [15]. Notably PBO-incorporated LLINs (Veeralin®LN, manufactured by VKA Polymers, Tamil Nadu, India) were distributed in late 2023. In Kanyamwa Kologi Ward, there is one level four hospital and seven health centers.

Eligibility criteria {10}

As the ceiling nets are installed per structure, we set the inclusion criteria on a structural basis. The inclusion criteria for the installation of the ceiling nets are (1) residential structures with at least one permanent resident aged 18 years or older in the household, (2) informed consent provided by a resident in the household, and (3) house structure amenable to ceiling net installation 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 structure, confirmed by at least two visits by community health promoters (CHPs), (2) dwelling structure to be vacated or destroyed within the study period, (3) not applicable house structure for the ceiling net installation, and (4) non-residential structures (school, shop, kitchen, storage, and toilet). The inclusion 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 Olyset®Plus 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.

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.

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 adding Olyset®Plus ceiling nets to the standard malaria control program. Thus, in the control arm, no Olyset®Plus 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.

Intervention description {11a}

In the intervention arm, Olyset®Plus 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 [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.

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.

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.

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

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

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.

Outcomes {12}

Epidemiological domain: The primary outcome will be symptomatic malaria case incidence, defined as axillary temperature of ≥37·5°C or a history of fever in the preceding 48 hours, and positive mRDT, in children aged 6 months to 14 years enrolled in the cohort, monitored with biweekly visit and passive case detection in the health facilities during an 18-month follow-up. The secondary outcomes will be (1) the prevalence of *Plasmodium* infections by PCR in all age groups at 6, 12, and 18 months post-intervention, (2) time to first infection defined as the number of days between the start of the intervention and the first PCR positive diagnosis in the cohort of children during the 18-month follow-up period, (3) spillover effect measured with the above-mentioned prevalence parameter, and (4) infection incidence by PCR in the prospective cohort of children aged 6 months to 14 years over 18 months.

Entomological domain: The primary outcome will be the density of the primary malaria vectors, species composition and sporozoite infection rates. Malaria vector density will be determined using CDC light trap, and species composition and sporozoite infection rates will be determined by microscopy and PCR. The secondary outcomes of the entomology domains will be (1) changes in EIR as a measure of malaria transmission and (2) prevalence of *kdr* 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 Olyset®Plus 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 at 6, 12, and 18 months post-intervention.

Cost-effectiveness domain: The primary outcome will be the incremental cost-effectiveness of adding Olyset®Plus 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 Olyset®Plus 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 [16]. All the sample sizes will be recalculated based on the baseline data, which will be collected about one month before the ceiling net installation.

Epidemiological survey

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 between-cluster 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 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 the number of clusters with 50 individuals per cluster, for the secondary outcome of malaria prevalence by PCR for 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 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.

Implementation {16c}

After the baseline survey, covariate-constrained randomization will be used to allocate the 44 clusters across the two study arms. 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. An independent statistician will perform the randomization. Local study assistants will perform participant

enrollment.

Assignment of interventions: Blinding

Who will be blinded {17a}

Due to the visibility of the Olyset®Plus ceiling net, neither the trial participants nor the members of the study team who take part in field activities can be blinded. However, laboratory- and office-based personnel (e.g., microscopists, laboratory technicians, and data analysts) will be blinded to the identity and intervention status of the trial participants since all biological specimens will be identified by a unique numeric study identifier, and personal information will be removed before analyses.

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 they need to be unblinded.

Data collection and management

Plans for assessment and collection of outcomes {18a}

Baseline survey

A baseline survey targeting 50 enumeration areas (comprising one or two villages) in the study area will be conducted shortly before the ceiling net intervention to obtain data to assure the balance of the cluster allocation and obtain basic demographic data. The baseline survey includes a questionnaire for all households, mRDT testing of all children aged 6 months to 14 years, and an entomological survey of randomly sampled households. We modified the questionnaire used in the 2020 Kenya Malaria Indicator Survey (KMIS) mainly to quantify the SES of each household and bed net usage. In addition, we add questions to quantify the favorability of ceiling nets before the intervention.

Cohort monitoring

Incidence of clinical malaria in the prospective cohort will be estimated by both active and passive case

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 finger-prick 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℃. The dried blood spots will be used for the determination of malaria status by PCR [17].

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.

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.

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.

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 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

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.

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

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.

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 for the within-cluster correlation of responses.

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. The distance of 400 m was chosen as the spillover effect appears to attenuate at this distance based on previous reports [19].

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) [20] to document the implementation processes of the ceiling nets, and the Evidence integration triangle framework[21] 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[22]. Data from ethnographic, focus group discussions, key informant interview will be summarized using content thematic analysis. Pre- and post-intervention acceptability to install Olyset®Plus ceiling net intervention will be compared to actual consent using logistic regressions.

Cost-effectiveness

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 (≤ 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}

In the cohort, non-adherence to the intervention can be identified by bi-weekly 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 hot-deck imputation methods if the missing fraction for the covariate is <5% or appropriate multiple imputation approaches if the missing fraction for a covariable are ≥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, which aim to monitor the progress of the trial.

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

Because this intervention is considered to be of a low-risk nature, this study does not have a data monitoring committee. For additional credibility about study quality, the researchers will consult a third statistician, if necessary.

Adverse event reporting and harms {22}

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.

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.

Dissemination plans {31a}

Study results will be shared with the 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. Suggestions from the participants will also help shape the future improvement of the intervention.

Discussion

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 [24] [2–6]. Novel interventions that are cost-effective and widely accepted by local communities are urgently needed to contain the spread of artemisinin-resistant *P. falciparum* in sub-Saharan Africa.

Early results from our cluster randomized controlled trial of Olyset®Plus 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 [25].

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 trial, contamination between intervention and control clusters cannot be excluded, as buffer zones between intervention and control clusters cannot be created due to geographic proximity of houses and villages in the ward. A recent study, however, has shown that the spillover effect of interventions on malaria can extend to 3 km [26], so buffer zones of a few hundred meters, as set out in many studies, may not be sufficient. We will try to eliminate such contamination effects by integrating spatial data into our statistical model. Second, 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 in-depth 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-PBO-incorporated 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 [2]. Given the abundance of PBO-incorporated LLINs in the region, it is important to assess the effectiveness of the Olyset®Plus 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 [27]. When these new LLINs become widely available, the effectiveness of pyrethroid-PBO ceiling nets needs to be re-investigated.

Trial status

The Baseline survey was started on April 8, 2024. The recruitment of the intervention participants will be in June 2024. The current protocol is version 5.0 as of April 18.

Abbreviations

ACT: artemisinin-based combination therapy

CHP: community health promoter

CRCT: cluster-randomized controlled trial

CV: coefficient of variation

kdr: knockdown resistance

KHIS: Kenya Health Information System

ITN: insecticide treated nets

IRS: indoor residual spraying

LLIN: long-lasting insecticidal nets

MKU: Mount Kenya University

PBO: piperonyl butoxide

RDT: rapid diagnosis tests

Declarations

Acknowledgements

We would like to express our sincere gratitude to this study's participants, field, and laboratory staff. In addition, we acknowledge the collaboration and support of health offices in Homa Bay County, Kenya.

Authors' contributions {31b}

AK and JG are co-principal investigators. YKK, WK, and AK developed the original concept. All authors discussed and contributed to the study protocol. YKK, WK, PO, BM, TO, CWC, JK, SM, and MK drafted the manuscript. YKK, WK, CWC, MK, GO, and JG contributed to the revisions of the draft of the

manuscript. DY participated as a senior statistician. YKK and MK drafted the statistical analysis plan (SAP) and WK, CWC, and DY revised. The authors read and approved the final manuscript and SAP.

Funding {4}

YKK and MK were financially supported by the Japan Society for the Promotion of Science. AK and JG received support from JICA/AMED joint research project (SATREPS) (Grant no. 20JM0110020H0002), Hitachi Fund Support for Research Related to Infectious Diseases, and Sumitomo Chemical Corporation. The funding bodies play no role in the study design, data collection, analysis, interpretation, and publication.

Availability of data and materials {29}

The study regimes, consent forms, assent forms, and study-related materials are accessible from the corresponding author. The final trial dataset will be available to all investigators. The corresponding author will make the de-identified datasets and source codes for all analysis available upon reasonable request.

Patient and public involvement

Although the study design was developed through discussions among the researchers, consultations with the local population were conducted prior to initiating the baseline survey, and their input was incorporated into the study. Community involvement will also be ongoing during the implementation of interventions and research activities.

Ethics approval and consent to participate {24}

Ethics approval was received from Mount Kenya University Institutional Scientific Ethics Review Committee (MKU-ISERC) and is under the review from the Ethics Committee in Osaka Metropolitan University.

Written informed consents will be sought from study participants before the baseline survey, installation of ceiling nets, each cross-sectional survey, and the start of prospective cohort surveys. Participants have the right to withdraw from the study at any time, and the option to withhold previously collected samples from any future analyses and studies.

The samples collected in this study may potentially be used for other research purposes. This is clearly stated in the informed consent form. In such cases, we will obtain the necessary ethical approval and provide participants with the chance to opt-out from this. All experiments will be carried out in adherence to WHO requirements and the Declaration of Helsinki.

Consent for publication {32}

We will not present identifying images or other personal or clinical details of participants. The participant information materials and informed consent form are available from the corresponding author on request.

Competing interests {28}

This study was partially supported by a research grant from Sumitomo Chemical Corporation.

References

1. Noor AM, Alonso PL. The message on malaria is clear: progress has stalled. The Lancet. 2022. p. 1777.

2. Rosenthal PJ, Björkman A, Dhorda M, Djimde A, Dondorp AM, Gaye O, et al. Cooperation in Countering Artemisinin Resistance in Africa: Learning from COVID-19. Am J Trop Med Hyg. 2022;106: 1568–1570.

3. Stokes BH, Ward KE, Fidock DA. Evidence of Artemisinin-Resistant Malaria in Africa. The New England journal of medicine. 2022. pp. 1385–1386.

4. Mihreteab S, Platon L, Berhane A, Stokes BH, Warsame M, Campagne P, et al. Increasing Prevalence of Artemisinin-Resistant HRP2-Negative Malaria in Eritrea. N Engl J Med. 2023;389: 1191–1202.

5. Fola AA, Feleke SM, Mohammed H, Brhane BG, Hennelly CM, Assefa A, et al. Plasmodium falciparum resistant to artemisinin and diagnostics have emerged in Ethiopia. Nature Microbiology. 2023;8: 1911–1919.

6. World Health Organization. World malaria report 2023. 2023.

7. Larson PS, Minakawa N, Dida GO, Njenga SM, Ionides EL, Wilson ML. Insecticide-treated net use before and after mass distribution in a fishing community along Lake Victoria, Kenya: successes and unavoidable pitfalls. Malar J. 2014;13: 466.

8. Minakawa N, Dida GO, Sonye GO, Futami K, Kaneko S. Unforeseen misuses of bed nets in fishing villages along Lake Victoria. Malar J. 2008;7: 165.

9. Kagaya W, Chan CW, Kongere J, Kanoi BN, Ngara M, Omondi P, et al. Evaluation of the protective efficacy of Olyset®Plus ceiling net on reducing malaria prevalence in children in Lake Victoria Basin, Kenya: study protocol for a cluster-randomized controlled trial. Trials. 2023;24: 354.

10. Homabay County | Ndhiwa Municipality. [cited 13 Feb 2024]. Available: https://www.homabay.go.ke/department/ndhiwa-municipality

11. Ndhiwa, Homa Bay, KE Climate Zone, Monthly Averages, Historical Weather Data. [cited 13 Feb 2024]. Available: https://weatherandclimate.com/kenya/homa-bay/ndhiwa

12. Statistics KNB of SNKNB of. 2019 Kenya Population and Housing Census Reports. 28 Feb 2020 [cited 13 Feb 2024]. Available: https://housingfinanceafrica.org/documents/2019-kenya-population-and-housing-census-reports/

13. Ndhiwa Constituency Schools | ShuleZote. [cited 13 Feb 2024]. Available: https://shulezote.co.ke/place/constituency/migori/ndhiwa/?page=1

14. VectorLink-Kenya-2021-End-of-Spray-Report-Submision-Approved-July-23-2021-sxf-CL.pdf. Available: https://d1u4sg1s9ptc4z.cloudfront.net/uploads/2021/09/VectorLink-Kenya-2021-End-of-Spray-Report-Submision-Approved-July-23-2021-sxf-CL.pdf

15. End-of-Spray-Report-Kenya-2023.pdf. Available: https://d1u4sg1s9ptc4z.cloudfront.net/uploads/2023/10/End-of-Spray-Report-Kenya-2023.pdf

16. Hayes RJ, Bennett S. Simple sample size calculation for cluster-randomized trials. Int J Epidemiol. 1999;28: 319–326.

17. Isozumi R, Fukui M, Kaneko A, Chan CW, Kawamoto F, Kimura M. Improved detection of malaria cases in island settings of Vanuatu and Kenya by PCR that targets the Plasmodium mitochondrial cytochrome c oxidase III (cox3) gene. Parasitol Int. 2015;64: 304–308.

18. Multerer L, Glass TR, Vanobberghen F, Smith T. Analysis of contamination in cluster randomized trials of malaria interventions. Trials. 2021;22: 613.

19. Hawley WA, Phillips-Howard PA, ter Kuile FO, Terlouw DJ, Vulule JM, Ombok M, et al. Community-wide effects of permethrin-treated bed nets on child mortality and malaria morbidity in western Kenya. Am J Trop Med Hyg. 2003;68: 121–127.

20. Miller CJ, Barnett ML, Baumann AA, Gutner CA, Wiltsey-Stirman S. The FRAME-IS: a framework for documenting modifications to implementation strategies in healthcare. Implement Sci. 2021;16: 36.

21. Glasgow RE, Green LW, Taylor MV, Stange KC. An evidence integration triangle for aligning science with policy and practice. Am J Prev Med. 2012;42: 646–654.

22. Chun Tie Y, Birks M, Francis K. Grounded theory research: A design framework for novice researchers. SAGE Open Med. 2019;7: 2050312118822927.

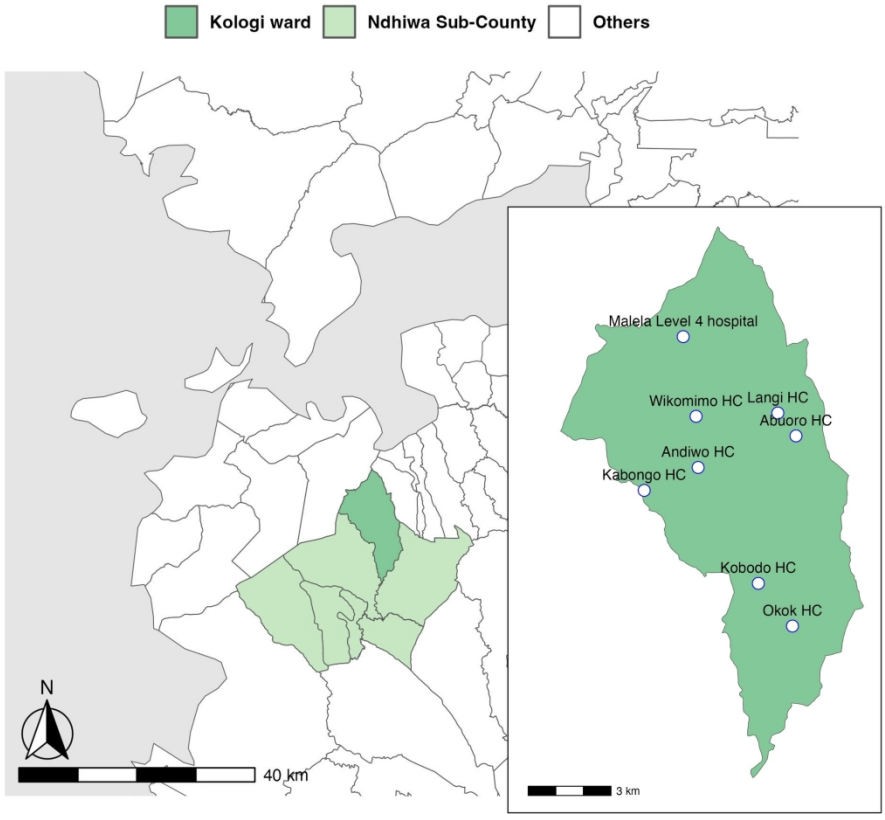
23. Minakawa N, Kawada H, Kongere JO, Sonye GO, Lutiali PA, Awuor B, et al. Effectiveness of screened ceilings over the current best practice in reducing malaria prevalence in western Kenya: a cluster randomised controlled trial. Parasitology. 2022;149: 1–39.

24. Imwong M, Dhorda M, Myo Tun K, Thu AM, Phyo AP, Proux S, et al. Molecular epidemiology of resistance to antimalarial drugs in the Greater Mekong subregion: an observational study. Lancet Infect Dis. 2020;20: 1470–1480.

25. Cohen JM, Smith DL, Cotter C, Ward A, Yamey G, Sabot OJ, et al. Malaria resurgence: a systematic review and assessment of its causes. Malar J. 2012;11: 122.

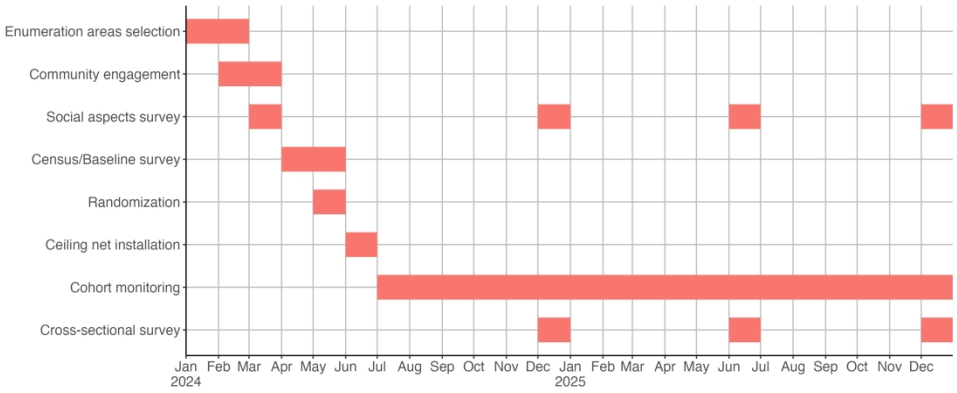
26. Benjamin-Chung J, Li H, Nguyen A, Heitmann GB, Bennett A, Ntuku H, et al. Targeted malaria elimination interventions reduce Plasmodium falciparum infections up to 3 kilometers away. medRxiv. 2023. doi:10.1101/2023.09.19.23295806

27. Mosha JF, Matowo NS, Kulkarni MA, Messenger LA, Lukole E, Mallya E, et al. Effectiveness of long-lasting insecticidal nets with pyriproxyfen–pyrethroid, chlorfenapyr–pyrethroid, or piperonyl butoxide–pyrethroid versus pyrethroid only against malaria in Tanzania: final-year results of a four-arm, single-blind, cluster-randomised trial. Lancet Infect Dis. 2024;24: 87–97.



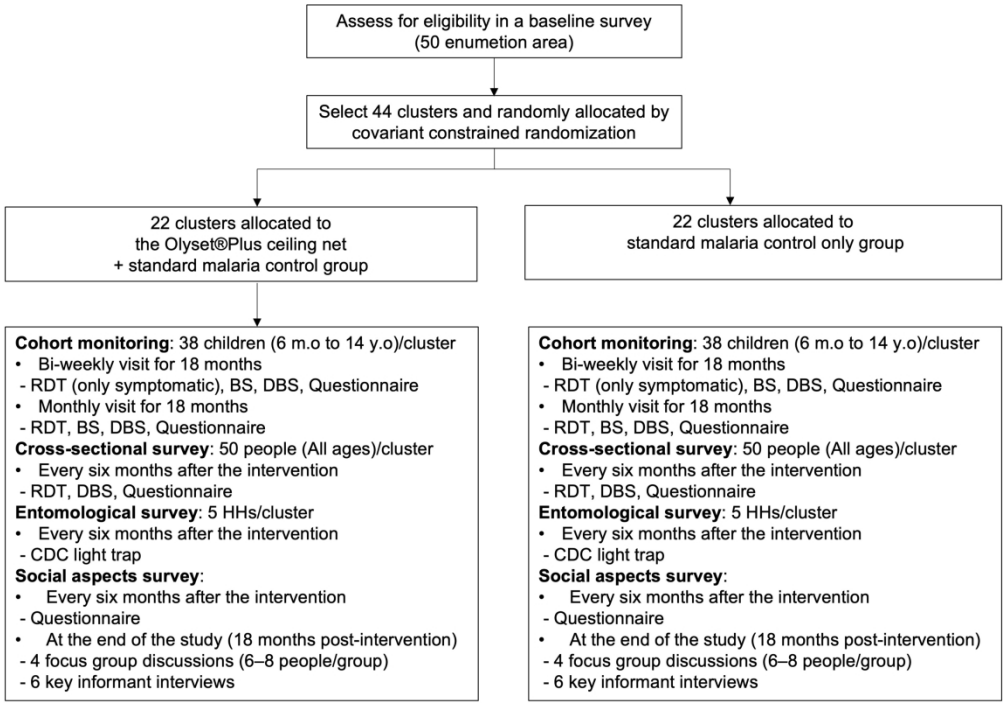
Map of the study area. Inset shows the locations of the level four hospital and seven health centers (HC) in Kanyamwa Kologi Ward.

216x179mm (300 x 300 DPI)



The schedule of trial activities.

774x322mm (118 x 118 DPI)



CONSORT flow diagram and the detail of each survey.

254x178mm (300 x 300 DPI)

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

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, 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[1]. All the sample sizes will be recalculated based on the baseline data, which will be collected before the ceiling net installation.

