UGANDA PBO NET STUDY

Study Title: Impact of long-lasting insecticide treated bednets with and without piperonyl butoxide (PBO) on malaria indicators in Uganda: a cluster-randomised trial

Funded by: The Against Malaria Foundation

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Study summary

Title	**Impact of long-lasting insecticide treated bednets with and without piperonyl butoxide (PBO) on malaria indicators in Uganda: a cluster-randomised trial**
Primary objective	*To evaluate the impact of combination LLINs (with PBO), as compared to conventional LLINs (without PBO), on parasite prevalence, in Eastern and Western Uganda.* We will test the hypothesis that parasite prevalence will be lower in intervention clusters (health sub-districts [HSDs] randomised to receive PBO nets), than in control clusters (HSDs randomised to conventional nets) overall, and stratified by region (Eastern and Western regions).
Secondary objectives	1 To evaluate the impact of PermaNet 3.0 (with PBO), as compared to PermaNet 2.0 (without PBO), on parasite prevalence. 2 To evaluate the impact of Olyset Plus (with PBO), as compared to Olyset Net (without PBO), on parasite prevalence. 3 To determine factors associated with effectiveness of LLINs with PBO, as compared to LLINs without PBO, including the level of insecticide resistance. 4 To assess net survivorship, durability, and bio-efficacy in Uganda. We will conduct cross-sectional surveys to determine net survivorship, attrition, and use, and will supplement these with laboratory assessments of net durability and bio-efficacy.
Study site	The study will be conducted in 48 districts in Eastern and Western Uganda, covering a wide range of epidemiological settings with varying levels of malaria transmission and insecticide resistance.
Cluster randomisation	A cluster has been defined as a HSD; 104 clusters have been included in the study. Adaptive randomisation was used to accommodate the number of LLINs available, which varied by manufacturer. Clusters have been randomised to receive one of 4 types of LLINs: (1) PermaNet 2.0 [n=37], (2) PermaNet 3.0 [n=32], (3) Olyset Net [n=15], and (4) Olyset Plus [n=20]
Intervention	A universal LLIN distribution campaign will be led by the National Malaria Control Programme and partners. LLINs will be distributed at the level of cluster (HSD).
Evaluation methods & sample size	**1) Cross-sectional surveys.** At baseline (prior to distributing LLINs), and up to 4 times after nets are distributed (at 6, 12, 18 and 24-30 months after distribution), randomly selected households will be surveyed from each of the clusters. The survey will include a household questionnaire and clinical & laboratory evaluation of children aged 2-10 years. We will survey 50 households in each cluster (n=5,200), aiming to recruit all eligible children in each household (approximately 10,400 children) per survey. **2) Entomology surveys.** Mosquitoes from 5-10 randomly selected households in all 104 clusters using prokopack aspirators, aiming to collect 30-50 mosquitoes per cluster for genotypic monitoring. Mosquitoes will also be collected from 10-15 purposely selected households in 12 sentinel site clusters for phenotypic monitoring. Collections will be carried out concurrently with the cross-sectional surveys. **3) Insecticide resistance monitoring.** Insecticide resistance will be measured using genotypic and phenotypic assays. Genotyping will be done on mosquitos collected from all 104 clusters. Mosquitoes species will be identified, and *A. gambiae* and *A. arabiensis* will be screened for key insecticide target sites (e.g. Vgsc) together with variants in metabolic resistance genes (e.g. Gste4, Cyp4j5, and Coeae1d). Phenotypic assays will be done on specimens from up to 12 sentinel sites, up to 6 per region, using permethrin, deltamethrin, permethrin + PBO and deltamethrin + PBO. **4) LLIN survivorship, durability and bio-efficacy**. Information on net survivorship and use will be collected in the cross-sectional surveys. One year after distribution of nets, we will quantify net durability using the WHO Vector Control Working Group methodology, and will conduct standard WHO cone bioassays on 100 bar-coded nets collected from the community. Net durability assessments will be repeated at 24-30 months, funding permitting.
Primary outcome	The primary outcome of the trial will be parasite prevalence (defined as the proportion of thick blood smears that are positive for asexual parasites) in children aged 2-10 years in the cross-sectional surveys.
Secondary outcomes	**1) Cross-sectional surveys:** Prevalence of anaemia and mean haemoglobin (in children < 5 years) **2) Insecticide resistance monitoring:** Prevalence of molecular markers associated with insecticide resistance, prevalence of phenotypic insecticide resistance. **3) LLIN survivorship, durability and bio-efficacy:** Survivorship: prevalence of nets present, and in use; Durability: proportionate hole index; Bio-efficacy: knock down rate, mortality rate