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 between-cluster 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[2]. 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

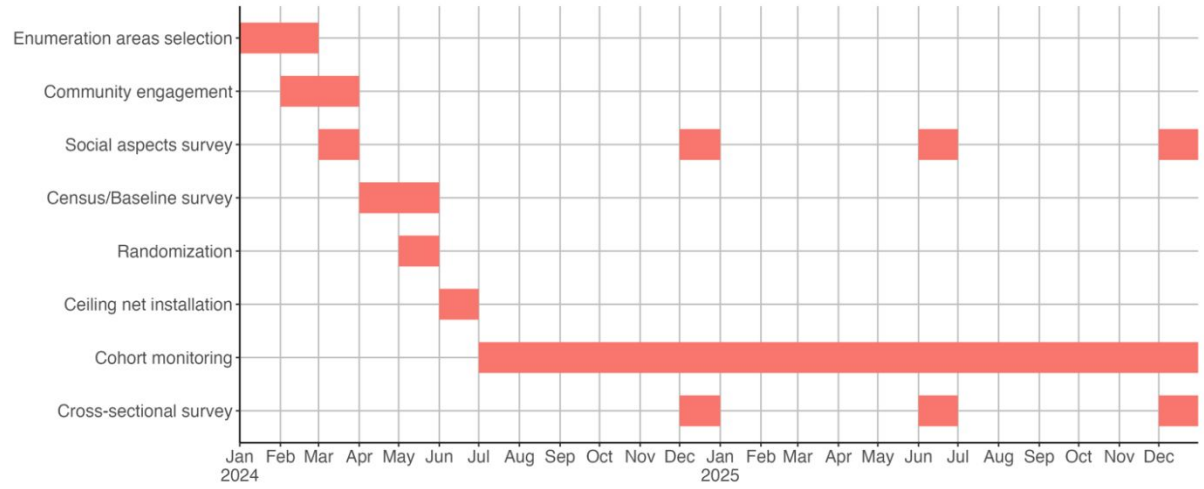


Figure1: Timetable of trial activities

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

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.

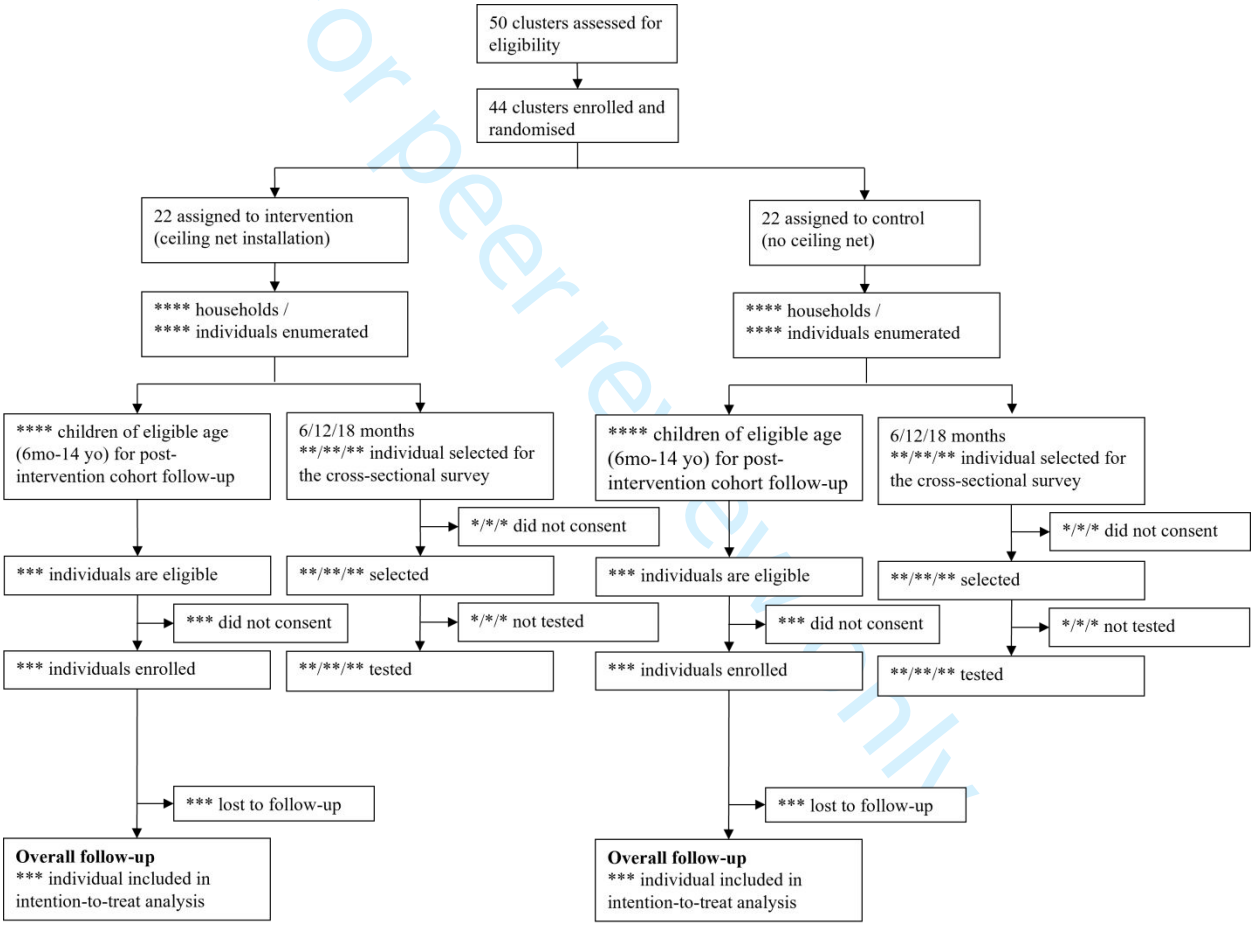


Figure 2: A schematic flow diagram of cluster allocation and study participant selection.

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.

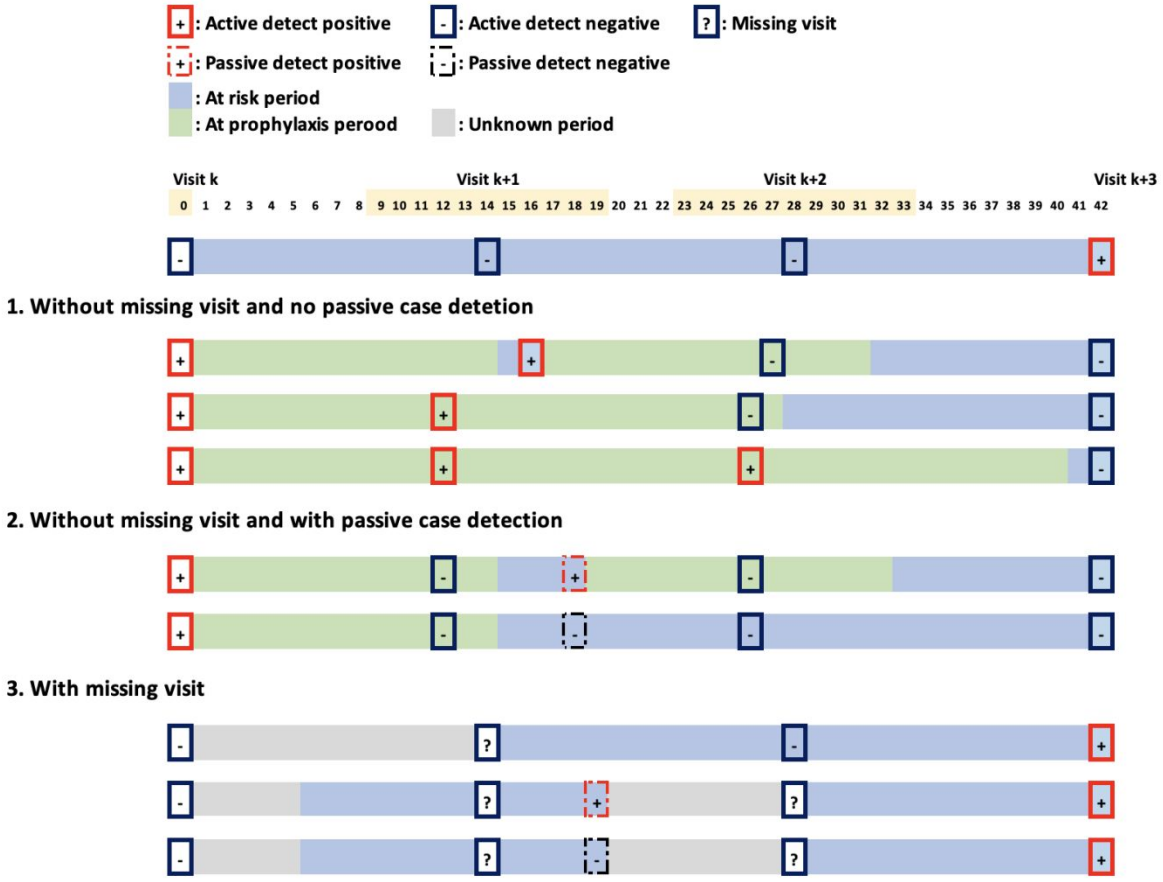
For the overall incidence rate calculation, the time at the risk will be adjusted by subtracting the 14 days of "protection period" of ACT. If a participant misses a particular visit or a second positive is considered a carryover from the previous infection, the period is not included in the at-risk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



No. of event	Person-days	Incidence rate
	42	0.02
	13	0.08
	14	0.00
	2	0.00
	14	0.07
	30	0.00
	28	0.04
	28	0.07
	28	0.04

Figure 3: Specific patterns for incidence rate calculation.

Analysis methods

We will follow the CONSORT guidelines extended for CRT[3] 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, $\boldsymbol{x}_{k,i}$ 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 $\left(1 - \exp\left(\hat{\beta}\right)\right) \times 100\%$, 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[4].

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

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[5]. 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.

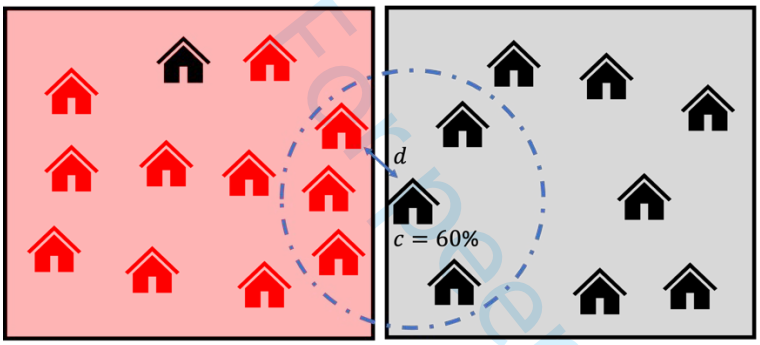


Figure 4: The distance to the nearest discordant household and the coverage of treatment.

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 ≥5%, 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 (≤ 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 https://www.R-project.org/.)

References

1. Hayes, R. J. & Bennett, S. Simple sample size calculation for cluster-randomized trials. *Int. J. Epidemiol.* **28**, 319–326 (1999).
2. Kagaya, W. *et al.* Evaluation of the protective efficacy of Olyset®Plus ceiling net on reducing malaria prevalence in children in Lake Victoria Basin, Kenya: study protocol for a cluster-randomized controlled trial. *Trials* **24**, 354 (2023).
3. Campbell, M. K., Piaggio, G., Elbourne, D. R. & Altman, D. G. Consort 2010 statement: extension to cluster randomised trials. *BMJ* **345**, (2012).
4. Multerer, L., Glass, T. R., Vanobberghen, F. & Smith, T. Analysis of contamination in cluster randomized trials of malaria interventions. *Trials* **22**, 613 (2021).

5. Hawley, W. A. *et al.* Community-wide effects of permethrin-treated bed nets on child mortality and malaria morbidity in western Kenya. *Am. J. Trop. Med. Hyg.* **68**, 121–127 (2003).

BMJ Open

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

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2024-087832.R1
Article Type:	Protocol
Date Submitted by the Author:	21-Nov-2024
Complete List of Authors:	Ko, Yura; Karolinska Institute, 1Department of Microbiology, Tumor and Cell Biology (MTC); Tohoku University Kagaya, Wataru; Nagasaki University, Omondi, Protus; Osaka Metropolitan University Musyoka, Kelvin ; Osaka Metropolitan University Okai, Takatsugu; Osaka Metropolitan University Chan, Chim; Osaka Metropolitan University Kongere, James; Osaka Metropolitan University; Center for Research in Tropical Medicine and Community Development Opiyo, Victor; Center for Research in Tropical Medicine and Community Development Oginga, Jared; Center for Research in Tropical Medicine and Community Development Mungai, Samuel; Mount Kenya University; United States International University Africa Kanoi, Bernard; Mount Kenya University Kanamori, Mariko ; Stockholm University; Kyoto University Yoneoka, Daisuke; National Institute of Infectious Diseases (KNBS), Kenya National Bureau of Statistics; Kenya National Bureau of Statistics Keitany, Kibor; Kenya National Malaria Control Program Songok, Elijah; Kenya Medical Research Institute, Okomo, Gordon ; Ministry of Health Minakawa, Noboru; Nagasaki University Gitaka, Jesse; Mount Kenya University, Research and Innovation Kaneko, Akira; Karolinska Institute, 1Department of Microbiology, Tumor and Cell Biology (MTC); Osaka Metropolitan University
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Infectious diseases, Public health
Keywords:	Malaria, Mosquito Vectors, Infection control < INFECTIOUS DISEASES

Title

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

Authors

Yura K Ko[1,2], Wataru Kagaya[3], Protus Omondi[4], Kelvin B. Musyoka[4], Takatsugu Okai[4], Chim W. Chan[4], James Kongere[4,5], Victor Opiyo[5], Jared Oginga[5], Samuel M. Mbugua[6,7,8], Bernard N. Kanoi[6,8], Mariko Kanamori[9,10], Daisuke Yoneoka[11], Kenya National Bureau of Statistics (KNBS)[12], Kibor Keitany[13], Elijah Songok[14], Gordon Okomo[15], Noboru Minakawa[16], Jesse Gitaka[6,8](*), Akira Kaneko[1,4,16](*)

[1]Department of Microbiology, Tumor and Cell Biology (MTC), Karolinska Institutet, Sweden

[2]Department of Virology, Tohoku University Graduate School of Medicine, Japan

[3]Department of Ecoepidemiology, Institute of Tropical Medicine (NEKKEN), Nagasaki University, Japan

[4]Department of Virology and Parasitology, Graduate School of Medicine, Osaka Metropolitan University, Japan

[5]Center for Research in Tropical Medicine and Community Development, Kenya

[6]Center for Research in Infectious Diseases, Directorate of Research and Innovation, Mount Kenya University, Kenya

[7]School of pharmacy and health sciences, United States International University Africa, Kenya

[8]Center for Malaria Elimination, Mount Kenya University, Kenya

[9]Department of Public Health Sciences, Stockholm University, Sweden

[10]Institute for the Future of Human Society, Kyoto University, Japan

[11]Center for Surveillance, Immunization, and Epidemiologic Research, National Institute of Infectious Diseases, Japan

[12]Kenya National Bureau of Statistics, Kenya

[13]National Malaria Control Programme, Ministry of Health, Kenya

[14]Kenya Medical Research Institute, Kenya

[15]Department of Health, Homa Bay County, Kenya

[16]Department of Vector Ecology and Environment, Institute of Tropical Medicine (NEKKEN), Nagasaki University, Japan

Correspondence to: Wataru Kagaya, Jesse Gitaka

*Senior joint authors

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 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.

Methods: A cluster randomized controlled trial is designed to evaluate the impact of pyrethroid-PBO 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 (pyrethroid-PBO 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 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.

Trial registration: UMIN000053873

Keywords

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

Administrative information

Title {1}	Evaluation of the protective efficacy of Olyset®Plus ceiling net on reducing malaria incidence in children in the Great Lake Region, Kenya: study protocol for a cluster-randomized controlled trial
Trial registration {2a and 2b}.	UMIN000053873
Protocol version {3}	Version 6.0
Funding {4}	This work is supported by the Japan International Cooperation Agency (JICA) and Japan Agency for Medical Research and Development (AMED) under the Science and Technology Research Partnership for Sustainable Development Goals (SATREPS) program.
Author details {5a}	Osaka Metropolitan University, Japan Nagasaki University, Japan Tohoku University, Japan National Institute of Infectious Diseases, Japan Mount Kenya University, Kenya National Malaria Control Programme, Nairobi, Kenya Kenya National Bureau of Statistics, Nairobi, Kenya Kenya Medical Research Institute, Kenya Homa Bay County, Kenya Karolinska Institutet, Sweden

	Stockholm University, Sweden
Name and contact information for the trial sponsor {5b}	Department of Virology and Parasitology/Research Center for Infectious Diseases, Graduate School of Medicine, Osaka Metropolitan University (OMU), Japan 1–4-3, Asahimachi, Abeno, Osaka, Osaka, Japan, 545–8585 TEL: + 81–6-6645–3760 Website: https://ocuparasitology.com/en/ Directorate of Research and Innovation, Mount Kenya University (MKU), Kenya General Kago Road, Thika, Kiambu, Kenya Website: https://www.mku.ac.ke
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.

Strength and limitations of this study

- This is a second cluster-randomized controlled trial of a novel vector control tool, pyrethroid-PBO ceiling net, to evaluate its efficacy in reducing malaria incidence among children.
- The implementation of monthly active screening within the prospective cohort population established in each cluster facilitates the assessment of infection incidence.
- The incorporation of multidisciplinary outcomes, encompassing social aspects and cost-effectiveness analyses, provides valuable insights for the potential future deployment of this intervention within integrated malaria control strategies.
- One of the anticipated limitations is the possible contamination between intervention and control clusters because we will not set a buffer zone due to the geographical proximity among clusters.

Introduction

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 [2], Uganda [3], Eritrea [4], Ethiopia [5], and the United Republic of Tanzania [6] 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 one of the key factors in reducing the impact of LLIN on the malaria burden, together with insufficient provision in the mass net distribution program or shortening durability of nets [7]. In the Lake Victoria basin, alternative uses of LLIN for fishing and protecting crops and chicks are well-known local behaviors [8,9] as reported in other endemic areas [10]. 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 (Sumitomo Chemical) ceiling net. The benefit of installing the pyrethroid-PBO ceiling net in addition to conventional LLINs is detailed elsewhere [11]. Briefly, the pyrethroid-PBO ceiling net provides a combination of physical and chemical protection against mosquitoes

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 ceiling nets on malaria morbidity and transmission in the Lake Victoria basin of Kenya. Preliminary data 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 combining various tools to maximize the impact of the malaria control program, it is important to understand 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.

Objectives {7}

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

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.

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 covariate-constrained 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.

Methods: Participants, interventions and outcomes

Study setting {9}

Location and administrative structure

Ndhiwa (713.5 km²) 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 poultry [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℃. The relative humidity remains elevated year-round, fluctuating between 75% to 85%

[17].

Demographics

The population of Kanyamwa Kologi Ward is approximately 33,000 according to the 2019 national census [18]. The dominant ethnic group in the region is Luo and the primary languages are DhoLuo, Kiswahili, and English. There are 172 primary and 36 secondary schools in Ndhiwa Sub-County [19]. Within Kanyamwa Kologi Ward, there are 28 primary and 7 secondary schools.

Malaria epidemiology and control measures

Based on the KHIS, there were 429.1 and 457.2 confirmed malaria cases per 1,000 population in Ndhiwa Sub-County and Kanyamwa Kologi Ward, respectively, in 2023. The primary malaria vector in the sub-county is *Anopheles funestus*, which prefers feeding on humans. Although *An. arabiensis* exhibits predominantly zoophilic behavior, it is also a significant malaria vector in our study area [20]. In Homa Bay County, LLINs have been distributed every three years since the early 2000s, and IRS and the RTS,S malaria vaccine have been piloted in several areas since 2018 and 2019, respectively [21]. Notably PBO-incorporated LLINs (Veeralin®LN, manufactured by VKA Polymers, Tamil Nadu, India) were distributed in late 2023. In Kanyamwa Kologi Ward, there is one level four hospital and seven health centers.

Eligibility criteria {10}

As the ceiling nets are installed per structure, we set the inclusion criteria on a structural basis. The inclusion criteria for the installation of the ceiling nets are (1) residential structures with at least one permanent resident aged 18 years or older in the household, (2) informed consent provided by a resident in the household, and (3) house structure amenable to ceiling net installation 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 structure, confirmed by at least two visits by community health promoters (CHPs), (2) dwelling structure to be vacated or destroyed within the study period, (3) non-eligible house structure for the ceiling net installation, and (4) non-residential structures (school, shop, kitchen, storage, and toilet). The inclusion

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.

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.

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

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.

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.

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.

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

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.

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

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

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. To monitor the long-term impact of the intervention, the research team may conduct additional cross-sectional surveys 2 and 3 years post-intervention to monitor further parasite transmission in the population.

Outcomes {12}

Epidemiological domain: The primary outcome will be symptomatic malaria case incidence, defined as axillary temperature of ≥37·5°C or a history of fever in the preceding 48 hours, and positive RDT, in children aged 6 months to 14 years enrolled in the cohort, monitored with a monthly visit and passive case detection in the health facilities during an 18-month follow-up. The secondary outcomes will be (1) the prevalence of *Plasmodium* infections by PCR in all age groups at 6, 12, and 18 months post-intervention, (2) the prevalence of *Plasmodium* infections by PCR among individuals without the ceiling net in all age groups at 6, 12, and 18 months post-intervention, and (3) infection incidence by PCR in the prospective cohort of children aged 6 months to 14 years over 18 months.

Entomological domain: The primary outcome will be the density of the primary malaria vectors, species composition and sporozoite infection rates. Indoor malaria vector density will be determined using CDC light trap, and species composition and sporozoite infection rates will be determined by microscopy and

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.

Epidemiological survey

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 between-cluster 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 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.

Implementation {16c}

After the baseline survey, covariate-constrained randomization will be used to allocate the 44 clusters across the two study arms. 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. An independent statistician will perform the randomization. Local study assistants will perform participant enrollment.

Assignment of interventions: Blinding

Who will be blinded {17a}

Due to the visibility of the pyrethroid-PBO ceiling net, neither the trial participants nor the members of the study team who take part in field activities can be blinded. However, laboratory- and office-based personnel (e.g., microscopists, laboratory technicians, and data analysts) will be blinded to the identity and intervention status of the trial participants since all biological specimens will be identified by a unique numeric study identifier, and personal information will be removed before analyses.

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 they need to be unblinded.

Data collection and management

Questionnaires for the baseline survey, cohort surveys, and post-intervention cross-sectional surveys are provided in the supplementary file.

Plans for assessment and collection of outcomes {18a}

Census and baseline cross-sectional survey

In Kanyamwa Kologi Ward, 85 census enumeration areas (EAs) are defined by the 2019 Kenya Population and Housing Census. Births, deaths, and migrations in each EA are regularly updated by CHPs using the integrated community health system maintained by the Ministry of Health. Fifty EAs are randomly selected for our baseline survey, during which demographic information of all individuals is updated. To ensure balanced cluster allocation, the baseline survey includes a questionnaire for all households, RDT testing of all children aged 6 months to 14 years, and an entomological survey of randomly sampled households. We modified the questionnaire used in the 2020 Kenya Malaria Indicator Survey (KMIS) mainly to quantify the SES of each household and bed net usage. In addition, we add questions to quantify the favorability of ceiling nets before the intervention.

Cohort monitoring

Incidence of clinical malaria in the prospective cohort will be estimated by both active and passive case detections. For active case detection, we will conduct home visits every four weeks. From all cohort participants, axillary temperature will be measured using a digital thermometer, and *Plasmodium* infection status will be determined by RDT and PCR. 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. 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 finger-prick 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℃. 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

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.

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 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.

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.

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].

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.

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 (≤ 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 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 hot-deck imputation methods if the missing fraction for the covariate is <5% or appropriate multiple imputation approaches if the missing fraction for a covariable are ≥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}

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 self-reported 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.

Dissemination plans {31a}

Study results will be shared with the 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. Suggestions from the participants will also help shape the future improvement of the intervention.

Discussion

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 cost-effective and widely accepted by local communities are urgently needed to contain the spread of artemisinin-resistant *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 trial, contamination between intervention and control clusters cannot be excluded, as buffer zones between intervention and control clusters cannot be created due to geographic proximity of houses and villages in the ward. A recent study, however, has shown that the spillover effect of interventions on malaria can extend to 3 km [33], so buffer zones of a few hundred meters, as set out in many studies, may not be sufficient. We will try to eliminate such contamination effects by integrating spatial data into our statistical model. Second,

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 in-depth 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-PBO-incorporated 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.

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.

Abbreviations

ACT: artemisinin-based combination therapy

CHP: community health promoter

CRCT: cluster-randomized controlled trial

CV: coefficient of variation

KHIS: Kenya Health Information System

ITN: insecticide treated nets

IRS: indoor residual spraying

LLIN: long-lasting insecticidal nets

MKU: Mount Kenya University

PBO: piperonyl butoxide

RDT: rapid diagnosis tests

VGSC: Voltage gated sodium channel

Declarations

Acknowledgements

We would like to express our sincere gratitude to this study's participants, field, and laboratory staff. In addition, we acknowledge the collaboration and support of health offices in Homa Bay County, Kenya.

Authors' contributions {31b}

AK and JG are co-principal investigators. AK is the guarantor. YKK, WK, and AK developed the original concept. All authors discussed and contributed to the study protocol. YKK, WK, PO, KBM, JK, VO, JO, SMM, KNBS, KK, ES, GO, and AK contributed the preparation of the baseline survey. YKK, WK, PO, BM, TO, CWC, JK, SM, and MK drafted the manuscript. YKK, WK, CWC, MK, GO, and JG contributed to the revisions of the draft of the manuscript. DY participated as a senior statistician. YKK and MK drafted the statistical analysis plan (SAP) and WK, CWC, and DY revised. The authors read and approved the final manuscript and SAP.

Funding {4}

AK and JG received support from JICA/AMED joint research project (SATREPS) (Grant no. 20JM0110020H0002), Hitachi Fund Support for Research Related to Infectious Diseases, and Sumitomo

Chemical Corporation. The funding bodies play no role in the study design, data collection, analysis, interpretation, and publication.

Availability of data and materials {29}

The study regimes, consent forms, assent forms, and study-related materials are accessible from the corresponding author. The final trial dataset will be available to all investigators. The corresponding author will make the de-identified datasets and source codes for all analysis available upon reasonable request.

Patient and public involvement

Although the study design was developed through discussions among the researchers, consultations with the local population were conducted prior to initiating the baseline survey, and their input was incorporated into the study. Community involvement will also be ongoing during the implementation of interventions and research activities.

Ethics approval and consent to participate {24}

Ethics approvals were received from Mount Kenya University Institutional Scientific Ethics Review Committee (MKU-ISERC) (approval number: 2565) and the Ethics Committee in Osaka Metropolitan University (approval number: 2024-068).

Written informed consents will be sought from study participants before the baseline survey, installation of ceiling nets, each cross-sectional survey, and the start of prospective cohort surveys. In cross-sectional and cohort surveys, informed assent will be obtained from children under the age of 15 who can understand the study at a level appropriate for their development, in addition to the consent of a parent or legal guardian. Participants have the right to withdraw from the study at any time, and the option to withhold previously collected samples from any future analyses and studies.

The samples collected in this study may potentially be used for other research purposes. This is clearly stated in the informed consent form. In such cases, we will obtain the necessary ethical approval and provide participants with the chance to opt-out from this. All experiments will be carried out in adherence to WHO requirements and the Declaration of Helsinki.

Consent for publication {32}

We will not present identifying images or other personal or clinical details of participants. The participant information materials and informed consent form are available from the corresponding author on request.

Competing interests {28}

AK and JG were partially supported by a research grant from Sumitomo Chemical Corporation. Other authors had no competing interests.

References

1. Noor AM, Alonso PL. The message on malaria is clear: progress has stalled. The Lancet. 2022. p. 1777.

2. Rosenthal PJ, Björkman A, Dhorda M, Djimde A, Dondorp AM, Gaye O, et al. Cooperation in Countering Artemisinin Resistance in Africa: Learning from COVID-19. Am J Trop Med Hyg. 2022;106: 1568–1570.

3. Stokes BH, Ward KE, Fidock DA. Evidence of Artemisinin-Resistant Malaria in Africa. The New England journal of medicine. 2022. pp. 1385–1386.

4. Mihreteab S, Platon L, Berhane A, Stokes BH, Warsame M, Campagne P, et al. Increasing Prevalence of Artemisinin-Resistant HRP2-Negative Malaria in Eritrea. N Engl J Med. 2023;389: 1191–1202.

5. Fola AA, Feleke SM, Mohammed H, Brhane BG, Hennelly CM, Assefa A, et al. Plasmodium falciparum resistant to artemisinin and diagnostics have emerged in Ethiopia. Nature Microbiology. 2023;8: 1911–1919.

6. World Health Organization. World malaria report 2023. 2023.

7. Bhatt S, Weiss DJ, Mappin B, Dalrymple U, Cameron E, Bisanzio D, et al. Coverage and system efficiencies of insecticide-treated nets in Africa from 2000 to 2017. Elife. 2015;4. doi:10.7554/eLife.09672

8. Larson PS, Minakawa N, Dida GO, Njenga SM, Ionides EL, Wilson ML. Insecticide-treated net use before and after mass distribution in a fishing community along Lake Victoria, Kenya: successes and unavoidable pitfalls. Malar J. 2014;13: 466.

9. Minakawa N, Dida GO, Sonye GO, Futami K, Kaneko S. Unforeseen misuses of bed nets in fishing villages along Lake Victoria. Malar J. 2008;7: 165.

10. Santos EM, Coalson JE, Munga S, Agawo M, Jacobs ET, Klimentidis YC, et al. "After those nets are torn, most people use them for other purposes": an examination of alternative bed net use in western Kenya. Malar J. 2020;19: 272.

11. Kagaya W, Chan CW, Kongere J, Kanoi BN, Ngara M, Omondi P, et al. Evaluation of the protective efficacy of Olyset®Plus ceiling net on reducing malaria prevalence in children in Lake Victoria Basin, Kenya: study protocol for a cluster-randomized controlled trial. Trials. 2023;24: 354.

12. Fernandez Montoya L, Alafo C, Martí-Soler H, Máquina M, Comiche K, Cuamba I, et al. Overlaying human and mosquito behavioral data to estimate residual exposure to host-seeking mosquitoes and the protection of bednets in a malaria elimination setting where indoor residual spraying and nets were deployed together. PLoS One. 2022;17: e0270882.

13. Ladu HI, Shuaibu U, Pulford J. Reasons for mosquito net non-use in malaria-endemic countries: A review of qualitative research published between 2011 and 2021. Trop Med Int Health. 2024;29: 647–656.

14. Minakawa N, Kawada H, Kongere JO, Sonye GO, Lutiali PA, Awuor B, et al. Effectiveness of screened ceilings over the current best practice in reducing malaria prevalence in western Kenya: a cluster randomised controlled trial. Parasitology. 2022;149: 1–39.

15. Idris Z, Chan CW, Kongere J, Gitaka J, Logedi J, Omar A, et al. High and Heterogeneous Prevalence of Asymptomatic and Sub-microscopic Malaria Infections on Islands in Lake Victoria, Kenya. Sci Rep. 2016;6: 1–13.

16. Homabay County | Ndhiwa Municipality. [cited 13 Feb 2024]. Available: https://www.homabay.go.ke/department/ndhiwa-municipality

17. Ndhiwa, Homa Bay, KE Climate Zone, Monthly Averages, Historical Weather Data. [cited 13 Feb 2024]. Available: https://weatherandclimate.com/kenya/homa-bay/ndhiwa

18. Statistics KNB of SNKNB of. 2019 Kenya Population and Housing Census Reports. 28 Feb 2020 [cited 13 Feb 2024]. Available: https://housingfinanceafrica.org/documents/2019-kenya-population-and-housing-census-reports/

19. Ndhiwa Constituency Schools | ShuleZote. [cited 13 Feb 2024]. Available: https://shulezote.co.ke/place/constituency/migori/ndhiwa/?page=1

20. VectorLink-Kenya-2021-End-of-Spray-Report-Submision-Approved-July-23-2021-sxf-CL.pdf. Available: https://d1u4sg1s9ptc4z.cloudfront.net/uploads/2021/09/VectorLink-Kenya-2021-End-of-Spray-Report-Submision-Approved-July-23-2021-sxf-CL.pdf

21. End-of-Spray-Report-Kenya-2023.pdf. Available: https://d1u4sg1s9ptc4z.cloudfront.net/uploads/2023/10/End-of-Spray-Report-Kenya-2023.pdf

22. Hayes RJ, Bennett S. Simple sample size calculation for cluster-randomized trials. Int J Epidemiol. 1999;28: 319–326.

23. Isozumi R, Fukui M, Kaneko A, Chan CW, Kawamoto F, Kimura M. Improved detection of malaria cases in island settings of Vanuatu and Kenya by PCR that targets the Plasmodium mitochondrial cytochrome c oxidase III (cox3) gene. Parasitol Int. 2015;64: 304–308.

24. Multerer L, Glass TR, Vanobberghen F, Smith T. Analysis of contamination in cluster randomized trials of malaria interventions. Trials. 2021;22: 613.

25. Hawley WA, Phillips-Howard PA, ter Kuile FO, Terlouw DJ, Vulule JM, Ombok M, et al. Community-wide effects of permethrin-treated bed nets on child mortality and malaria morbidity in western Kenya. Am J Trop Med Hyg. 2003;68: 121–127.

26. Miller CJ, Barnett ML, Baumann AA, Gutner CA, Wiltsey-Stirman S. The FRAME-IS: a framework for documenting modifications to implementation strategies in healthcare. Implement Sci. 2021;16: 36.

27. Glasgow RE, Green LW, Taylor MV, Stange KC. An evidence integration triangle for aligning science with policy and practice. Am J Prev Med. 2012;42: 646–654.

28. Chun Tie Y, Birks M, Francis K. Grounded theory research: A design framework for novice researchers. SAGE Open Med. 2019;7: 2050312118822927.

29. Wager S, Athey S. Estimation and inference of heterogeneous treatment effects using random forests. J Am Stat Assoc. 2018;113: 1228–1242.

30. van der Laan MJ, Polley EC, Hubbard AE. Super learner. Stat Appl Genet Mol Biol. 2007;6: Article25.

31. Imwong M, Dhorda M, Myo Tun K, Thu AM, Phyo AP, Proux S, et al. Molecular epidemiology of resistance to antimalarial drugs in the Greater Mekong subregion: an observational study. Lancet Infect Dis. 2020;20: 1470–1480.

32. Cohen JM, Smith DL, Cotter C, Ward A, Yamey G, Sabot OJ, et al. Malaria resurgence: a systematic review and assessment of its causes. Malar J. 2012;11: 122.

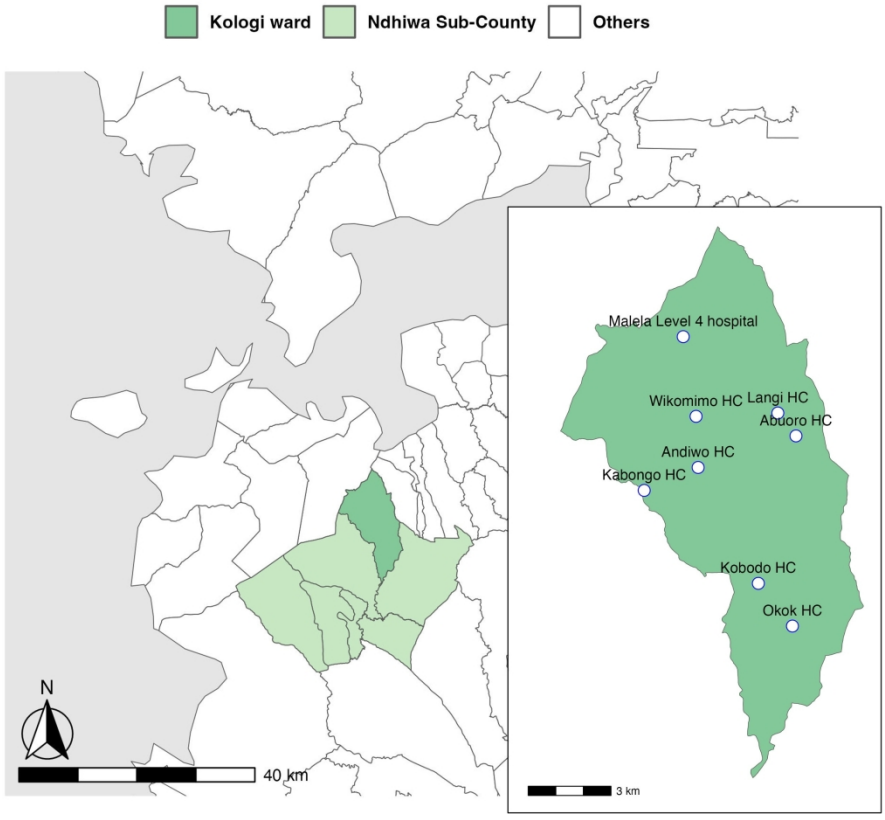
33. Benjamin-Chung J, Li H, Nguyen A, Barratt Heitmann G, Bennett A, Ntuku H, et al. Extension of efficacy range for targeted malaria-elimination interventions due to spillover effects. Nat Med. 2024. doi:10.1038/s41591-024-03134-z

34. Mosha JF, Matowo NS, Kulkarni MA, Messenger LA, Lukole E, Mallya E, et al. Effectiveness of long-lasting insecticidal nets with pyriproxyfen–pyrethroid, chlorfenapyr–pyrethroid, or piperonyl butoxide–pyrethroid versus pyrethroid only against malaria in Tanzania: final-year results of a four-arm, single-blind, cluster-randomised trial. Lancet Infect Dis. 2024;24: 87–97.

Figure 1: Map of the study area. Inset shows the locations of the level four hospital and seven health centers (HC) in Kanyamwa Kologi Ward.

Figure 2: The schedule of trial activities.

Figure 3: CONSORT flow diagram and the detail of each survey



Map of the study area. Inset shows the locations of the level four hospital and seven health centers (HC) in Kanyamwa Kologi Ward.

216x179mm (330 x 330 DPI)

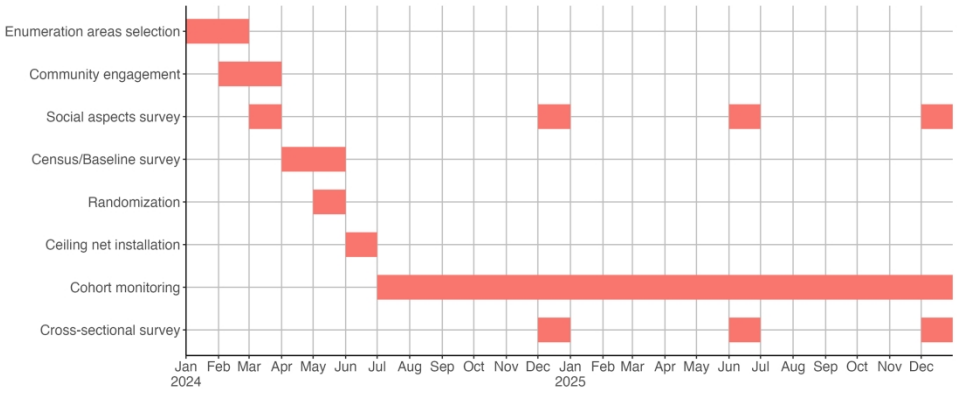
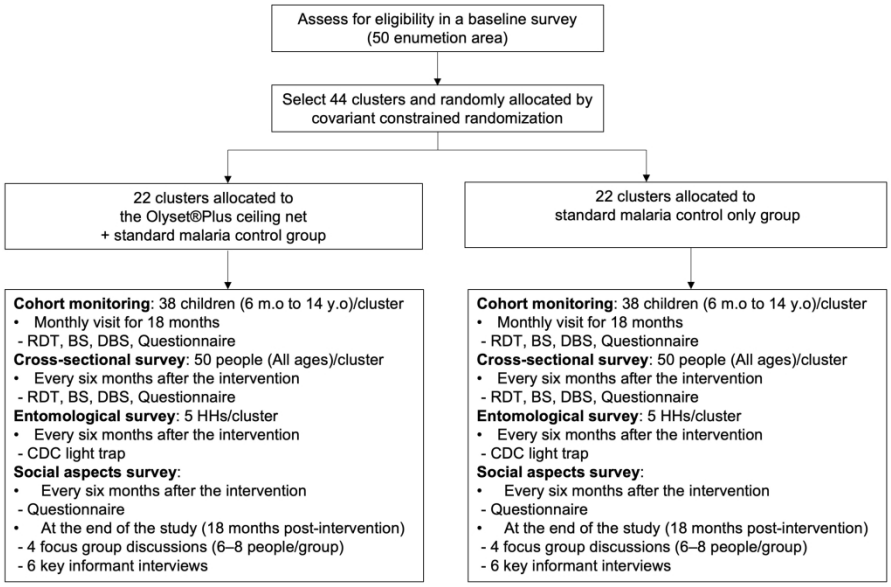


Figure 2: The schedule of trial activities.

304x127mm (300 x 300 DPI)



CONSORT flow diagram and the detail of each survey

288x186mm (300 x 300 DPI)

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.

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[1]. All sample sizes will be recalculated based on the baseline data, which will be collected before the ceiling net installation.

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 between-cluster 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[2]. 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

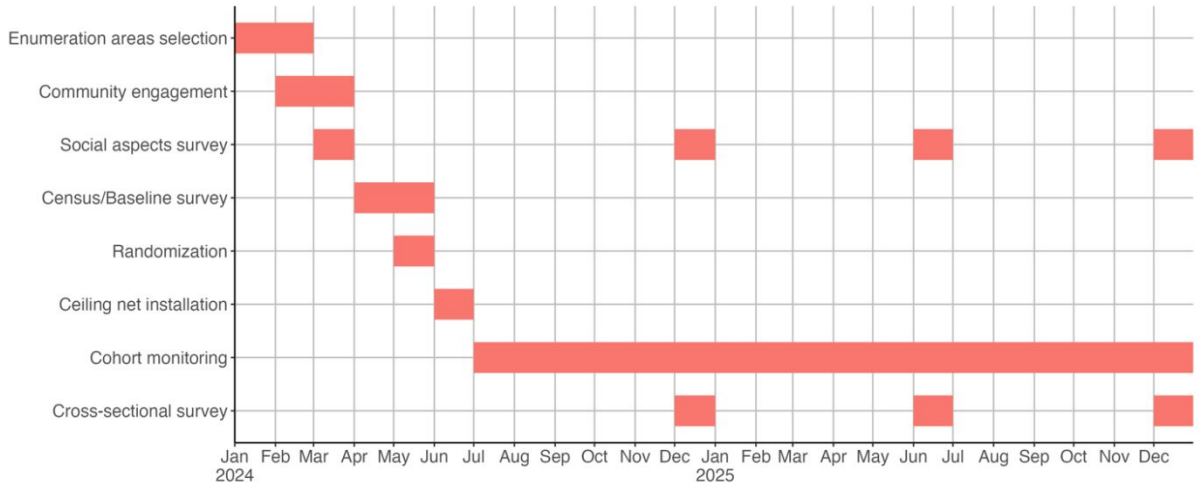


Figure1: Timetable of trial activities

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.

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

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.