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Abbreviations & acronyms

ACT	artemisinin-based combination therapy
AL	artemether-lumefantrine
AMF	The Against Malaria Foundation
CAB	community advisory board
CORPS	community owner resource person
DFID	UK's Department for International Development
EDTA	ethylene-diamine-tetra-acetic acid
ELISA	enzyme-linked immunosorbent assay
EIR	entomologic inoculation rate
GIS	geographical information systems
GPS	global positioning system
HSD	health sub-district
IDRC	Infectious Disease Research Collaboration
IRB	institutional review board
IRS	indoor residual spraying
ITN	insecticide treated bednet
LLIN	long-lasting insecticide treated bed net
LSHTM	London School of Hygiene and Tropical Medicine
MoH	Ministry of Health
PBO	Piperonyl butoxide
PCR	polymerase chain reaction
PHI	proportionate hole index
PMI	US President's Malaria Initiative
PRISM	Programme for Resistance, Immunology, Surveillance and Modelling of Malaria in Uganda
QDS	questionnaire development system
RDT	rapid diagnostic test
SBCC	social behaviour change communication
SOMREC	School of Medicine Research and Ethics Committee, Makerere University
SOP	standard operating procedure
UCSF	University of California, San Francisco
UMSP	Uganda Malaria Surveillance Project
UNCST	Uganda National Council of Science and Technology
WHO	World Health Organisation

1 Background

1.1 Introduction

Over the last 15 years, malaria control interventions have been scaled-up dramatically across Africa, resulting in an estimated 40% decrease in the incidence of disease due to *P. falciparum* between 2000 and 2015 [1]. However, despite these encouraging trends, decreases in the burden of malaria have not been uniform across Africa and have been slowest in countries with the highest burden, such as Uganda [2]. In Uganda, coverage of key malaria control strategies, including long-lasting insecticidal nets (LLINs), indoor residual spraying of insecticide (IRS), and treatment of malaria cases with artemisinin-based combination therapy (ACTs), has increased substantially. However, overall progress toward control of malaria in Uganda has been slow [3, 4], and recent evidence suggests that gains may be fragile in high transmission areas, if effective control measures are not sustained [2, 5].

1.2 Impact of malaria control interventions in Uganda

Our research group has been well-positioned to estimate the impact of population-level control interventions implemented under operational settings using data from our malaria surveillance sites. In Tororo district, a LLIN distribution campaign was carried out in Nov 2013, and in Dec 2014, IRS with the carbamate bendiocarb was implemented for the first time (Figure 1). We utilised data from a comprehensive surveillance programme, including health facility and cohort data among children, to evaluate temporal trends in the test positivity rate and incidence of malaria, respectively, and entomological data to evaluate trends in the human biting rate. Surprisingly, although the LLIN distribution campaign substantially increased coverage levels, it had little impact on clinical malaria indicators, based on time-series analysis [4]. However, the addition of three rounds of IRS at ~6 month intervals was associated with significant reductions in all key indicators (Figure 1).

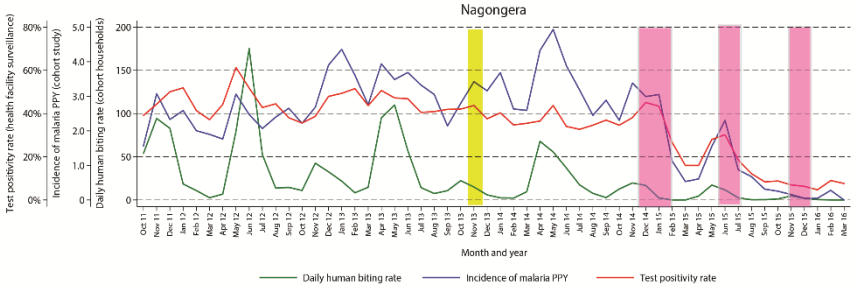

Figure 1. Impact of vector control on key malaria indicators in Tororo district. Monthly trends following delivery of LLINs (yellow bar) and multiple rounds of IRS (pink bars) in Nagongera sub-county, Tororo, showing significant reductions in the incidence of malaria (RR=0.13, 95% CI 0.07-0.27, p<0.001), test positivity rate (RR=0.54, 95% CI 0.49-0.60, p<0.001), and human biting rate (RR=0.29, 95% CI 0.17-0.50, p<0.001).