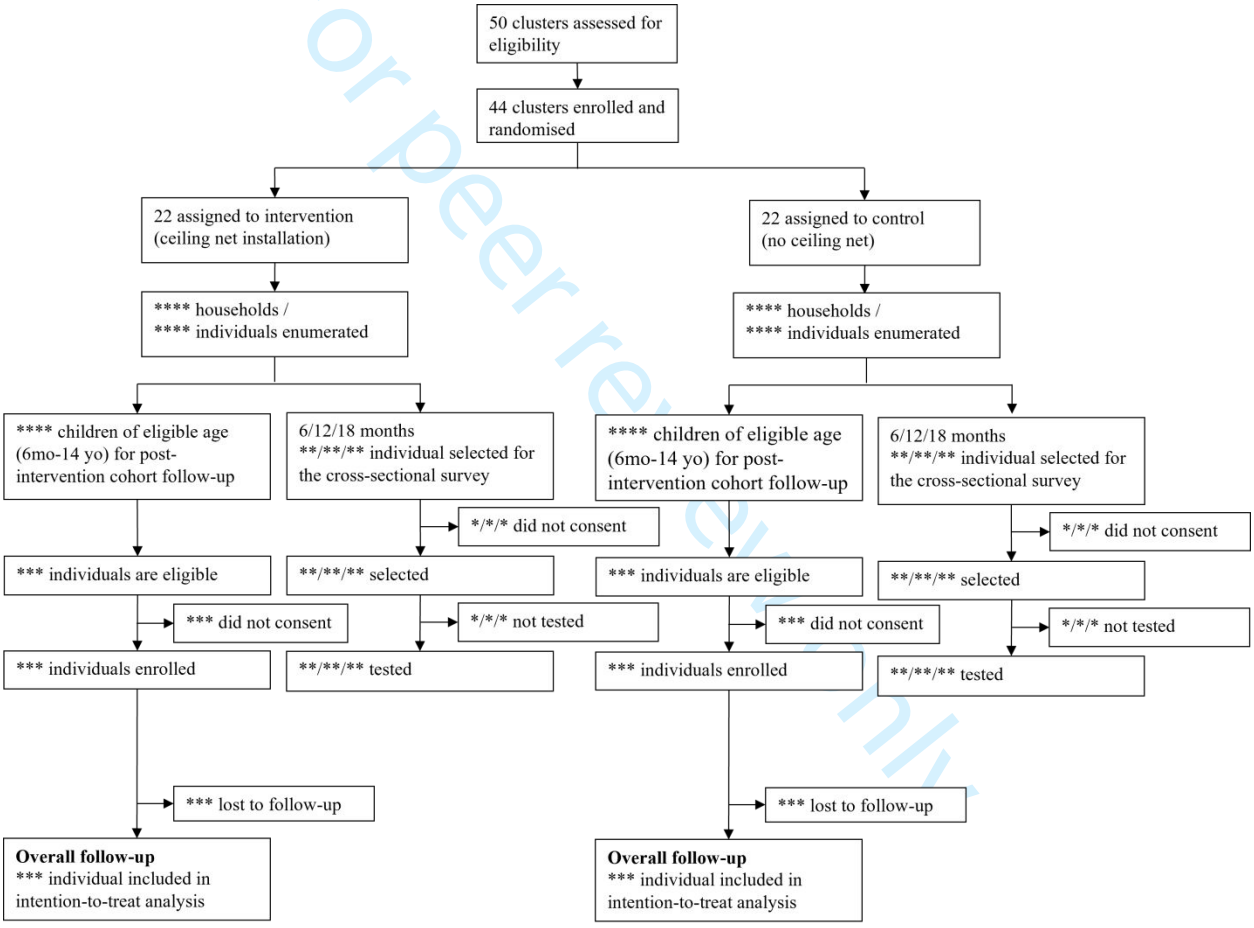


Figure 2: A schematic flow diagram of cluster allocation and study participant selection.

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 by PCR at 6, 12, and 18 months post-intervention in all age groups among intervention and control clusters.
2. 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 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

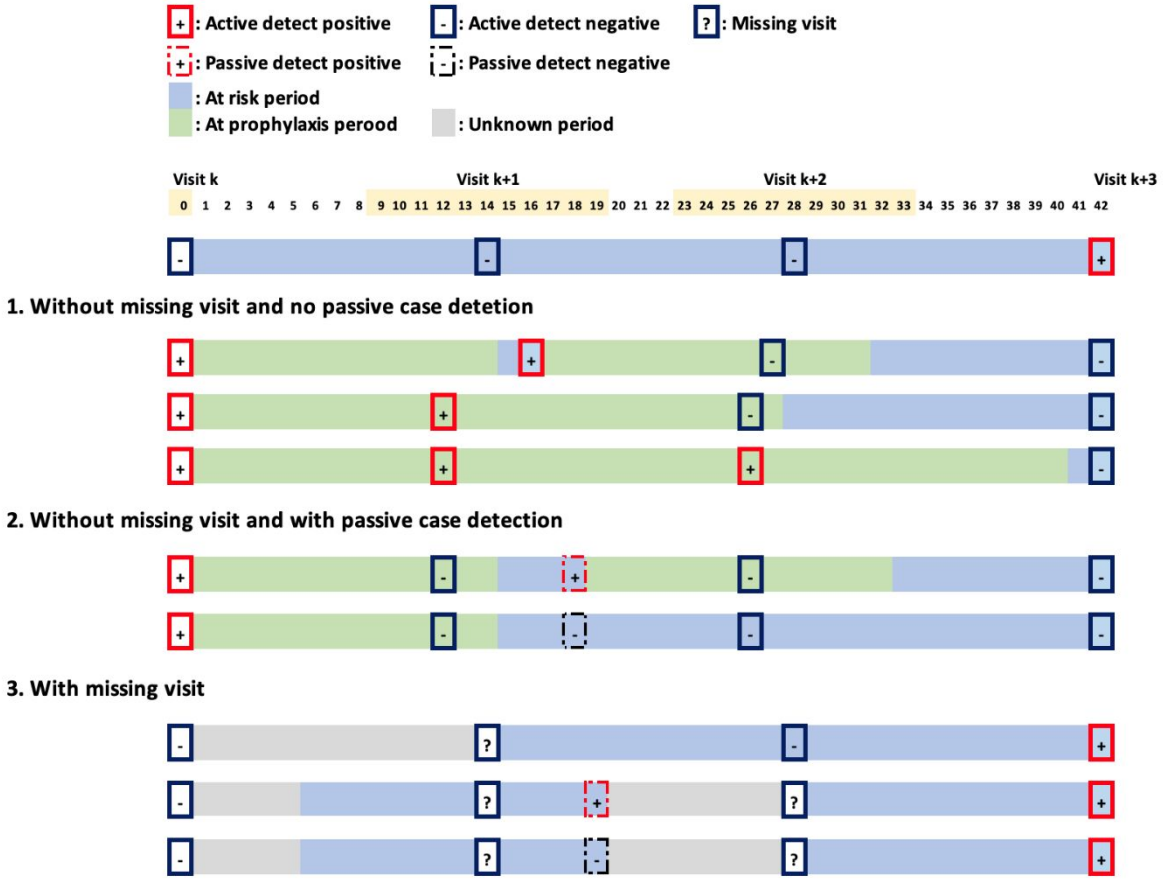
of "protection period" of ACT. If a participant misses a particular visit or a second positive is considered a carryover from the previous infection, the period is not included in the at-risk period.

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 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[3]. 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.



No. of event	Person-days	Incidence rate
	42	0.02
	13	0.08
	14	0.00
	2	0.00
	14	0.07
	30	0.00
	28	0.04
	28	0.07
	28	0.04

Figure 3: Specific patterns for case incidence rate calculation.

Analysis methods

We will follow the CONSORT guidelines extended for CRT[4] 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:

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

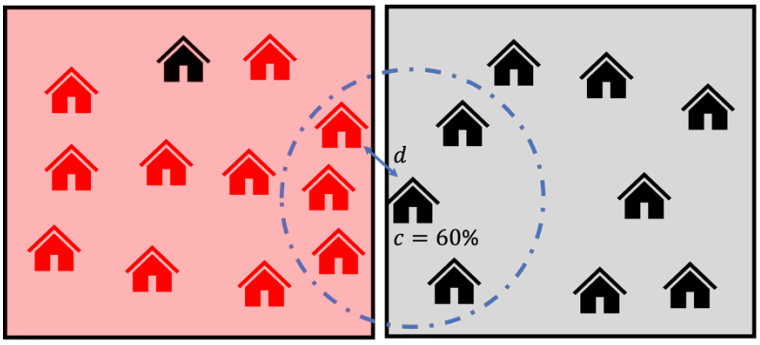
where $\mu_{k,i}$ is the mean incidence rate of individual i in cluster k, $\boldsymbol{x}_{k,i}$ is the covariate vector including individual and cluster level data, z_k is the Gaussian-type random effect at the cluster level. The protective efficacy will be estimated by $\left(1 - \exp\left(\hat{\beta}\right)\right) \times 100\%$, 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[5].

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[6]. 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.



: 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 ≥5%, 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 (≤ 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 https://www.R-project.org/.)

References

1. Hayes, R. J. & Bennett, S. Simple sample size calculation for cluster-randomized trials. *Int. J. Epidemiol.* **28**, 319–326 (1999).
2. Kagaya, W. *et al.* Evaluation of the protective efficacy of Olyset®Plus ceiling net on reducing malaria prevalence in children in Lake Victoria Basin, Kenya: study protocol for a cluster-randomized controlled trial. *Trials* **24**, 354 (2023).
3. Bennett, A. *et al.* A longitudinal cohort to monitor malaria infection incidence during mass drug administration in Southern Province, Zambia. *Am. J. Trop. Med. Hyg.* **103**, 54–65 (2020).
4. Campbell, M. K., Piaggio, G., Elbourne, D. R. & Altman, D. G. Consort 2010 statement: extension to cluster randomised trials. *BMJ* **345**, (2012).
5. Multerer, L., Glass, T. R., Vanobberghen, F. & Smith, T. Analysis of contamination in cluster randomized trials of malaria interventions. *Trials* **22**, 613 (2021).

6. Hawley, W. A. *et al.* Community-wide effects of permethrin-treated bed nets on child mortality and malaria morbidity in western Kenya. *Am. J. Trop. Med. Hyg.* **68**, 121–127 (2003).

0. Consent form

Please complete the survey below.

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.	◯ Yes ◯ No
Name of participant	_____
Signature of participant	_____
Name of witness	_____
Signature of witness	_____
Do you have a child to participate in the study?	◯ Yes ◯ No
Check the following box.	◯ I DO CONSENT: I do agree my child to take part in this study. ◯ I DO NOT CONSENT: I do not wish my child to participate in this study.
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	_____
Signature of witness	_____

id1 _____

id2 _____

id3 _____

"[id1]-[id2]-[id3]"

Please fix the structure ID above on the roof in front of the door.

Date _____

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?
- ◯ PIPED INTO DWELLING
- ◯ PIPED TO YARD/PLOT
- ◯ PIPED TO NEIGHBOR
- ◯ PUBLIC TAP/STANDPIPE
- ◯ DUG PROTECTED WELL
- ◯ DUG UNPROTECTED WELL
- ◯ WATER FROM PROTECTED SPRING
- ◯ WATER FROM UNPROTECTED SPRING
- ◯ RAINWATER
- ◯ TANKER TRUCK
- ◯ CART WITH SMALL TANK
- ◯ SURFACE WATER (RIVER/DAM/LAKE/POND/STREAM /IRRIGATION CHANNEL)
- ◯ BOTTLED WATER
- ◯ OTHER

Specify it. _____

What is the main source of water used by your household for other purposes such as cooking and handwashing?
- ◯ PIPED INTO DWELLING
- ◯ PIPED TO YARD/PLOT
- ◯ PIPED TO NEIGHBOR
- ◯ PUBLIC TAP/STANDPIPE
- ◯ DUG PROTECTED WELL
- ◯ DUG UNPROTECTED WELL
- ◯ WATER FROM PROTECTED SPRING
- ◯ WATER FROM UNPROTECTED SPRING
- ◯ RAINWATER
- ◯ TANKER TRUCK
- ◯ CART WITH SMALL TANK
- ◯ SURFACE WATER (RIVER/DAM/LAKE/POND/STREAM/C /IRRIGATION CHANNEL)
- ◯ OTHER

Specify it.	_____
Where is that water source located?	◯ IN OWN DWELLING ◯ IN OWN YARD/PLOT ◯ ELSEWHERE
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.	◯ FLUSH TO PIPED SEWER SYSTEM ◯ FLUSH TO SEPTIC TANK ◯ FLUSH TO PIT LATRINE ◯ FLUSH TO SOMEWHERE ELSE ◯ FLUSH, DON'T KNOW WHERE ◯ VENTILATED IMPROVED PIT LATRINE ◯ PIT LATRINE WITH SLAB ◯ PIT LATRINE WITHOUT SLAB/OPEN PIT ◯ COMPOSTING TOILET ◯ BUCKET TOILET ◯ HANGING TOILET/HANGING LATRINE ◯ NO FACILITY/BUSH/FIELD ◯ OTHER
Specify it.	_____
Do you share this toilet facility with other households?	◯ Yes ◯ No
Including your own compound, how many households use this toilet facility?	◯ LESS THAN 10 HOUSEHOLDS ◯ 10 OR MORE HOUSEHOLDS ◯ DON'T KNOW
Including your own household, how many households use this toilet facility (if less than 10)?	_____
Where is this toilet facility located?	◯ IN OWN DWELLING ◯ IN OWN YARD/PLOT ◯ ELSEWHERE
In your household, what type of cooking device (cookstove) is mainly used for cooking?	◯ ELECTRIC STOVE ◯ SOLAR COOKER ◯ LIQUEFIED PETROLEUM GAS (LPG)/COOKING GAS STOV ◯ PIPED NATURAL GAS STOVE ◯ BIOGAS STOVE ◯ LIQUID FUEL STOVE ◯ MANUFACTURED SOLID FUEL STOVE (i.g. Jiko) ◯ THREE STONE STOVE/OPENFIRE ◯ NO FOOD COOKED IN THE HOUSEHOLD ◯ OTHER
Specify it.	_____

What type of fuel or energy source is mainly used in this cookstove?	◯ ALCOHOL/ETHANOL ◯ GASOLINE/DIESEL ◯ KEROSENE/PARAFFIN ◯ COAL/LIGNITE ◯ CHARCOAL ◯ WOOD ◯ STRAW/SHRUBS/GRASS ◯ AGRICULTURAL CROP ◯ ANIMAL DUNG/WASTE ◯ PROCESSED BIOMASS (PELLETS) OR WOODCHIPS ◯ GARBAGE/PLASTIC ◯ SAWDUST ◯ OTHER
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? - Horses	_____
How many of the following (animals) livestock does this household own? - Donkeys	_____
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?	◯ Yes ◯ No
Do you know how many acres of agricultural land do members of this household own?	◯ Yes ◯ No
How many acres of agricultural land do members of this household own? ACRES	_____
Does your household have:	☐ Electricity? ☐ A radio? ☐ A television? ☐ A fixedlinetelephone? ☐ A computer? ☐ A refrigerator? ☐ A solarpanel? ☐ A table? ☐ A chair? ☐ A sofa? ☐ A bed? ☐ A cupboard? ☐ A clock? ☐ A microwave oven? ☐ A DVD player? ☐ A CD player?
Does any member of this compound own:	☐ A wrist watch? ☐ A mobile phone? ☐ A bicycle? ☐ A motorcycle or motor scooter? ☐ An animal-drawn cart? ☐ A car or truck? ☐ A boat with a motor?
Does any member of this household have an account in a bank or other financial institution?	◯ Yes ◯ No
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?	◯ Yes ◯ No
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

Does your household have any bed nets?	◯ Yes ◯ No
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.	☐ Air flow disturbance ☐ Heat ☐ Appearance ☐ Pets ☐ Fire ☐ Social culture and religious factor ☐ Others
Specify it	_____
Do you have any concerns about the ceiling net? Select all that apply.	☐ Air flow disturbance ☐ Heat ☐ Appearance ☐ Pets ☐ Fire ☐ Social culture and religious factor ☐ No concern ☐ Others
Specify it	_____
OBSERVE MAIN MATERIAL OF THE FLOOR OF THE DWELLING/SLEEPING ROOM. RECORD OBSERVATION.	◯ EARTH/SAND ◯ DUNG ◯ WOOD PLANKS ◯ PALM/BAMBOO ◯ PARQUET OR POLISHED WOOD ◯ VINYL OR ASPHALT STRIPS ◯ CERAMIC TILES ◯ CEMENT ◯ CARPET ◯ OTHER
Specify it.	_____

OBSERVE MAIN MATERIAL OF THE ROOF OF THE DWELLING. RECORD OBSERVATION.	◯ NO ROOF ◯ THATCH/PALM LEAF ◯ RUSTIC MAT ◯ PALM/BAMBOO ◯ WOOD PLANKS ◯ CARDBOARD ◯ IRON SHEETS ◯ WOOD ◯ CALAMINE/CEMENT FIBER ◯ BRICK/CLAY TILES ◯ CEMENT ◯ ROOFING SHINGLES ◯ OTHER
Specify it.	_____
OBSERVE MAIN MATERIAL OF THE EXTERIOR WALLS OF THE DWELLING. RECORD OBSERVATION.	◯ NO WALLS ◯ WOOD WITH MUD ◯ IRON SHEET ◯ BRICKS ◯ CANE/PALM/TRUNKS ◯ BAMBOO WITH MUD ◯ STONE WITH MUD ◯ UNCOVERED ADOBE ◯ PLYWOOD ◯ CARDBOARD ◯ REUSED WOOD ◯ CEMENT ◯ STONE WITH LIME/CEMENT ◯ CEMENT BLOCKS ◯ COVERED ADOBE ◯ WOOD PLANKS/SHINGLES ◯ OTHER
Specify it.	_____
OBSERVE EAVES OF THE DWELLING. RECORD OBSERVATION.	◯ Open ◯ Partly open ◯ Close
OBSERVE BEAMS OF THE DWELLING. RECORD OBSERVATION.	◯ No vertical beam ◯ One vertical beam ◯ More than one vertical beams
Tick all that apply	☐ 2 or more vertical beams in the same room ☐ Ceiling board/ Flat roof ☐ The roof is very low ☐ The room is used for kitchen ☐ None
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

Is there a child living in this structure? "Living" means that the child usually stay in the household. If the child is usually staying at a boarding school, but now he/she is staying in this house because of a school closure, that is not regarded as "living".	◯ Yes ◯ No

Once you complete, "Show More Save Options">"Save & Go to Next Form"

2. Children

Please complete the survey below.

Thank you!

Skip this page because there is no children and "Show More Save Options">"Save & Go to Next Form".

Now we would like to record the names of all children aged under 18.

But RDT tests are for children from 6 month to 14 years old.

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?

Last name _____

Is the child a boy or a girl?

◯ BOY
◯ GIRL

Was that a single or multiple pregnancy?

◯ SING
◯ 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.

Is the child living with you?

◯ Yes
◯ No

"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".

Has the child been ill with a fever at any time in the last 2 weeks?

◯ YES
◯ NO
◯ DON'T KNOW

At any time during the illness, did the child have blood taken from a finger or heel for testing?	◯ YES ◯ NO ◯ DON'T KNOW
Were you told by a healthcare provider that the child had malaria?	◯ YES ◯ NO ◯ DON'T KNOW
Did you seek advice or treatment for the illness from any source?	◯ Yes ◯ No
How many times did you seek advice or treatment for the illness from any source?	_____
Where did you first 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'	◯ GOVERNMENT HOSPITAL ◯ GOVERNMENT HEALTH CENTER ◯ GOVERNMENT DISPENSARY ◯ GOVERNMENT MOBILE CLINIC ◯ COMMUNITY HEALTH WORKER/FIELD WORKER ◯ PRIVATE HOSPITAL ◯ PRIVATE CLINIC ◯ PHARMACY ◯ PRIVATE DOCTOR ◯ PRIVATE MOBILE CLINIC ◯ COMMUNITY HEALTH WORKER ◯ SHOP ◯ TRADITIONAL PRACTITIONER ◯ MARKET ◯ ITINERANT DRUG SELLER ◯ OTHER
Specify it.	_____
Where did you second 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'	◯ GOVERNMENT HOSPITAL ◯ GOVERNMENT HEALTH CENTER ◯ GOVERNMENT DISPENSARY ◯ GOVERNMENT MOBILE CLINIC ◯ COMMUNITY HEALTH WORKER/FIELD WORKER ◯ PRIVATE HOSPITAL ◯ PRIVATE CLINIC ◯ PHARMACY ◯ PRIVATE DOCTOR ◯ PRIVATE MOBILE CLINIC ◯ COMMUNITY HEALTH WORKER ◯ SHOP ◯ TRADITIONAL PRACTITIONER ◯ MARKET ◯ ITINERANT DRUG SELLER ◯ OTHER
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'	◯ GOVERNMENT HOSPITAL ◯ GOVERNMENT HEALTH CENTER ◯ GOVERNMENT DISPENSARY ◯ GOVERNMENT MOBILE CLINIC ◯ COMMUNITY HEALTH WORKER/FIELD WORKER ◯ PRIVATE HOSPITAL ◯ PRIVATE CLINIC ◯ PHARMACY ◯ PRIVATE DOCTOR ◯ PRIVATE MOBILE CLINIC ◯ COMMUNITY HEALTH WORKER ◯ SHOP ◯ TRADITIONAL PRACTITIONER ◯ MARKET ◯ ITINERANT DRUG SELLER ◯ OTHER
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?	◯ Yes ◯ No
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?	◯ SAME DAY ◯ NEXT DAY ◯ TWO DAYS AFTER FEVER ◯ THREE OR MORE DAYS AFTER FEVER ◯ DON'TKNOW
Has [mis_wo213_1] received a malaria vaccine?	◯ Yes ◯ No

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

RDT result for Pan	◯ Negative ◯ Positive

If there is another child, press "Show More Save Options">"Save & Add New Instance

otherwise, press "Show More Save Options">Go to Next Form".

3. Adults

Please complete the survey below.

Thank you!

Now, we would like to record the names of all adults who live in this household on a permanent or weekly basis.
Do not include a person who stays only a few days in a month.

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

◯ Permanent Resident
◯ Weekly Resident
◯ Monthly Resident
◯ Others

Answer his/her age with...

◯ birthday
◯ age
◯ age group

Birthday _____

Age _____ (years old)

Age group

◯ High school
◯ After high school
◯ Was born before the independence of Kenya

Sex

◯ Male
◯ Female
◯ Other
◯ Prefer not to say

Relation to the structure head	◯ 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
Relation to the compound head	◯ 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
Please repeat until you record all the members. ("Show More Save Options">"Save & Add New Instance"). Once you complete all the member, "Show More Save Options">"Save & Go to Next Form".	
Note	_____

4. NET

Please complete the survey below.

Thank you!

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?

- ◯ Yes
- ◯ No

How many months ago did your household get the mosquito net?
IF LESS THAN ONE MONTH AGO, RECORD '00'.

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10
- ◯ 11
- ◯ 12
- ◯ 13
- ◯ 14
- ◯ 15
- ◯ 16
- ◯ 17
- ◯ 18
- ◯ 19
- ◯ 20
- ◯ 21
- ◯ 22
- ◯ 23
- ◯ 24
- ◯ 25
- ◯ 26
- ◯ 27
- ◯ 28
- ◯ 29
- ◯ 30
- ◯ 31
- ◯ 32
- ◯ 33
- ◯ 34
- ◯ 35
- ◯ 36
- ◯ MORE THAN 36 MONTHS AGO
- ◯ NOT SURE

OBSERVE OR ASK BRAND/TYPE OF MOSQUITO NET.	◯ OLYSET (SUPANET EXTRA) ◯ PERMANET (SUPANET EXTRA) ◯ VEERALIN ◯ NETPROTECT ◯ YORKOOL ◯ DAWAPLUS ◯ OTHER/DON'T KNOW BRAND (LLIN) ◯ OTHER TYPE (NOT LLIN) ◯ DON'T KNOW TYPE
Did you get the net through a distribution campaign, during an antenatal care visit, or during a child welfare visit?	◯ YES, MASS DISTRIBUTION CAMPAIGN ◯ YES, ANTENATAL CARE VISIT ◯ YES, CHILD WELFARE VISIT ◯ NO
Where did you get the net?	◯ GOVERNMENT HEALTH FACILITY ◯ PRIVATE HEALTH FACILITY ◯ PHARMACY ◯ SHOP/MARKET ◯ CHP ◯ RELIGIOUS INSTITUTION ◯ SCHOOL ◯ OTHER ◯ DON'T KNOW
Did anyone sleep under this mosquito net last night?	◯ YES ◯ NO ◯ NOT SURE
Who slept under this mosquito net last night? RECORD THE PERSON'S NAME. IF THERE ARE MORE THAN ONE, RECORD ALL THE NAME CONNECTING BY ",".	_____
What was the main reason this net was not used last night?	◯ TOO HOT ◯ DON'T LIKE NET SHAPE/COLOR/SIZE ◯ DON'T LIKE SMELL ◯ UNABLE TO HANG NET ◯ SLEPT OUTDOORS ◯ USUAL USER DIDN'T SLEEP HERE LAST NIGHT ◯ NO MOSQUITOES/NO MALARIA ◯ EXTRA NET/SAVING FOR LATER ◯ NET TOO SMALL/SHORT ◯ NET BROUGHT BED BUGS ◯ OTHER
Specify it	_____
Note	_____

If there is another net, press "Show More Save Options">"Save & Add New Instance

otherwise, press "Save & Exit Form".

Questionnaire

Please complete the survey below.

Thank 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.	◯ Moved out from the area (will never come back) ◯ Travel to another village in Ndhiwa ◯ Travel to Homa Bay County other than Ndhiwa ◯ Travel to Another county in Kenya ◯ Travel to Another country ◯ Refuse ◯ Do not know (Could not find) ◯ Others
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?	☐ Another house in your village ☐ Another village in Ndhiwa ☐ Homa Bay County other than Ndhiwa ☐ Another county in Kenya ☐ Another country

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 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? (Please refer to the booklet)	◯ Yes ◯ No
Did [name_f] have the following symptoms at any point in the past four weeks?	☐ Fever ☐ Chills ☐ Profuse sweating ☐ Muscle/joint pain ☐ Abdominal pain ☐ Diarrhoea ☐ Nausea ☐ Vomiting ☐ Irritability ☐ Refusal to feed ☐ Prostration (difficulty to sit upright) ☐ Alteration in the level of consciousness ☐ Convulsions or coma ☐ Difficulty in breathing/respiratory distress ☐ Jaundice ☐ Others ☐ None
Please list other symptoms [name_f] experienced in the past four weeks.	_____
How many times did the child visit health facilities?	◯ One time ◯ Two time ◯ Three time ◯ More than three

When did [name_f]visit the health facility?

_____

(Please refer to the booklet)

Which health facility did [name_f] visit?

(Please refer to the booklet)

- ☐ Malela level 4 hospital
- ☐ Kabongo HC
- ☐ 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?

(Please refer to the booklet)

- ☐ Fever
- ☐ Headache
- ☐ Muscle pain
- ☐ Abdominal pain
- ☐ Nausea
- ☐ Vomiting
- ☐ Diarrhea
- ☐ Convulsions or coma
- ☐ Jaundice
- ☐ Rapid breathing
- ☐ Difficulty in breathing/respiratory distress
- ☐ Pale conjunctivae/palms
- ☐ Loss of reactivity
- ☐ Others

When did the symptom start?

_____

(Please refer to the booklet)

Was [name_f] diagnosed with malaria?

(Please refer to the booklet)

- ◯ Yes
- ◯ No

What was the diagnosis?

_____

Did [name_f] take any treatment or medication?

(Please refer to the booklet)

- ◯ Yes
- ◯ No

What treatment or medication did [name_f] receive from the health facility?

(Please refer to the booklet)

- ☐ AL
- ☐ DHAP
- ☐ OTHER ACT (NOT AL OR DHAP)
- ☐ 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

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?

(Please refer to the booklet)

- ☐ Malela level 4 hospital
- ☐ Kabongo HC
- ☐ 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?

(Please refer to the booklet)

- ☐ Fever
- ☐ Headache
- ☐ Muscle pain
- ☐ Abdominal pain
- ☐ Nausea
- ☐ Vomiting
- ☐ Diarrhea
- ☐ Convulsions or coma
- ☐ Jaundice
- ☐ Rapid breathing
- ☐ Difficulty in breathing/respiratory distress
- ☐ Pale conjunctivae/palms
- ☐ Loss of reactivity
- ☐ Others

When did the symptoms for the first visit start?

_____

(Please refer to the booklet)

Was [name_f] diagnosed with malaria for the first visit?

(Please refer to the booklet)

- ◯ Yes
- ◯ No

What was the diagnosis?

_____

Did [name_f] take any treatment or medication for the first visit?

(Please refer to the booklet)

- ◯ Yes
- ◯ No

What treatment or medication did [name_f] receive from the health facility?

(Please refer to the booklet)

- ☐ AL
- ☐ DHAP
- ☐ OTHER ACT (NOT AL OR DHAP)
- ☐ 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

Please list other medications [name_f] received from the health facility.

_____

When did [name_f] SECOND visit the health facility?

_____

(Please refer to the booklet)

Which health facility did [name_f] second visit?

(Please refer to the booklet)

- ☐ Malela level 4 hospital
- ☐ Kabongo HC
- ☐ 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 second visit? (Please refer to the booklet)	☐ Fever ☐ Headache ☐ Muscle pain ☐ Abdominal pain ☐ Nausea ☐ Vomiting ☐ Diarrhea ☐ Convulsions or coma ☐ Jaundice ☐ Rapid breathing ☐ Difficulty in breathing/respiratory distress ☐ Pale conjunctivae/palms ☐ Loss of reactivity ☐ Others
When did the symptoms for the second visit start? (Please refer to the booklet)	_____
Was [name_f] diagnosed with malaria for the second visit? (Please refer to the booklet)	◯ Yes ◯ No
What was the diagnosis?	_____
Did [name_f] take any treatment or medication for the second visit? (Please refer to the booklet)	◯ Yes ◯ No
What treatment or medication did [name_f] receive from the health facility? (Please refer to the booklet)	☐ AL ☐ DHAP ☐ OTHER ACT (NOT AL OR DHAP) ☐ 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
Please list other medications [name_f] received from the health facility.	_____

When did [name_f] THIRD visit the health facility?

_____

(Please refer to the booklet)

Which health facility did [name_f] third visit?

(Please refer to the booklet)

- ☐ Malela level 4 hospital
- ☐ Kabongo HC
- ☐ 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 third visit?

(Please refer to the booklet)

- ☐ Fever
- ☐ Headache
- ☐ Muscle pain
- ☐ Abdominal pain
- ☐ Nausea
- ☐ Vomiting
- ☐ Diarrhea
- ☐ Convulsions or coma
- ☐ Jaundice
- ☐ Rapid breathing
- ☐ Difficulty in breathing/respiratory distress
- ☐ Pale conjunctivae/palms
- ☐ Loss of reactivity
- ☐ Others

When did the symptoms for the third visit start?

_____

(Please refer to the booklet)

Was [name_f] diagnosed with malaria for the third visit?

(Please refer to the booklet)

- ◯ Yes
- ◯ No

What was the diagnosis?

_____

Did [name_f] take any treatment or medication for the third visit?

(Please refer to the booklet)

- ◯ Yes
- ◯ No

What treatment or medication did [name_f] receive from the health facility? (Please refer to the booklet)	☐ AL ☐ DHAP ☐ OTHER ACT (NOT AL OR DHAP) ☐ 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
Please list other medications [name_f] received from the health facility.	_____
Did [name_f] take treatment or medication from the following in the past four weeks?	☐ No ☐ Friends ☐ Relatives ☐ Pharmacy/chemist ☐ Traditional healers
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) ☐ OTHER ANTIMALARIAL ☐ AMOXICILLIN ☐ COTRIMOXAZOLE ☐ OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP) ☐ OTHER ANTIBIOTIC MEDICINE (INJECTION/IV) ☐ ASPIRIN ☐ PARACETAMOL/PANADOL/ACETAMINOPHEN ☐ IBUPROFEN ☐ OTHER ☐ DON'TKNOW
Please list other medications [name_f] took from the friends.	_____

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) ☐ OTHER ANTIMALARIAL ☐ AMOXICILLIN ☐ COTRIMOXAZOLE ☐ OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP) ☐ OTHER ANTIBIOTIC MEDICINE (INJECTION/IV) ☐ ASPIRIN ☐ PARACETAMOL/PANADOL/ACETAMINOPHEN ☐ IBUPROFEN ☐ OTHER ☐ DON'TKNOW
Please list other medications [name_f] took from the relatives.	_____
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 (INJECTION/IV) ☐ OTHER ANTIMALARIAL ☐ AMOXICILLIN ☐ COTRIMOXAZOLE ☐ OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP) ☐ OTHER ANTIBIOTIC MEDICINE (INJECTION/IV) ☐ ASPIRIN ☐ PARACETAMOL/PANADOL/ACETAMINOPHEN ☐ IBUPROFEN ☐ OTHER ☐ DON'TKNOW
Please list other medications [name_f] took from the pharmacy.	_____

What medications did [name_f] take from the traditional healer?	☐ AL ☐ DHAP ☐ OTHER ACT (NOT AL OR DHAP) ☐ 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
Please list other medications [name_f] took from the traditional healer.	_____
Does [name_f] have the following symptoms now or in the last 24 hours?	☐ Fever ☐ Chills ☐ Profuse sweating ☐ Muscle/joint pain ☐ Abdominal pain ☐ Diarrhoea ☐ Nausea ☐ Vomiting ☐ Irritability ☐ Refusal to feed ☐ Prostration (difficulty to sit upright) ☐ Alteration in the level of consciousness ☐ Convulsions or coma ☐ Difficulty in breathing/respiratory distress ☐ Jaundice ☐ Others ☐ None
Please list other symptoms [name_f] experience now or in the last 24 hours.	_____
Did [name_f] receive the malaria vaccine within four weeks?	◯ Yes ◯ No
How many times has [name_f] received the malaria vaccine, including the latest one?	◯ 1 dose ◯ 2 doses ◯ 3 doses ◯ 4 doses ◯ Don't know
Does the structure where [name_f] usually sleeps have ceiling nets?	◯ Yes ◯ No

Sample

Please complete the survey below.

Thank you!

	_____
Cohort 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?	◯ Yes ◯ No
Thick and thin blood films?	◯ Yes ◯ No
RDT results for P.f	◯ Negative ◯ Positive
RDT results for Pan	◯ Negative ◯ Positive

Participant questionnaire

Please complete the survey below.

Thank 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")	_____
First name	_____
Middle name	_____
Last name	_____
Age	_____ (years old)
Does [name_f] know the birthday?	◯ Yes ◯ No
Birthday	_____
The birthday and your age are contradicting. Please check the true age again.	
Sex	◯ Male ◯ Female ◯ Other ◯ Prefer not to say
Longitude	_____
Latitude	_____
This participant is available for the survey.	◯ Yes ◯ No

Please select the reason why the participant is not available.	◯ Moved out from the area (will never come back) ◯ Travel to another village in Ndhiwa ◯ Travel to Homa Bay County other than Ndhiwa ◯ Travel to Another county in Kenya ◯ Travel to Another country ◯ Refuse ◯ Do not know (Could not find) ◯ Others
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?	☐ Another house in your village ☐ Another village in Ndhiwa ☐ Homa Bay County other than Ndhiwa ☐ Another county in Kenya ☐ Another country
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 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 Ndhiwa?	_____
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] have any symptoms at any point in the past four weeks?	◯ Yes ◯ No ◯ Don't know

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

What treatment or medication did [name_f] receive from the health facility?	☐ AL ☐ DHAP ☐ OTHER ACT (NOT AL OR DHAP) ☐ 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
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?	◯ Yes ◯ No
Did [name_f] take treatment or medication from the following in the past four weeks?	☐ Friends ☐ Relatives ☐ Pharmacy/chemist ☐ Traditional healers
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) ☐ 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

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) ☐ 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 relatives.	_____
Do you know the names of medications from the pharmacy/chemist?	◯ Yes ◯ No
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 (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 pharmacy.	_____
Do you know the names of medications from the traditional healer?	◯ Yes ◯ No

What medications did [name_f] take from the traditional healer?	☐ AL ☐ DHAP ☐ OTHER ACT (NOT AL OR DHAP) ☐ 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
Please list other medications [name_f] took from the traditional healer.	_____
Does [name_f] have any symptoms now or in the last 24 hours?	◯ Yes ◯ No
Does [name_f] have the following symptoms now or in the last 24 hours?	☐ Fever ☐ Chills ☐ Profuse sweating ☐ Muscle/joint pain ☐ Abdominal pain ☐ Diarrhoea ☐ Nausea ☐ Vomiting ☐ Irritability ☐ Refusal to feed ☐ Prostration (difficulty to sit upright) ☐ Alteration in the level of consciousness ☐ Convulsions or coma ☐ Difficulty in breathing/respiratory distress ☐ Jaundice ☐ Cough ☐ Rash ☐ Itches ☐ Others
Please list other symptoms [name_f] experience now or in the last 24 hours.	_____
Has [name_f] received a malaria vaccine? Please refer to the mother-child book.	◯ Yes ◯ No
How many times has [name_f] received the malaria vaccine? Please refer to the mother-child book.	◯ 1 dose ◯ 2 doses ◯ 3 doses ◯ 4 doses ◯ Don't know
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?	◯ Yes ◯ No
Thick and thin blood films?	◯ Yes ◯ No
RDT results for P.f	◯ Negative ◯ Positive
RDT results for Pan	◯ Negative ◯ Positive

Head questionnaire

Please complete the survey below.

Thank you!

_____

Who is the respondent?

*If the respondent are not sure about the answer(s), he/she can be helped by the other members.

- ◯ Head
- ◯ Primary care taker
- ◯ Participant
- ◯ Others

What is the respondent's relation to the participant?

- ◯ 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

What is the condition of the ceiling net?

- ◯ No damage
- ◯ Damaged and not repaired
- ◯ Damaged but repaired
- ◯ Removed
- ◯ Not installed

How many hole(s) does/did it have?
(regardless of the size)
(mark 0 if no hole)

_____

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
- ◯ smaller than the fist
- ◯ larger than the fist

What is/was the reason of the damage?

- ◯ Accident during the cleaning
- ◯ Animal
- ◯ Caught a fire
- ◯ Unknown
- ◯ Others

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?	◯ Good ◯ Damaged
Presence of gaps between battens and the wall	◯ Yes ◯ No
Do you agree with the following potential positive sides of the ceiling net?	☐ Stop mosquito entering the house ☐ Stop other insects/animals entering the house ☐ Durability of the ceiling nets ☐ To beautify the house ☐ Household coverage ☐ Keep the room cool ☐ Others
Please specify.	_____
Do you agree with the following potential negative sides of the ceiling net?	☐ It makes room too hot ☐ It reduces the storage space a the top of the w all ☐ Fixing looks untidy ☐ It is hard to clean ☐ Dirt/debris trapped by the ceiling net ☐ Rewiring of power lines ☐ Others
Please specify.	_____
Other features in the ceiling net (if any).	_____
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?	◯ 100 KSH ◯ 300 KSH ◯ 500 KSH ◯ 1000 KSH ◯ 2000 KSH ◯ 5000 KSH ◯ More than 10,000 KSH
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?	◯ Yes ◯ No

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

BMJ Open

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

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2024-087832.R2
Article Type:	Protocol
Date Submitted by the Author:	16-Dec-2024
Complete List of Authors:	Ko, Yura; Karolinska Institute, 1Department of Microbiology, Tumor and Cell Biology (MTC); Tohoku University Kagaya, Wataru; Nagasaki University, Omondi, Protus; Osaka Metropolitan University Musyoka, Kelvin ; Osaka Metropolitan University Okai, Takatsugu; Osaka Metropolitan University Chan, Chim; Osaka Metropolitan University Kongere, James; Osaka Metropolitan University; Center for Research in Tropical Medicine and Community Development Opiyo, Victor; Center for Research in Tropical Medicine and Community Development Oginga, Jared; Center for Research in Tropical Medicine and Community Development Mungai, Samuel; Mount Kenya University; United States International University Africa Kanoi, Bernard; Mount Kenya University Kanamori, Mariko ; Stockholm University; Kyoto University Yoneoka, Daisuke; National Institute of Infectious Diseases (KNBS), Kenya National Bureau of Statistics; Kenya National Bureau of Statistics Keitany, Kibor; Kenya National Malaria Control Program Songok, Elijah; Kenya Medical Research Institute, Okomo, Gordon ; Ministry of Health Minakawa, Noboru; Nagasaki University Gitaka, Jesse; Mount Kenya University, Research and Innovation Kaneko, Akira; Karolinska Institute, 1Department of Microbiology, Tumor and Cell Biology (MTC); Osaka Metropolitan University
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Infectious diseases, Public health
Keywords:	Malaria, Mosquito Vectors, Infection control < INFECTIOUS DISEASES

Title

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

Authors

Yura K Ko[1,2], Wataru Kagaya[3], Protus Omondi[4], Kelvin B. Musyoka[4], Takatsugu Okai[4], Chim W. Chan[4], James Kongere[4,5], Victor Opiyo[5], Jared Oginga[5], Samuel M. Mbugua[6,7,8], Bernard N. Kanoi[6,8], Mariko Kanamori[9,10], Daisuke Yoneoka[11], Kenya National Bureau of Statistics (KNBS)[12], Kibor Keitany[13], Elijah Songok[14], Gordon Okomo[15], Noboru Minakawa[16], Jesse Gitaka[6,8](*), Akira Kaneko[1,4,16](*)

[1]Department of Microbiology, Tumor and Cell Biology (MTC), Karolinska Institutet, Sweden

[2]Department of Virology, Tohoku University Graduate School of Medicine, Japan

[3]Department of Ecoepidemiology, Institute of Tropical Medicine (NEKKEN), Nagasaki University, Japan

[4]Department of Virology and Parasitology, Graduate School of Medicine, Osaka Metropolitan University, Japan

[5]Center for Research in Tropical Medicine and Community Development, Kenya

[6]Center for Research in Infectious Diseases, Directorate of Research and Innovation, Mount Kenya University, Kenya

[7]School of pharmacy and health sciences, United States International University Africa, Kenya

[8]Center for Malaria Elimination, Mount Kenya University, Kenya

[9]Department of Public Health Sciences, Stockholm University, Sweden

[10]Institute for the Future of Human Society, Kyoto University, Japan

[11]Center for Surveillance, Immunization, and Epidemiologic Research, National Institute of Infectious Diseases, Japan

[12]Kenya National Bureau of Statistics, Kenya

[13]National Malaria Control Programme, Ministry of Health, Kenya

[14]Kenya Medical Research Institute, Kenya

[15]Department of Health, Homa Bay County, Kenya

[16]Department of Vector Ecology and Environment, Institute of Tropical Medicine (NEKKEN), Nagasaki University, Japan

Correspondence to: Wataru Kagaya, Jesse Gitaka

*Senior joint authors

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 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.

Methods: A cluster randomized controlled trial is designed to evaluate the impact of pyrethroid-PBO 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 (pyrethroid-PBO 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 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.

Trial registration: UMIN000053873

Keywords

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

Administrative information

Title {1}	Evaluation of the protective efficacy of Olyset®Plus ceiling net on reducing malaria incidence in children in the Great Lake Region, Kenya: study protocol for a cluster-randomized controlled trial
Trial registration {2a and 2b}.	UMIN000053873
Protocol version {3}	Version 6.0
Funding {4}	This work is supported by the Japan International Cooperation Agency (JICA) and Japan Agency for Medical Research and Development (AMED) under the Science and Technology Research Partnership for Sustainable Development Goals (SATREPS) program.
Author details {5a}	Osaka Metropolitan University, Japan Nagasaki University, Japan Tohoku University, Japan National Institute of Infectious Diseases, Japan Mount Kenya University, Kenya National Malaria Control Programme, Nairobi, Kenya Kenya National Bureau of Statistics, Nairobi, Kenya Kenya Medical Research Institute, Kenya Homa Bay County, Kenya Karolinska Institutet, Sweden

	Stockholm University, Sweden
Name and contact information for the trial sponsor {5b}	Department of Virology and Parasitology/Research Center for Infectious Diseases, Graduate School of Medicine, Osaka Metropolitan University (OMU), Japan 1–4-3, Asahimachi, Abeno, Osaka, Osaka, Japan, 545–8585 TEL: + 81–6-6645–3760 Website: https://ocuparasitology.com/en/ Directorate of Research and Innovation, Mount Kenya University (MKU), Kenya General Kago Road, Thika, Kiambu, Kenya Website: https://www.mku.ac.ke
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.