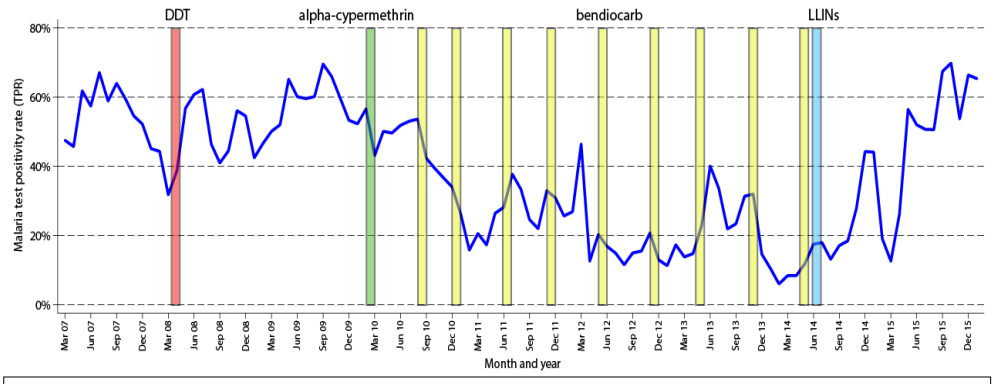

Figure 2. Impact of vector control on malaria test positivity rate in Apac. Monthly trends in malaria test positivity rate (TPR, blue line) in Apac following delivery of multiple rounds of IRS with different insecticides (red, green, yellow bars) and universal distribution of LLINs (light blue bar).

In 2009, IRS was successfully implemented in 10 districts in northern Uganda with high transmission intensity. In 2014, IRS was discontinued in these districts due to limited funding, with the hope that gains would be sustained by LLINs. In Apac district we have been able to monitor trends in malaria morbidity

before, during and after IRS and distribution of LLINs (Figure 2). Prior to implementation of IRS, transmission intensity in Apac district was one of the highest ever recorded, with an annual EIR of >1,500 infective bites PPY [6]. Malaria test positivity rates ranged from 70-80% in children and 30-50% in adults, with little change after IRS with a pyrethroid in early 2010. In late 2010, the IRS program switched to a carbamate class of insecticide. Rounds of IRS were continued approximately every 6 months until May 2014, and during this period test positivity rates decreased markedly to < 20% in children and 10% in adults. Following discontinuation of IRS a universal LLIN distribution program was implemented with the hopes of maintaining gains achieved by IRS. However, within 4 months of discontinuing IRS test positivity rates began to rise dramatically, reaching pre-IRS levels. The trends in test positivity rate from the surveillance Apac, as well as Tororo, suggest that that pyrethroid resistance may be limiting the impact of LLINs, and negatively impacting malaria control in Uganda.

1.3 LLINs and insecticide resistance

LLINs have been shown to reduce malaria morbidity and mortality across a range of epidemiological settings [7, 8], and the scale-up of nets is estimated to have been responsible for 69% of *P. falciparum* cases averted in Africa between 2000 and 2015 [1]. The World Health Organisation (WHO) recommends universal coverage of populations at risk, defined as one net for every two people to achieve community benefits [9]. In Uganda, LLINs are the primary vector control intervention, and considerable effort has been made to achieve universal coverage. However, to date, LLINs have not had the desired impact on malaria burden in Uganda [4]. High levels of pyrethroid resistance in malaria vectors may be contributing to the limited impact of LLINs (Figure 3) [4, 10]. All LLINs are currently treated with pyrethroid insecticides due to their