Strength and limitations of this study

- This is a second cluster-randomized controlled trial of a novel vector control tool, pyrethroid-PBO ceiling net, to evaluate its efficacy in reducing malaria incidence among children.
- The implementation of monthly active screening within the prospective cohort population established in each cluster facilitates the assessment of infection incidence.
- The incorporation of multidisciplinary outcomes, encompassing social aspects and cost-effectiveness analyses, provides valuable insights for the potential future deployment of this intervention within integrated malaria control strategies.
- One of the anticipated limitations is the possible contamination between intervention and control clusters because we will not set a buffer zone due to the geographical proximity among clusters.

Introduction

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 [2], Uganda [3], Eritrea [4], Ethiopia [5], and the United Republic of Tanzania [6] 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 one of the key factors in reducing the impact of LLIN on the malaria burden, together with insufficient provision in the mass net distribution program or shortening durability of nets [7]. In the Lake Victoria basin, alternative uses of LLIN for fishing and protecting crops and chicks are well-known local behaviors [8,9] as reported in other endemic areas [10]. 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 (Sumitomo Chemical) ceiling net. The benefit of installing the pyrethroid-PBO ceiling net in addition to conventional LLINs is detailed elsewhere [11]. Briefly, the pyrethroid-PBO ceiling net provides a combination of physical and chemical protection against mosquitoes

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 ceiling nets on malaria morbidity and transmission in the Lake Victoria basin of Kenya. Preliminary data 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 combining various tools to maximize the impact of the malaria control program, it is important to understand 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.

Objectives {7}

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

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.

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 covariate-constrained 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.

Methods: Participants, interventions and outcomes

Study setting {9}

Location and administrative structure

Ndhiwa (713.5 km²) 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 poultry [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℃. The relative humidity remains elevated year-round, fluctuating between 75% to 85%

[17].

Demographics

The population of Kanyamwa Kologi Ward is approximately 33,000 according to the 2019 national census [18]. The dominant ethnic group in the region is Luo and the primary languages are DhoLuo, Kiswahili, and English. There are 172 primary and 36 secondary schools in Ndhiwa Sub-County [19]. Within Kanyamwa Kologi Ward, there are 28 primary and 7 secondary schools.

Malaria epidemiology and control measures

Based on the KHIS, there were 429.1 and 457.2 confirmed malaria cases per 1,000 population in Ndhiwa Sub-County and Kanyamwa Kologi Ward, respectively, in 2023. The primary malaria vector in the sub-county is *Anopheles funestus*, which prefers feeding on humans. Although *An. arabiensis* exhibits predominantly zoophilic behavior, it is also a significant malaria vector in our study area [20]. In Homa Bay County, LLINs have been distributed every three years since the early 2000s, and IRS and the RTS,S malaria vaccine have been piloted in several areas since 2018 and 2019, respectively [21]. Notably PBO-incorporated LLINs (Veeralin®LN, manufactured by VKA Polymers, Tamil Nadu, India) were distributed in late 2023. In Kanyamwa Kologi Ward, there is one level four hospital and seven health centers.

Eligibility criteria {10}

As the ceiling nets are installed per structure, we set the inclusion criteria on a structural basis. The inclusion criteria for the installation of the ceiling nets are (1) residential structures with at least one permanent resident aged 18 years or older in the household, (2) informed consent provided by a resident in the household, and (3) house structure amenable to ceiling net installation 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 structure, confirmed by at least two visits by community health promoters (CHPs), (2) dwelling structure to be vacated or destroyed within the study period, (3) non-eligible house structure for the ceiling net installation, and (4) non-residential structures (school, shop, kitchen, storage, and toilet). The inclusion

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.

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.

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

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.

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.

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.

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

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.

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

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

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. To monitor the long-term impact of the intervention, the research team may conduct additional cross-sectional surveys 2 and 3 years post-intervention to monitor further parasite transmission in the population.

Outcomes {12}

Epidemiological domain: The primary outcome will be symptomatic malaria case incidence, defined as axillary temperature of ≥37·5°C or a history of fever in the preceding 48 hours, and positive RDT, in children aged 6 months to 14 years enrolled in the cohort, monitored with a monthly visit and passive case detection in the health facilities during an 18-month follow-up. The secondary outcomes will be (1) the prevalence of *Plasmodium* infections by PCR in all age groups at 6, 12, and 18 months post-intervention and (2) infection incidence by PCR in the prospective cohort of children aged 6 months to 14 years over 18 months.

Entomological domain: The primary outcome will be the density of the primary malaria vectors, species composition and sporozoite infection rates. Indoor malaria vector density will be determined using CDC light trap, and species composition and sporozoite infection rates will be determined by microscopy and 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.

Epidemiological survey

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 between-cluster 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 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.

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.

Implementation {16c}

After the baseline survey, covariate-constrained randomization will be used to allocate the 44 clusters across the two study arms. 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. An independent statistician will perform the randomization. Local study assistants will perform participant enrollment.

Assignment of interventions: Blinding

Who will be blinded {17a}

Due to the visibility of the pyrethroid-PBO ceiling net, neither the trial participants nor the members of the study team who take part in field activities can be blinded. However, laboratory- and office-based personnel (e.g., microscopists, laboratory technicians, and data analysts) will be blinded to the identity and intervention status of the trial participants since all biological specimens will be identified by a unique numeric study identifier, and personal information will be removed before analyses.

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 they need to be unblinded.

Data collection and management

Questionnaires for the baseline survey, cohort surveys, and post-intervention cross-sectional surveys are provided in the supplementary file.

Plans for assessment and collection of outcomes {18a}

Census and baseline cross-sectional survey

In Kanyamwa Kologi Ward, 85 census enumeration areas (EAs) are defined by the 2019 Kenya Population and Housing Census. Births, deaths, and migrations in each EA are regularly updated by CHPs using the integrated community health system maintained by the Ministry of Health. Fifty EAs are randomly selected for our baseline survey, during which demographic information of all individuals is updated. To ensure balanced cluster allocation, the baseline survey includes a questionnaire for all households, RDT testing of all children aged 6 months to 14 years, and an entomological survey of randomly sampled households. We modified the questionnaire used in the 2020 Kenya Malaria Indicator Survey (KMIS) mainly to quantify the SES of each household and bed net usage. In addition, we add questions to quantify the favorability of ceiling nets before the intervention.

Cohort monitoring

Incidence of clinical malaria in the prospective cohort will be estimated by both active and passive case detections. For active case detection, we will conduct home visits every four weeks. From all cohort participants, axillary temperature will be measured using a digital thermometer, and *Plasmodium* infection status will be determined by RDT and PCR. 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. 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 finger-prick 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℃. 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

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.

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 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.

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.

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].

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.

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 (≤ 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 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 hot-deck imputation methods if the missing fraction for the covariate is <5% or appropriate multiple imputation approaches if the missing fraction for a covariable are ≥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}

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 self-reported 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.

Dissemination plans {31a}

Study results will be shared with the 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. Suggestions from the participants will also help shape the future improvement of the intervention.

Discussion

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 cost-effective and widely accepted by local communities are urgently needed to contain the spread of artemisinin-resistant *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 trial, contamination between intervention and control clusters cannot be excluded, as buffer zones between intervention and control clusters cannot be created due to geographic proximity of houses and villages in the ward. A recent study, however, has shown that the spillover effect of interventions on malaria can extend to 3 km [33], so buffer zones of a few hundred meters, as set out in many studies, may not be sufficient. We will try to eliminate such contamination effects by integrating spatial data into our statistical model. Second,

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 in-depth 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-PBO-incorporated 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.

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.

Abbreviations

ACT: artemisinin-based combination therapy

CHP: community health promoter

CRCT: cluster-randomized controlled trial

CV: coefficient of variation

KHIS: Kenya Health Information System

ITN: insecticide treated nets

IRS: indoor residual spraying

LLIN: long-lasting insecticidal nets

MKU: Mount Kenya University

PBO: piperonyl butoxide

RDT: rapid diagnosis tests

VGSC: Voltage gated sodium channel

Declarations

Acknowledgements

We would like to express our sincere gratitude to this study's participants, field, and laboratory staff. In addition, we acknowledge the collaboration and support of health offices in Homa Bay County, Kenya.

Authors' contributions {31b}

AK and JG are co-principal investigators. AK is the guarantor. YKK, WK, and AK developed the original concept. All authors discussed and contributed to the study protocol. YKK, WK, PO, KBM, JK, VO, JO, SMM, KNBS, KK, ES, GO, and AK contributed the preparation of the baseline survey. YKK, WK, PO, BM, TO, CWC, JK, SM, and MK drafted the manuscript. YKK, WK, CWC, MK, GO, and JG contributed to the revisions of the draft of the manuscript. DY participated as a senior statistician. YKK and MK drafted the statistical analysis plan (SAP) and WK, CWC, and DY revised. The authors read and approved the final manuscript and SAP.

Funding {4}

AK and JG received support from JICA/AMED joint research project (SATREPS) (Grant no. 20JM0110020H0002), Hitachi Fund Support for Research Related to Infectious Diseases, and Sumitomo

Chemical Corporation. The funding bodies play no role in the study design, data collection, analysis, interpretation, and publication.

Availability of data and materials {29}

The study regimes, consent forms, assent forms, and study-related materials are accessible from the corresponding author. The final trial dataset will be available to all investigators. The corresponding author will make the de-identified datasets and source codes for all analysis available upon reasonable request.

Patient and public involvement

Although the study design was developed through discussions among the researchers, consultations with the local population were conducted prior to initiating the baseline survey, and their input was incorporated into the study. Community involvement will also be ongoing during the implementation of interventions and research activities.

Ethics approval and consent to participate {24}

Ethics approvals were received from Mount Kenya University Institutional Scientific Ethics Review Committee (MKU-ISERC) (approval number: 2565) and the Ethics Committee in Osaka Metropolitan University (approval number: 2024-068).

Written informed consents will be sought from study participants before the baseline survey, installation of ceiling nets, each cross-sectional survey, and the start of prospective cohort surveys. In cross-sectional and cohort surveys, informed assent will be obtained from children under the age of 15 who can understand the study at a level appropriate for their development, in addition to the consent of a parent or legal guardian. Participants have the right to withdraw from the study at any time, and the option to withhold previously collected samples from any future analyses and studies.

The samples collected in this study may potentially be used for other research purposes. This is clearly stated in the informed consent form. In such cases, we will obtain the necessary ethical approval and provide participants with the chance to opt-out from this. All experiments will be carried out in adherence to WHO requirements and the Declaration of Helsinki.

Consent for publication {32}

We will not present identifying images or other personal or clinical details of participants. The participant information materials and informed consent form are available from the corresponding author on request.

Competing interests {28}

AK and JG were partially supported by a research grant from Sumitomo Chemical Corporation. Other authors had no competing interests.

References

1. Noor AM, Alonso PL. The message on malaria is clear: progress has stalled. The Lancet. 2022. p. 1777.

2. Rosenthal PJ, Björkman A, Dhorda M, Djimde A, Dondorp AM, Gaye O, et al. Cooperation in Countering Artemisinin Resistance in Africa: Learning from COVID-19. Am J Trop Med Hyg. 2022;106: 1568–1570.

3. Stokes BH, Ward KE, Fidock DA. Evidence of Artemisinin-Resistant Malaria in Africa. The New England journal of medicine. 2022. pp. 1385–1386.

4. Mihreteab S, Platon L, Berhane A, Stokes BH, Warsame M, Campagne P, et al. Increasing Prevalence of Artemisinin-Resistant HRP2-Negative Malaria in Eritrea. N Engl J Med. 2023;389: 1191–1202.

5. Fola AA, Feleke SM, Mohammed H, Brhane BG, Hennelly CM, Assefa A, et al. Plasmodium falciparum resistant to artemisinin and diagnostics have emerged in Ethiopia. Nature Microbiology. 2023;8: 1911–1919.

6. World Health Organization. World malaria report 2023. 2023.

7. Bhatt S, Weiss DJ, Mappin B, Dalrymple U, Cameron E, Bisanzio D, et al. Coverage and system efficiencies of insecticide-treated nets in Africa from 2000 to 2017. Elife. 2015;4. doi:10.7554/eLife.09672

8. Larson PS, Minakawa N, Dida GO, Njenga SM, Ionides EL, Wilson ML. Insecticide-treated net use before and after mass distribution in a fishing community along Lake Victoria, Kenya: successes and unavoidable pitfalls. Malar J. 2014;13: 466.

9. Minakawa N, Dida GO, Sonye GO, Futami K, Kaneko S. Unforeseen misuses of bed nets in fishing villages along Lake Victoria. Malar J. 2008;7: 165.

10. Santos EM, Coalson JE, Munga S, Agawo M, Jacobs ET, Klimentidis YC, et al. "After those nets are torn, most people use them for other purposes": an examination of alternative bed net use in western Kenya. Malar J. 2020;19: 272.

11. Kagaya W, Chan CW, Kongere J, Kanoi BN, Ngara M, Omondi P, et al. Evaluation of the protective efficacy of Olyset®Plus ceiling net on reducing malaria prevalence in children in Lake Victoria Basin, Kenya: study protocol for a cluster-randomized controlled trial. Trials. 2023;24: 354.

12. Fernandez Montoya L, Alafo C, Martí-Soler H, Máquina M, Comiche K, Cuamba I, et al. Overlaying human and mosquito behavioral data to estimate residual exposure to host-seeking mosquitoes and the protection of bednets in a malaria elimination setting where indoor residual spraying and nets were deployed together. PLoS One. 2022;17: e0270882.

13. Ladu HI, Shuaibu U, Pulford J. Reasons for mosquito net non-use in malaria-endemic countries: A review of qualitative research published between 2011 and 2021. Trop Med Int Health. 2024;29: 647–656.

14. Minakawa N, Kawada H, Kongere JO, Sonye GO, Lutiali PA, Awuor B, et al. Effectiveness of screened ceilings over the current best practice in reducing malaria prevalence in western Kenya: a cluster randomised controlled trial. Parasitology. 2022;149: 1–39.

15. Idris Z, Chan CW, Kongere J, Gitaka J, Logedi J, Omar A, et al. High and Heterogeneous Prevalence of Asymptomatic and Sub-microscopic Malaria Infections on Islands in Lake Victoria, Kenya. Sci Rep. 2016;6: 1–13.

16. Homabay County | Ndhiwa Municipality. [cited 13 Feb 2024]. Available: https://www.homabay.go.ke/department/ndhiwa-municipality

17. Ndhiwa, Homa Bay, KE Climate Zone, Monthly Averages, Historical Weather Data. [cited 13 Feb 2024]. Available: https://weatherandclimate.com/kenya/homa-bay/ndhiwa

18. Statistics KNB of SNKNB of. 2019 Kenya Population and Housing Census Reports. 28 Feb 2020 [cited 13 Feb 2024]. Available: https://housingfinanceafrica.org/documents/2019-kenya-population-and-housing-census-reports/

19. Ndhiwa Constituency Schools | ShuleZote. [cited 13 Feb 2024]. Available: https://shulezote.co.ke/place/constituency/migori/ndhiwa/?page=1

20. VectorLink-Kenya-2021-End-of-Spray-Report-Submision-Approved-July-23-2021-sxf-CL.pdf. Available: https://d1u4sg1s9ptc4z.cloudfront.net/uploads/2021/09/VectorLink-Kenya-2021-End-of-Spray-Report-Submision-Approved-July-23-2021-sxf-CL.pdf

21. End-of-Spray-Report-Kenya-2023.pdf. Available: https://d1u4sg1s9ptc4z.cloudfront.net/uploads/2023/10/End-of-Spray-Report-Kenya-2023.pdf

22. Hayes RJ, Bennett S. Simple sample size calculation for cluster-randomized trials. Int J Epidemiol. 1999;28: 319–326.

23. Isozumi R, Fukui M, Kaneko A, Chan CW, Kawamoto F, Kimura M. Improved detection of malaria cases in island settings of Vanuatu and Kenya by PCR that targets the Plasmodium mitochondrial cytochrome c oxidase III (cox3) gene. Parasitol Int. 2015;64: 304–308.

24. Multerer L, Glass TR, Vanobberghen F, Smith T. Analysis of contamination in cluster randomized trials of malaria interventions. Trials. 2021;22: 613.

25. Hawley WA, Phillips-Howard PA, ter Kuile FO, Terlouw DJ, Vulule JM, Ombok M, et al. Community-wide effects of permethrin-treated bed nets on child mortality and malaria morbidity in western Kenya. Am J Trop Med Hyg. 2003;68: 121–127.

26. Miller CJ, Barnett ML, Baumann AA, Gutner CA, Wiltsey-Stirman S. The FRAME-IS: a framework for documenting modifications to implementation strategies in healthcare. Implement Sci. 2021;16: 36.

27. Glasgow RE, Green LW, Taylor MV, Stange KC. An evidence integration triangle for aligning science with policy and practice. Am J Prev Med. 2012;42: 646–654.

28. Chun Tie Y, Birks M, Francis K. Grounded theory research: A design framework for novice researchers. SAGE Open Med. 2019;7: 2050312118822927.

29. Wager S, Athey S. Estimation and inference of heterogeneous treatment effects using random forests. J Am Stat Assoc. 2018;113: 1228–1242.

30. van der Laan MJ, Polley EC, Hubbard AE. Super learner. Stat Appl Genet Mol Biol. 2007;6: Article25.

31. Imwong M, Dhorda M, Myo Tun K, Thu AM, Phyo AP, Proux S, et al. Molecular epidemiology of resistance to antimalarial drugs in the Greater Mekong subregion: an observational study. Lancet Infect Dis. 2020;20: 1470–1480.

32. Cohen JM, Smith DL, Cotter C, Ward A, Yamey G, Sabot OJ, et al. Malaria resurgence: a systematic review and assessment of its causes. Malar J. 2012;11: 122.

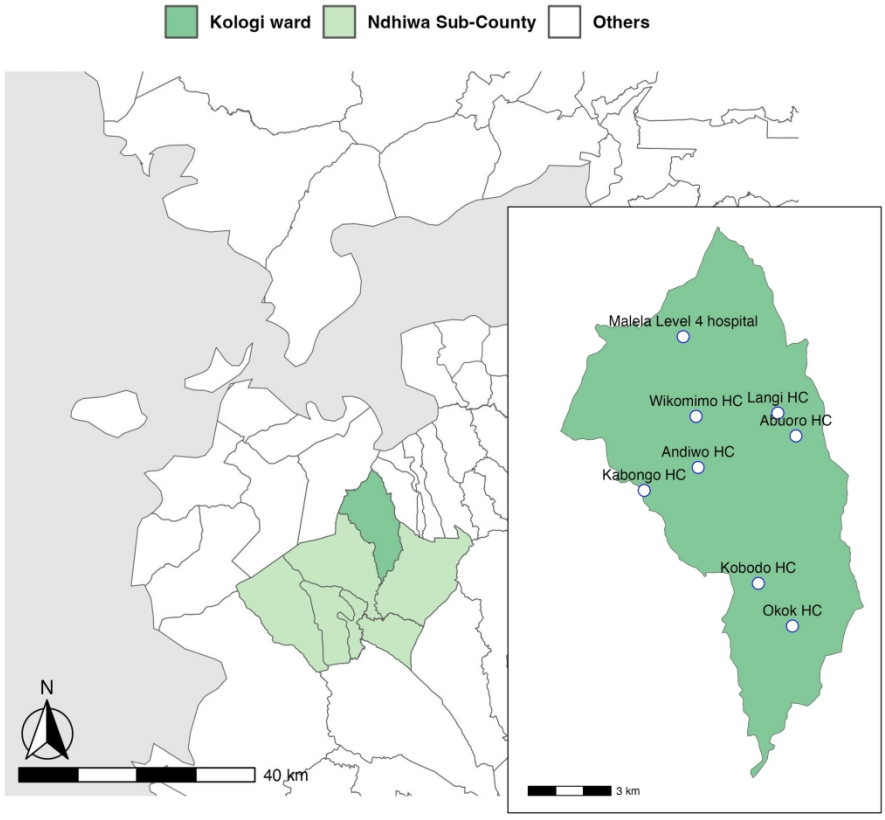
33. Benjamin-Chung J, Li H, Nguyen A, Barratt Heitmann G, Bennett A, Ntuku H, et al. Extension of efficacy range for targeted malaria-elimination interventions due to spillover effects. Nat Med. 2024. doi:10.1038/s41591-024-03134-z

34. Mosha JF, Matowo NS, Kulkarni MA, Messenger LA, Lukole E, Mallya E, et al. Effectiveness of long-lasting insecticidal nets with pyriproxyfen–pyrethroid, chlorfenapyr–pyrethroid, or piperonyl butoxide–pyrethroid versus pyrethroid only against malaria in Tanzania: final-year results of a four-arm, single-blind, cluster-randomised trial. Lancet Infect Dis. 2024;24: 87–97.

Figure 1: Map of the study area. Inset shows the locations of the level four hospital and seven health centers (HC) in Kanyamwa Kologi Ward.

Figure 2: The schedule of trial activities.

Figure 3: CONSORT flow diagram and the detail of each survey



Map of the study area. Inset shows the locations of the level four hospital and seven health centers (HC) in Kanyamwa Kologi Ward.

216x179mm (330 x 330 DPI)

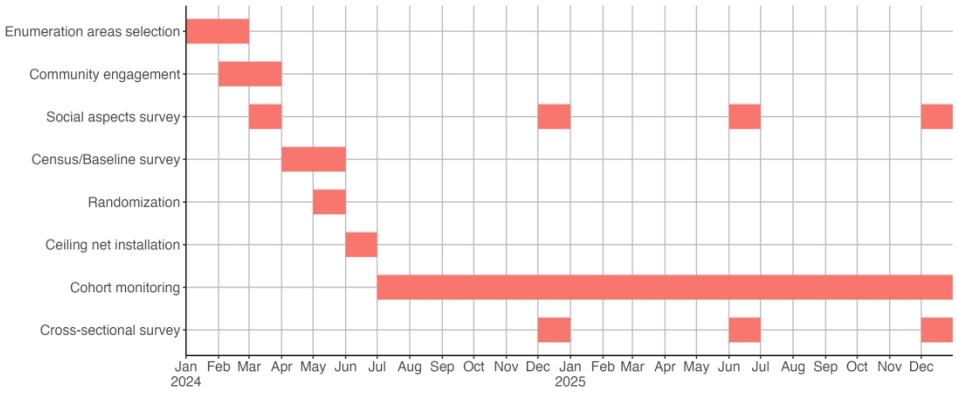
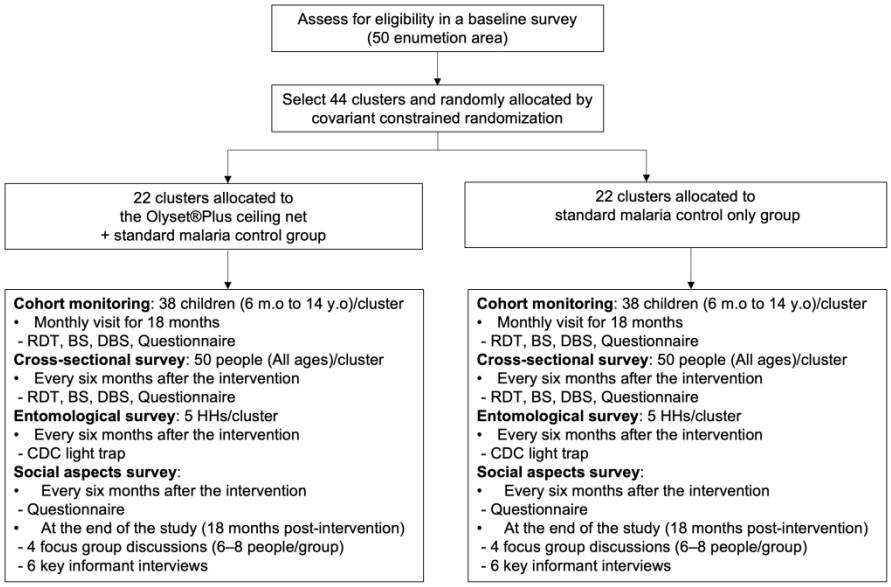


Figure 2: The schedule of trial activities.

304x127mm (310 x 310 DPI)



CONSORT flow diagram and the detail of each survey

288x186mm (330 x 330 DPI)

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.

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[1]. All sample sizes will be recalculated based on the baseline data, which will be collected before the ceiling net installation.

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 between-cluster 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[2]. 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

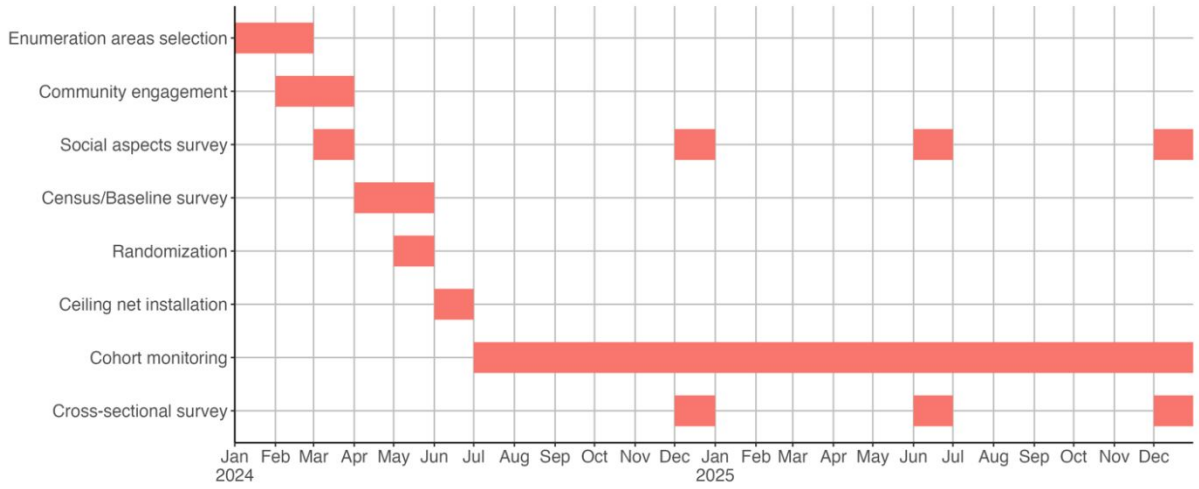


Figure1: Timetable of trial activities

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.

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

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.

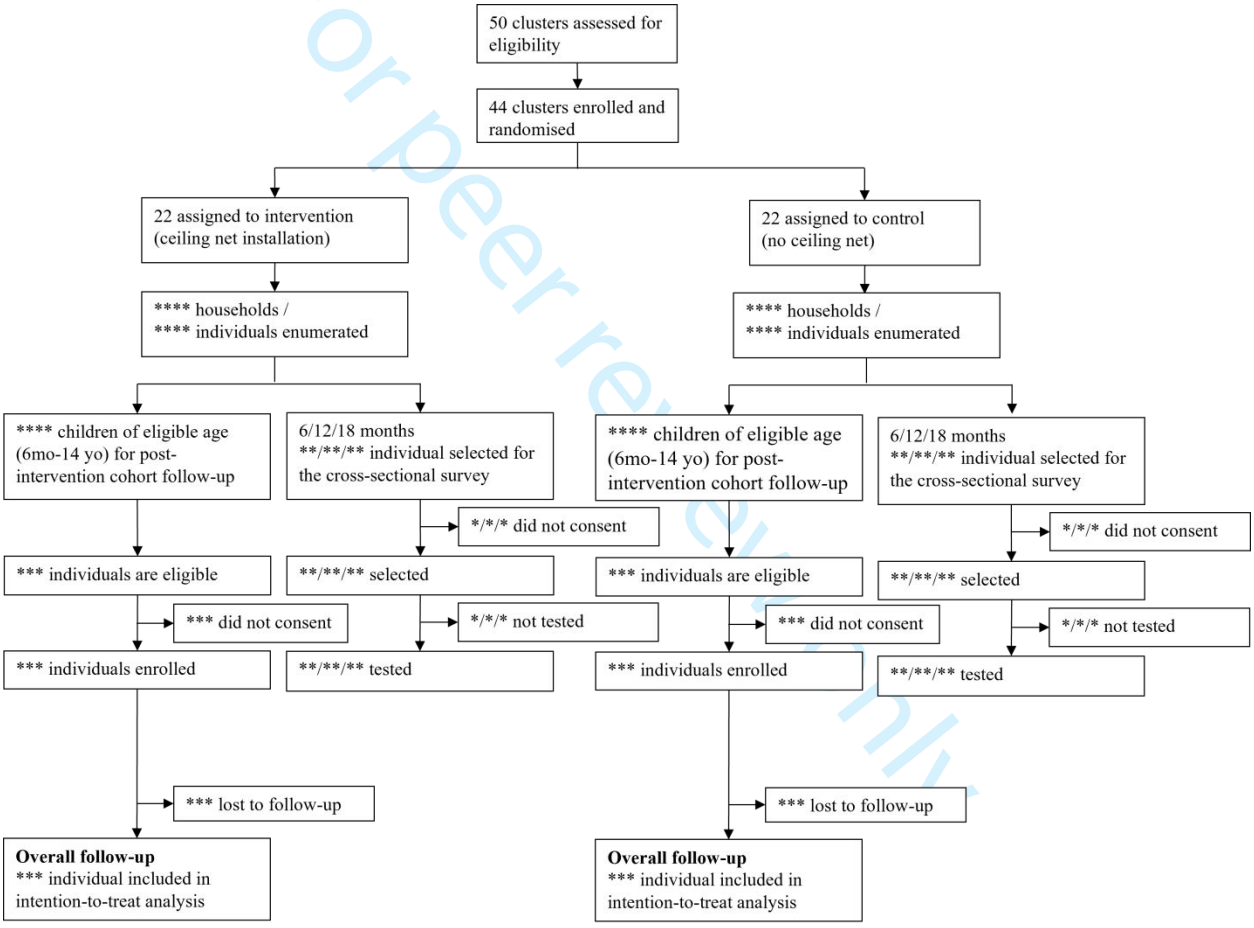


Figure 2: A schematic flow diagram of cluster allocation and study participant selection.

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 by PCR at 6, 12, and 18 months post-intervention in all age groups among intervention and control clusters.
2. 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 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

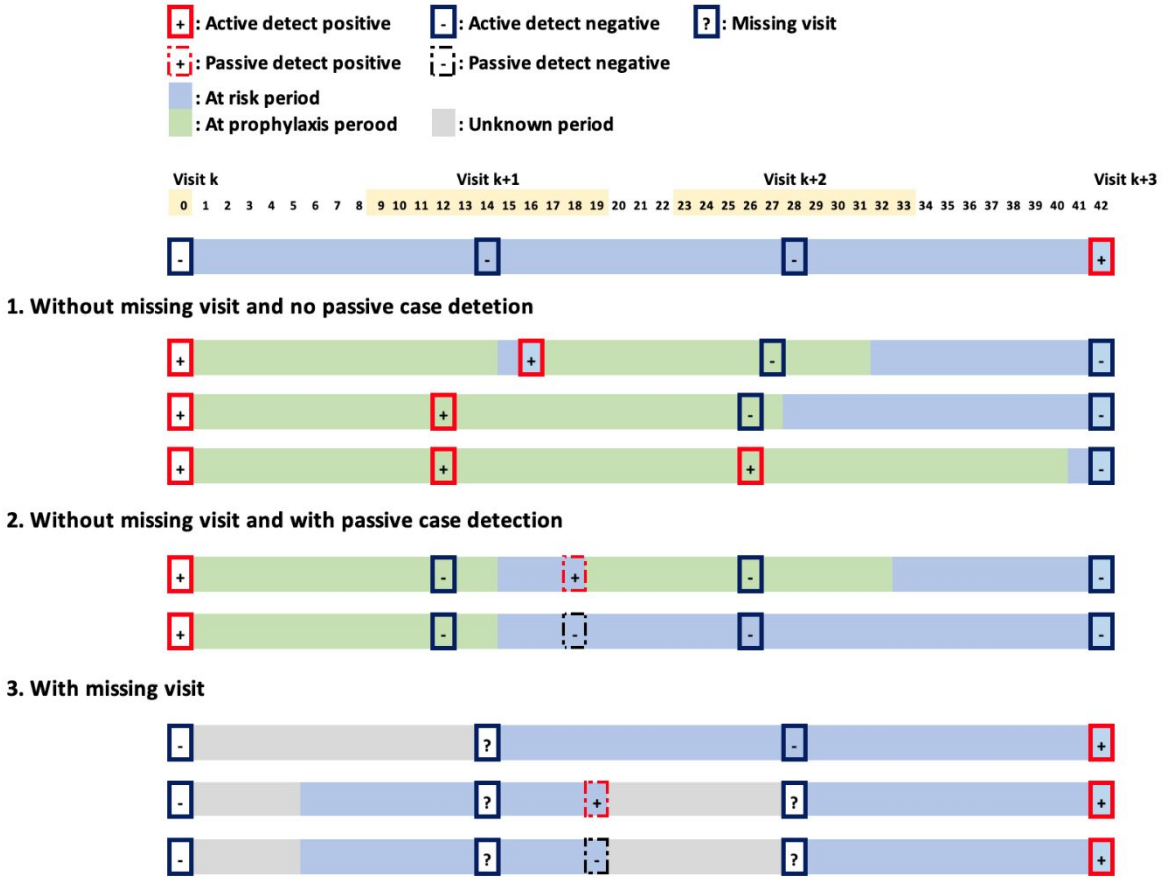
of "protection period" of ACT. If a participant misses a particular visit or a second positive is considered a carryover from the previous infection, the period is not included in the at-risk period.

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 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[3]. 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.



No. of event	Person-days	Incidence rate
	42	0.02
	13	0.08
	14	0.00
	2	0.00
	14	0.07
	30	0.00
	28	0.04
	28	0.07
	28	0.04

Figure 3: Specific patterns for case incidence rate calculation.

Analysis methods

We will follow the CONSORT guidelines extended for CRT[4] 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:

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

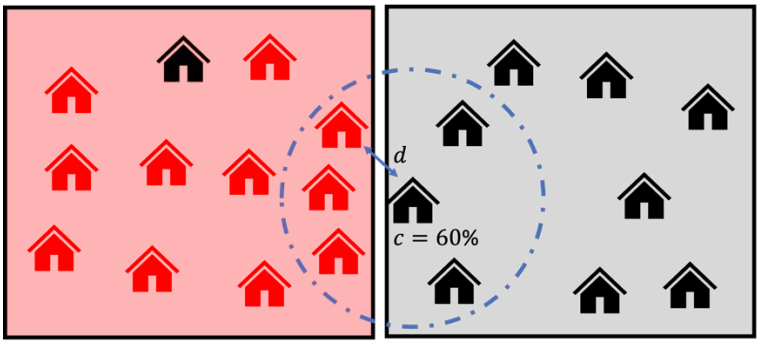
where $\mu_{k,i}$ is the mean incidence rate of individual i in cluster k, $\boldsymbol{x}_{k,i}$ is the covariate vector including individual and cluster level data, z_k is the Gaussian-type random effect at the cluster level. The protective efficacy will be estimated by $\left(1 - \exp\left(\hat{\beta}\right)\right) \times 100\%$, 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[5].

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[6]. 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.



: 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 ≥5%, 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 (≤ 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 https://www.R-project.org/.)

References

1. Hayes, R. J. & Bennett, S. Simple sample size calculation for cluster-randomized trials. *Int. J. Epidemiol.* **28**, 319–326 (1999).
2. Kagaya, W. *et al.* Evaluation of the protective efficacy of Olyset®Plus ceiling net on reducing malaria prevalence in children in Lake Victoria Basin, Kenya: study protocol for a cluster-randomized controlled trial. *Trials* **24**, 354 (2023).
3. Bennett, A. *et al.* A longitudinal cohort to monitor malaria infection incidence during mass drug administration in Southern Province, Zambia. *Am. J. Trop. Med. Hyg.* **103**, 54–65 (2020).
4. Campbell, M. K., Piaggio, G., Elbourne, D. R. & Altman, D. G. Consort 2010 statement: extension to cluster randomised trials. *BMJ* **345**, (2012).
5. Multerer, L., Glass, T. R., Vanobberghen, F. & Smith, T. Analysis of contamination in cluster randomized trials of malaria interventions. *Trials* **22**, 613 (2021).

6. Hawley, W. A. *et al.* Community-wide effects of permethrin-treated bed nets on child mortality and malaria morbidity in western Kenya. *Am. J. Trop. Med. Hyg.* **68**, 121–127 (2003).

0. Consent form

Please complete the survey below.

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.	◯ Yes ◯ No
Name of participant	_____
Signature of participant	_____
Name of witness	_____
Signature of witness	_____
Do you have a child to participate in the study?	◯ Yes ◯ No
Check the following box.	◯ I DO CONSENT: I do agree my child to take part in this study. ◯ I DO NOT CONSENT: I do not wish my child to participate in this study.
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	_____
Signature of witness	_____

id1 _____

id2 _____

id3 _____

"[id1]-[id2]-[id3]"

Please fix the structure ID above on the roof in front of the door.

Date _____

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?
- ◯ PIPED INTO DWELLING
- ◯ PIPED TO YARD/PLOT
- ◯ PIPED TO NEIGHBOR
- ◯ PUBLIC TAP/STANDPIPE
- ◯ DUG PROTECTED WELL
- ◯ DUG UNPROTECTED WELL
- ◯ WATER FROM PROTECTED SPRING
- ◯ WATER FROM UNPROTECTED SPRING
- ◯ RAINWATER
- ◯ TANKER TRUCK
- ◯ CART WITH SMALL TANK
- ◯ SURFACE WATER (RIVER/DAM/LAKE/POND/STREAM /IRRIGATION CHANNEL)
- ◯ BOTTLED WATER
- ◯ OTHER

Specify it. _____

What is the main source of water used by your household for other purposes such as cooking and handwashing?
- ◯ PIPED INTO DWELLING
- ◯ PIPED TO YARD/PLOT
- ◯ PIPED TO NEIGHBOR
- ◯ PUBLIC TAP/STANDPIPE
- ◯ DUG PROTECTED WELL
- ◯ DUG UNPROTECTED WELL
- ◯ WATER FROM PROTECTED SPRING
- ◯ WATER FROM UNPROTECTED SPRING
- ◯ RAINWATER
- ◯ TANKER TRUCK
- ◯ CART WITH SMALL TANK
- ◯ SURFACE WATER (RIVER/DAM/LAKE/POND/STREAM/C /IRRIGATION CHANNEL)
- ◯ OTHER

Specify it.	_____
Where is that water source located?	◯ IN OWN DWELLING ◯ IN OWN YARD/PLOT ◯ ELSEWHERE
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.	◯ FLUSH TO PIPED SEWER SYSTEM ◯ FLUSH TO SEPTIC TANK ◯ FLUSH TO PIT LATRINE ◯ FLUSH TO SOMEWHERE ELSE ◯ FLUSH, DON'T KNOW WHERE ◯ VENTILATED IMPROVED PIT LATRINE ◯ PIT LATRINE WITH SLAB ◯ PIT LATRINE WITHOUT SLAB/OPEN PIT ◯ COMPOSTING TOILET ◯ BUCKET TOILET ◯ HANGING TOILET/HANGING LATRINE ◯ NO FACILITY/BUSH/FIELD ◯ OTHER
Specify it.	_____
Do you share this toilet facility with other households?	◯ Yes ◯ No
Including your own compound, how many households use this toilet facility?	◯ LESS THAN 10 HOUSEHOLDS ◯ 10 OR MORE HOUSEHOLDS ◯ DON'T KNOW
Including your own household, how many households use this toilet facility (if less than 10)?	_____
Where is this toilet facility located?	◯ IN OWN DWELLING ◯ IN OWN YARD/PLOT ◯ ELSEWHERE
In your household, what type of cooking device (cookstove) is mainly used for cooking?	◯ ELECTRIC STOVE ◯ SOLAR COOKER ◯ LIQUEFIED PETROLEUM GAS (LPG)/COOKING GAS STOV ◯ PIPED NATURAL GAS STOVE ◯ BIOGAS STOVE ◯ LIQUID FUEL STOVE ◯ MANUFACTURED SOLID FUEL STOVE (i.g. Jiko) ◯ THREE STONE STOVE/OPENFIRE ◯ NO FOOD COOKED IN THE HOUSEHOLD ◯ OTHER
Specify it.	_____

What type of fuel or energy source is mainly used in this cookstove?	◯ ALCOHOL/ETHANOL ◯ GASOLINE/DIESEL ◯ KEROSENE/PARAFFIN ◯ COAL/LIGNITE ◯ CHARCOAL ◯ WOOD ◯ STRAW/SHRUBS/GRASS ◯ AGRICULTURAL CROP ◯ ANIMAL DUNG/WASTE ◯ PROCESSED BIOMASS (PELLETS) OR WOODCHIPS ◯ GARBAGE/PLASTIC ◯ SAWDUST ◯ OTHER
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? - Horses	_____
How many of the following (animals) livestock does this household own? - Donkeys	_____
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?	◯ Yes ◯ No
Do you know how many acres of agricultural land do members of this household own?	◯ Yes ◯ No
How many acres of agricultural land do members of this household own? ACRES	_____
Does your household have:	☐ Electricity? ☐ A radio? ☐ A television? ☐ A fixedlinetelephone? ☐ A computer? ☐ A refrigerator? ☐ A solarpanel? ☐ A table? ☐ A chair? ☐ A sofa? ☐ A bed? ☐ A cupboard? ☐ A clock? ☐ A microwave oven? ☐ A DVD player? ☐ A CD player?
Does any member of this compound own:	☐ A wrist watch? ☐ A mobile phone? ☐ A bicycle? ☐ A motorcycle or motor scooter? ☐ An animal-drawn cart? ☐ A car or truck? ☐ A boat with a motor?
Does any member of this household have an account in a bank or other financial institution?	◯ Yes ◯ No
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?	◯ Yes ◯ No
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

Does your household have any bed nets?	◯ Yes ◯ No
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.	☐ Air flow disturbance ☐ Heat ☐ Appearance ☐ Pets ☐ Fire ☐ Social culture and religious factor ☐ Others
Specify it	_____
Do you have any concerns about the ceiling net? Select all that apply.	☐ Air flow disturbance ☐ Heat ☐ Appearance ☐ Pets ☐ Fire ☐ Social culture and religious factor ☐ No concern ☐ Others
Specify it	_____
OBSERVE MAIN MATERIAL OF THE FLOOR OF THE DWELLING/SLEEPING ROOM. RECORD OBSERVATION.	◯ EARTH/SAND ◯ DUNG ◯ WOOD PLANKS ◯ PALM/BAMBOO ◯ PARQUET OR POLISHED WOOD ◯ VINYL OR ASPHALT STRIPS ◯ CERAMIC TILES ◯ CEMENT ◯ CARPET ◯ OTHER
Specify it.	_____

OBSERVE MAIN MATERIAL OF THE ROOF OF THE DWELLING. RECORD OBSERVATION.	◯ NO ROOF ◯ THATCH/PALM LEAF ◯ RUSTIC MAT ◯ PALM/BAMBOO ◯ WOOD PLANKS ◯ CARDBOARD ◯ IRON SHEETS ◯ WOOD ◯ CALAMINE/CEMENT FIBER ◯ BRICK/CLAY TILES ◯ CEMENT ◯ ROOFING SHINGLES ◯ OTHER
Specify it.	_____
OBSERVE MAIN MATERIAL OF THE EXTERIOR WALLS OF THE DWELLING. RECORD OBSERVATION.	◯ NO WALLS ◯ WOOD WITH MUD ◯ IRON SHEET ◯ BRICKS ◯ CANE/PALM/TRUNKS ◯ BAMBOO WITH MUD ◯ STONE WITH MUD ◯ UNCOVERED ADOBE ◯ PLYWOOD ◯ CARDBOARD ◯ REUSED WOOD ◯ CEMENT ◯ STONE WITH LIME/CEMENT ◯ CEMENT BLOCKS ◯ COVERED ADOBE ◯ WOOD PLANKS/SHINGLES ◯ OTHER
Specify it.	_____
OBSERVE EAVES OF THE DWELLING. RECORD OBSERVATION.	◯ Open ◯ Partly open ◯ Close
OBSERVE BEAMS OF THE DWELLING. RECORD OBSERVATION.	◯ No vertical beam ◯ One vertical beam ◯ More than one vertical beams
Tick all that apply	☐ 2 or more vertical beams in the same room ☐ Ceiling board/ Flat roof ☐ The roof is very low ☐ The room is used for kitchen ☐ None
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

Is there a child living in this structure? "Living" means that the child usually stay in the household. If the child is usually staying at a boarding school, but now he/she is staying in this house because of a school closure, that is not regarded as "living".	◯ Yes ◯ No

Once you complete, "Show More Save Options">"Save & Go to Next Form"

2. Children

Please complete the survey below.

Thank you!

Skip this page because there is no children and "Show More Save Options">"Save & Go to Next Form".

Now we would like to record the names of all children aged under 18.

But RDT tests are for children from 6 month to 14 years old.

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?

Last name _____

Is the child a boy or a girl?

◯ BOY
◯ GIRL

Was that a single or multiple pregnancy?

◯ SING
◯ 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.

Is the child living with you?

◯ Yes
◯ No

"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".

Has the child been ill with a fever at any time in the last 2 weeks?

◯ YES
◯ NO
◯ DON'T KNOW

At any time during the illness, did the child have blood taken from a finger or heel for testing?	◯ YES ◯ NO ◯ DON'T KNOW
Were you told by a healthcare provider that the child had malaria?	◯ YES ◯ NO ◯ DON'T KNOW
Did you seek advice or treatment for the illness from any source?	◯ Yes ◯ No
How many times did you seek advice or treatment for the illness from any source?	_____
Where did you first 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'	◯ GOVERNMENT HOSPITAL ◯ GOVERNMENT HEALTH CENTER ◯ GOVERNMENT DISPENSARY ◯ GOVERNMENT MOBILE CLINIC ◯ COMMUNITY HEALTH WORKER/FIELD WORKER ◯ PRIVATE HOSPITAL ◯ PRIVATE CLINIC ◯ PHARMACY ◯ PRIVATE DOCTOR ◯ PRIVATE MOBILE CLINIC ◯ COMMUNITY HEALTH WORKER ◯ SHOP ◯ TRADITIONAL PRACTITIONER ◯ MARKET ◯ ITINERANT DRUG SELLER ◯ OTHER
Specify it.	_____
Where did you second 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'	◯ GOVERNMENT HOSPITAL ◯ GOVERNMENT HEALTH CENTER ◯ GOVERNMENT DISPENSARY ◯ GOVERNMENT MOBILE CLINIC ◯ COMMUNITY HEALTH WORKER/FIELD WORKER ◯ PRIVATE HOSPITAL ◯ PRIVATE CLINIC ◯ PHARMACY ◯ PRIVATE DOCTOR ◯ PRIVATE MOBILE CLINIC ◯ COMMUNITY HEALTH WORKER ◯ SHOP ◯ TRADITIONAL PRACTITIONER ◯ MARKET ◯ ITINERANT DRUG SELLER ◯ OTHER
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'	◯ GOVERNMENT HOSPITAL ◯ GOVERNMENT HEALTH CENTER ◯ GOVERNMENT DISPENSARY ◯ GOVERNMENT MOBILE CLINIC ◯ COMMUNITY HEALTH WORKER/FIELD WORKER ◯ PRIVATE HOSPITAL ◯ PRIVATE CLINIC ◯ PHARMACY ◯ PRIVATE DOCTOR ◯ PRIVATE MOBILE CLINIC ◯ COMMUNITY HEALTH WORKER ◯ SHOP ◯ TRADITIONAL PRACTITIONER ◯ MARKET ◯ ITINERANT DRUG SELLER ◯ OTHER
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?	◯ Yes ◯ No
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?	◯ SAME DAY ◯ NEXT DAY ◯ TWO DAYS AFTER FEVER ◯ THREE OR MORE DAYS AFTER FEVER ◯ DON'TKNOW
Has [mis_wo213_1] received a malaria vaccine?	◯ Yes ◯ No

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

RDT result for Pan	◯ Negative ◯ Positive

If there is another child, press "Show More Save Options">"Save & Add New Instance

otherwise, press "Show More Save Options">Go to Next Form".

3. Adults

Please complete the survey below.

Thank you!

Now, we would like to record the names of all adults who live in this household on a permanent or weekly basis.
Do not include a person who stays only a few days in a month.

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

◯ Permanent Resident
◯ Weekly Resident
◯ Monthly Resident
◯ Others

Answer his/her age with...

◯ birthday
◯ age
◯ age group

Birthday _____

Age _____ (years old)

Age group

◯ High school
◯ After high school
◯ Was born before the independence of Kenya

Sex

◯ Male
◯ Female
◯ Other
◯ Prefer not to say

Relation to the structure head	◯ 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
Relation to the compound head	◯ 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
Please repeat until you record all the members. ("Show More Save Options">"Save & Add New Instance"). Once you complete all the member, "Show More Save Options">"Save & Go to Next Form".	
Note	_____

4. NET

Please complete the survey below.

Thank you!

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?

- ◯ Yes
- ◯ No

How many months ago did your household get the mosquito net?
IF LESS THAN ONE MONTH AGO, RECORD '00'.

- ◯ 0
- ◯ 1
- ◯ 2
- ◯ 3
- ◯ 4
- ◯ 5
- ◯ 6
- ◯ 7
- ◯ 8
- ◯ 9
- ◯ 10
- ◯ 11
- ◯ 12
- ◯ 13
- ◯ 14
- ◯ 15
- ◯ 16
- ◯ 17
- ◯ 18
- ◯ 19
- ◯ 20
- ◯ 21
- ◯ 22
- ◯ 23
- ◯ 24
- ◯ 25
- ◯ 26
- ◯ 27
- ◯ 28
- ◯ 29
- ◯ 30
- ◯ 31
- ◯ 32
- ◯ 33
- ◯ 34
- ◯ 35
- ◯ 36
- ◯ MORE THAN 36 MONTHS AGO
- ◯ NOT SURE

OBSERVE OR ASK BRAND/TYPE OF MOSQUITO NET.	◯ OLYSET (SUPANET EXTRA) ◯ PERMANET (SUPANET EXTRA) ◯ VEERALIN ◯ NETPROTECT ◯ YORKOOL ◯ DAWAPLUS ◯ OTHER/DON'T KNOW BRAND (LLIN) ◯ OTHER TYPE (NOT LLIN) ◯ DON'T KNOW TYPE
Did you get the net through a distribution campaign, during an antenatal care visit, or during a child welfare visit?	◯ YES, MASS DISTRIBUTION CAMPAIGN ◯ YES, ANTENATAL CARE VISIT ◯ YES, CHILD WELFARE VISIT ◯ NO
Where did you get the net?	◯ GOVERNMENT HEALTH FACILITY ◯ PRIVATE HEALTH FACILITY ◯ PHARMACY ◯ SHOP/MARKET ◯ CHP ◯ RELIGIOUS INSTITUTION ◯ SCHOOL ◯ OTHER ◯ DON'T KNOW
Did anyone sleep under this mosquito net last night?	◯ YES ◯ NO ◯ NOT SURE
Who slept under this mosquito net last night? RECORD THE PERSON'S NAME. IF THERE ARE MORE THAN ONE, RECORD ALL THE NAME CONNECTING BY ",".	_____
What was the main reason this net was not used last night?	◯ TOO HOT ◯ DON'T LIKE NET SHAPE/COLOR/SIZE ◯ DON'T LIKE SMELL ◯ UNABLE TO HANG NET ◯ SLEPT OUTDOORS ◯ USUAL USER DIDN'T SLEEP HERE LAST NIGHT ◯ NO MOSQUITOES/NO MALARIA ◯ EXTRA NET/SAVING FOR LATER ◯ NET TOO SMALL/SHORT ◯ NET BROUGHT BED BUGS ◯ OTHER
Specify it	_____
Note	_____

If there is another net, press "Show More Save Options">"Save & Add New Instance

otherwise, press "Save & Exit Form".

Questionnaire

Please complete the survey below.

Thank 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.	◯ Moved out from the area (will never come back) ◯ Travel to another village in Ndhiwa ◯ Travel to Homa Bay County other than Ndhiwa ◯ Travel to Another county in Kenya ◯ Travel to Another country ◯ Refuse ◯ Do not know (Could not find) ◯ Others
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?	☐ Another house in your village ☐ Another village in Ndhiwa ☐ Homa Bay County other than Ndhiwa ☐ Another county in Kenya ☐ Another country

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 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? (Please refer to the booklet)	◯ Yes ◯ No
Did [name_f] have the following symptoms at any point in the past four weeks?	☐ Fever ☐ Chills ☐ Profuse sweating ☐ Muscle/joint pain ☐ Abdominal pain ☐ Diarrhoea ☐ Nausea ☐ Vomiting ☐ Irritability ☐ Refusal to feed ☐ Prostration (difficulty to sit upright) ☐ Alteration in the level of consciousness ☐ Convulsions or coma ☐ Difficulty in breathing/respiratory distress ☐ Jaundice ☐ Others ☐ None
Please list other symptoms [name_f] experienced in the past four weeks.	_____
How many times did the child visit health facilities?	◯ One time ◯ Two time ◯ Three time ◯ More than three

When did [name_f]visit the health facility?

_____

(Please refer to the booklet)

Which health facility did [name_f] visit?

(Please refer to the booklet)

- ☐ Malela level 4 hospital
- ☐ Kabongo HC
- ☐ 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?

(Please refer to the booklet)

- ☐ Fever
- ☐ Headache
- ☐ Muscle pain
- ☐ Abdominal pain
- ☐ Nausea
- ☐ Vomiting
- ☐ Diarrhea
- ☐ Convulsions or coma
- ☐ Jaundice
- ☐ Rapid breathing
- ☐ Difficulty in breathing/respiratory distress
- ☐ Pale conjunctivae/palms
- ☐ Loss of reactivity
- ☐ Others

When did the symptom start?

_____

(Please refer to the booklet)

Was [name_f] diagnosed with malaria?

(Please refer to the booklet)

- ◯ Yes
- ◯ No

What was the diagnosis?

_____

Did [name_f] take any treatment or medication?

(Please refer to the booklet)

- ◯ Yes
- ◯ No

What treatment or medication did [name_f] receive from the health facility?

(Please refer to the booklet)

- ☐ AL
- ☐ DHAP
- ☐ OTHER ACT (NOT AL OR DHAP)
- ☐ 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

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?

(Please refer to the booklet)

- ☐ Malela level 4 hospital
- ☐ Kabongo HC
- ☐ 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?

(Please refer to the booklet)

- ☐ Fever
- ☐ Headache
- ☐ Muscle pain
- ☐ Abdominal pain
- ☐ Nausea
- ☐ Vomiting
- ☐ Diarrhea
- ☐ Convulsions or coma
- ☐ Jaundice
- ☐ Rapid breathing
- ☐ Difficulty in breathing/respiratory distress
- ☐ Pale conjunctivae/palms
- ☐ Loss of reactivity
- ☐ Others

When did the symptoms for the first visit start?

_____

(Please refer to the booklet)

Was [name_f] diagnosed with malaria for the first visit?

(Please refer to the booklet)

- ◯ Yes
- ◯ No

What was the diagnosis?

_____

Did [name_f] take any treatment or medication for the first visit?

(Please refer to the booklet)

- ◯ Yes
- ◯ No

What treatment or medication did [name_f] receive from the health facility?

(Please refer to the booklet)

- ☐ AL
- ☐ DHAP
- ☐ OTHER ACT (NOT AL OR DHAP)
- ☐ 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

Please list other medications [name_f] received from the health facility.

_____

When did [name_f] SECOND visit the health facility?

_____

(Please refer to the booklet)

Which health facility did [name_f] second visit?

(Please refer to the booklet)

- ☐ Malela level 4 hospital
- ☐ Kabongo HC
- ☐ 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 second visit? (Please refer to the booklet)	☐ Fever ☐ Headache ☐ Muscle pain ☐ Abdominal pain ☐ Nausea ☐ Vomiting ☐ Diarrhea ☐ Convulsions or coma ☐ Jaundice ☐ Rapid breathing ☐ Difficulty in breathing/respiratory distress ☐ Pale conjunctivae/palms ☐ Loss of reactivity ☐ Others
When did the symptoms for the second visit start? (Please refer to the booklet)	_____
Was [name_f] diagnosed with malaria for the second visit? (Please refer to the booklet)	◯ Yes ◯ No
What was the diagnosis?	_____
Did [name_f] take any treatment or medication for the second visit? (Please refer to the booklet)	◯ Yes ◯ No
What treatment or medication did [name_f] receive from the health facility? (Please refer to the booklet)	☐ AL ☐ DHAP ☐ OTHER ACT (NOT AL OR DHAP) ☐ 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
Please list other medications [name_f] received from the health facility.	_____

When did [name_f] THIRD visit the health facility?

_____

(Please refer to the booklet)

Which health facility did [name_f] third visit?

(Please refer to the booklet)

- ☐ Malela level 4 hospital
- ☐ Kabongo HC
- ☐ 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 third visit?

(Please refer to the booklet)

- ☐ Fever
- ☐ Headache
- ☐ Muscle pain
- ☐ Abdominal pain
- ☐ Nausea
- ☐ Vomiting
- ☐ Diarrhea
- ☐ Convulsions or coma
- ☐ Jaundice
- ☐ Rapid breathing
- ☐ Difficulty in breathing/respiratory distress
- ☐ Pale conjunctivae/palms
- ☐ Loss of reactivity
- ☐ Others

When did the symptoms for the third visit start?

_____

(Please refer to the booklet)

Was [name_f] diagnosed with malaria for the third visit?

(Please refer to the booklet)

- ◯ Yes
- ◯ No

What was the diagnosis?

_____

Did [name_f] take any treatment or medication for the third visit?

(Please refer to the booklet)

- ◯ Yes
- ◯ No

What treatment or medication did [name_f] receive from the health facility? (Please refer to the booklet)	☐ AL ☐ DHAP ☐ OTHER ACT (NOT AL OR DHAP) ☐ 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
Please list other medications [name_f] received from the health facility.	_____
Did [name_f] take treatment or medication from the following in the past four weeks?	☐ No ☐ Friends ☐ Relatives ☐ Pharmacy/chemist ☐ Traditional healers
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) ☐ OTHER ANTIMALARIAL ☐ AMOXICILLIN ☐ COTRIMOXAZOLE ☐ OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP) ☐ OTHER ANTIBIOTIC MEDICINE (INJECTION/IV) ☐ ASPIRIN ☐ PARACETAMOL/PANADOL/ACETAMINOPHEN ☐ IBUPROFEN ☐ OTHER ☐ DON'TKNOW
Please list other medications [name_f] took from the friends.	_____

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) ☐ OTHER ANTIMALARIAL ☐ AMOXICILLIN ☐ COTRIMOXAZOLE ☐ OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP) ☐ OTHER ANTIBIOTIC MEDICINE (INJECTION/IV) ☐ ASPIRIN ☐ PARACETAMOL/PANADOL/ACETAMINOPHEN ☐ IBUPROFEN ☐ OTHER ☐ DON'TKNOW
Please list other medications [name_f] took from the relatives.	_____
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 (INJECTION/IV) ☐ OTHER ANTIMALARIAL ☐ AMOXICILLIN ☐ COTRIMOXAZOLE ☐ OTHER ANTIBIOTIC MEDICINE (PILL/SYRUP) ☐ OTHER ANTIBIOTIC MEDICINE (INJECTION/IV) ☐ ASPIRIN ☐ PARACETAMOL/PANADOL/ACETAMINOPHEN ☐ IBUPROFEN ☐ OTHER ☐ DON'TKNOW
Please list other medications [name_f] took from the pharmacy.	_____

What medications did [name_f] take from the traditional healer?	☐ AL ☐ DHAP ☐ OTHER ACT (NOT AL OR DHAP) ☐ 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
Please list other medications [name_f] took from the traditional healer.	_____
Does [name_f] have the following symptoms now or in the last 24 hours?	☐ Fever ☐ Chills ☐ Profuse sweating ☐ Muscle/joint pain ☐ Abdominal pain ☐ Diarrhoea ☐ Nausea ☐ Vomiting ☐ Irritability ☐ Refusal to feed ☐ Prostration (difficulty to sit upright) ☐ Alteration in the level of consciousness ☐ Convulsions or coma ☐ Difficulty in breathing/respiratory distress ☐ Jaundice ☐ Others ☐ None
Please list other symptoms [name_f] experience now or in the last 24 hours.	_____
Did [name_f] receive the malaria vaccine within four weeks?	◯ Yes ◯ No
How many times has [name_f] received the malaria vaccine, including the latest one?	◯ 1 dose ◯ 2 doses ◯ 3 doses ◯ 4 doses ◯ Don't know
Does the structure where [name_f] usually sleeps have ceiling nets?	◯ Yes ◯ No

Sample

Please complete the survey below.

Thank you!

	_____
Cohort 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?	◯ Yes ◯ No
Thick and thin blood films?	◯ Yes ◯ No
RDT results for P.f	◯ Negative ◯ Positive
RDT results for Pan	◯ Negative ◯ Positive

Participant questionnaire

Please complete the survey below.

Thank 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")	_____
First name	_____
Middle name	_____
Last name	_____
Age	_____ (years old)
Does [name_f] know the birthday?	◯ Yes ◯ No
Birthday	_____
The birthday and your age are contradicting. Please check the true age again.	
Sex	◯ Male ◯ Female ◯ Other ◯ Prefer not to say
Longitude	_____
Latitude	_____
This participant is available for the survey.	◯ Yes ◯ No

Please select the reason why the participant is not available.	◯ Moved out from the area (will never come back) ◯ Travel to another village in Ndhiwa ◯ Travel to Homa Bay County other than Ndhiwa ◯ Travel to Another county in Kenya ◯ Travel to Another country ◯ Refuse ◯ Do not know (Could not find) ◯ Others
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?	☐ Another house in your village ☐ Another village in Ndhiwa ☐ Homa Bay County other than Ndhiwa ☐ Another county in Kenya ☐ Another country
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 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 Ndhiwa?	_____
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] have any symptoms at any point in the past four weeks?	◯ Yes ◯ No ◯ Don't know

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

What treatment or medication did [name_f] receive from the health facility?	☐ AL ☐ DHAP ☐ OTHER ACT (NOT AL OR DHAP) ☐ 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
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?	◯ Yes ◯ No
Did [name_f] take treatment or medication from the following in the past four weeks?	☐ Friends ☐ Relatives ☐ Pharmacy/chemist ☐ Traditional healers
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) ☐ 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

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) ☐ 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 relatives.	_____
Do you know the names of medications from the pharmacy/chemist?	◯ Yes ◯ No
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 (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 pharmacy.	_____
Do you know the names of medications from the traditional healer?	◯ Yes ◯ No

What medications did [name_f] take from the traditional healer?	☐ AL ☐ DHAP ☐ OTHER ACT (NOT AL OR DHAP) ☐ 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
Please list other medications [name_f] took from the traditional healer.	_____
Does [name_f] have any symptoms now or in the last 24 hours?	◯ Yes ◯ No
Does [name_f] have the following symptoms now or in the last 24 hours?	☐ Fever ☐ Chills ☐ Profuse sweating ☐ Muscle/joint pain ☐ Abdominal pain ☐ Diarrhoea ☐ Nausea ☐ Vomiting ☐ Irritability ☐ Refusal to feed ☐ Prostration (difficulty to sit upright) ☐ Alteration in the level of consciousness ☐ Convulsions or coma ☐ Difficulty in breathing/respiratory distress ☐ Jaundice ☐ Cough ☐ Rash ☐ Itches ☐ Others
Please list other symptoms [name_f] experience now or in the last 24 hours.	_____
Has [name_f] received a malaria vaccine? Please refer to the mother-child book.	◯ Yes ◯ No
How many times has [name_f] received the malaria vaccine? Please refer to the mother-child book.	◯ 1 dose ◯ 2 doses ◯ 3 doses ◯ 4 doses ◯ Don't know
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?	◯ Yes ◯ No
Thick and thin blood films?	◯ Yes ◯ No
RDT results for P.f	◯ Negative ◯ Positive
RDT results for Pan	◯ Negative ◯ Positive

Head questionnaire

Please complete the survey below.

Thank you!

_____

Who is the respondent?

*If the respondent are not sure about the answer(s), he/she can be helped by the other members.

- ◯ Head
- ◯ Primary care taker
- ◯ Participant
- ◯ Others

What is the respondent's relation to the participant?

- ◯ 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

What is the condition of the ceiling net?

- ◯ No damage
- ◯ Damaged and not repaired
- ◯ Damaged but repaired
- ◯ Removed
- ◯ Not installed

How many hole(s) does/did it have?
(regardless of the size)
(mark 0 if no hole)

_____

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
- ◯ smaller than the fist
- ◯ larger than the fist

What is/was the reason of the damage?

- ◯ Accident during the cleaning
- ◯ Animal
- ◯ Caught a fire
- ◯ Unknown
- ◯ Others

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?	◯ Good ◯ Damaged
Presence of gaps between battens and the wall	◯ Yes ◯ No
Do you agree with the following potential positive sides of the ceiling net?	☐ Stop mosquito entering the house ☐ Stop other insects/animals entering the house ☐ Durability of the ceiling nets ☐ To beautify the house ☐ Household coverage ☐ Keep the room cool ☐ Others
Please specify.	_____
Do you agree with the following potential negative sides of the ceiling net?	☐ It makes room too hot ☐ It reduces the storage space a the top of the w all ☐ Fixing looks untidy ☐ It is hard to clean ☐ Dirt/debris trapped by the ceiling net ☐ Rewiring of power lines ☐ Others
Please specify.	_____
Other features in the ceiling net (if any).	_____
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?	◯ 100 KSH ◯ 300 KSH ◯ 500 KSH ◯ 1000 KSH ◯ 2000 KSH ◯ 5000 KSH ◯ More than 10,000 KSH
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?	◯ Yes ◯ No

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