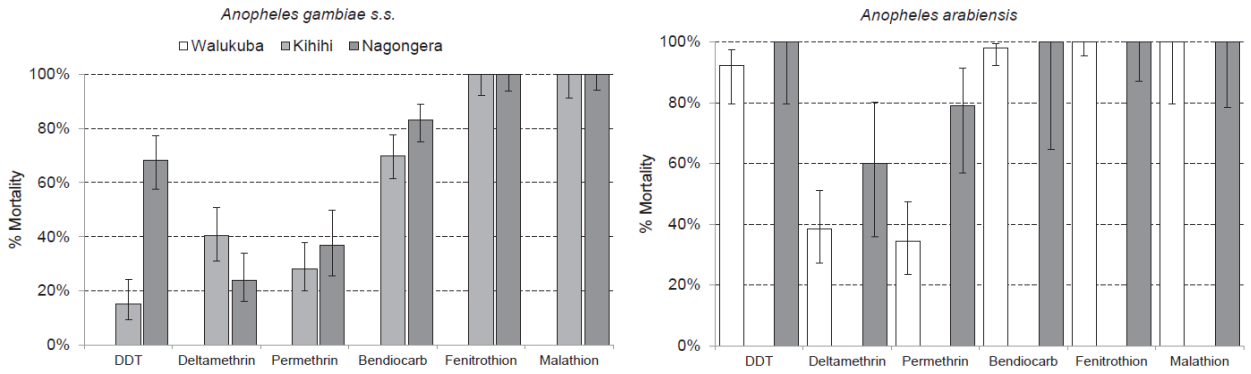

Figure 3. Insecticide resistance monitoring in Jinja (Walukuba sub-county), Kanungu (Kihihi) and Tororo (Nagongera). 24-hour mortality levels with 95% standard error bars for Anopheles gambiae s.s. (Kihihi and Nagongera only) and Anopheles arabiensis (Walukuba and Nagongera only) exposed for one hour to insecticide-treated papers impregnated with WHO diagnostic concentrations of insecticides. By WHO convention mortality of 98–100% indicates susceptibility; <98% is suggestive of resistance, and <90% is strongly suggestive of resistance.

favourable safety profile at low doses, repellent effects, and rapid killing. However, pyrethroid resistance, due to both target site mutations (kdr) and metabolic mechanisms, has been reported across Africa and could threaten malaria control [11]. As early as 2001, kdr mutations were observed in Ugandan *Anopheles gambiae* and *A. arabiensis*, and the problem has been growing [12, 13]. Recently pyrethroid resistance was also observed in the other major vector (*A. funestus)* in the west of the country [14]. Unpublished data suggests that pyrethroid resistance is widespread across Uganda and that the causal mechanisms include kdr, cytochrome P450s, carboxylestrases, and glutathione-s-transferases [15].

1.4 LLINs with PBO

The threat of pyrethroid resistance has generated interest in combining more than one insecticide mixture in LLINs. One approach is to combine a pyrethroid insecticide with a synergist, piperonyl butoxide (PBO), which is capable of inhibiting cytochrome P450s, and potentially overcoming pyrethroid resistance in anopheline vectors. Data showing that PBO synergist bioassays resulted in near complete recovery of

pyrethroid susceptibility is strongly supportive of the involvement of cytochrome P450s in mediating resistance [10], and suggests that one specific P450 *Cyp4j5* is reproducibly associated with pyrethroid resistance in Uganda and Kenya. Data from Tororo district in Uganda (Figure 4) suggest that two resistance associated mutations in COE and *Cyp4j5* occur at a frequency of approximately 50 to 60%. LLINs including PBO are anticipated to be more effective in areas where pyrethroid resistance is mediated by P450s. However, the impact of PBO LLINs is expected to vary according to the bioavailability and retention of PBO, and the level, intensity and mechanisms of insecticide resistance for local vectors, as well as across different transmission settings.

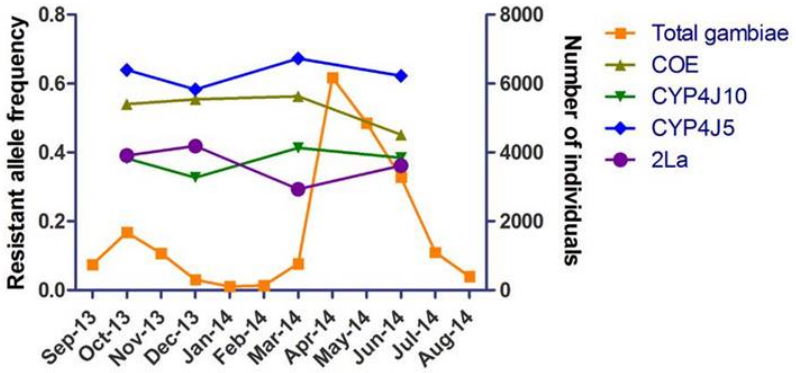

Figure 4. Mutations associated with insecticide resistance in Nagongera sub-county, Tororo district, Uganda. The two resistance associated mutations in COE and Cyp4j5 occur at a frequency of approximately 50% to 60%.

1.5 Characteristics and effectiveness of PBO LLINs

Two brands of PBO nets are currently recommended by the WHO [16, 17], including PermaNet® 3.0 (Vestergaard Frandsen SA, Denmark) and Olyset® Plus (Sumitomo Chemical). Although both nets incorporate PBO, the characteristics of the PBO nets, and of the conventional non-PBO nets produced by both companies (PermaNet® 2.0 and Olyset® Net), vary in terms of insecticide used, concentrations, net weight and construction (Table 1) [16, 17].

Table 1. Characteristics of combination (with PBO) and conventional (without PBO) LLINs

Net	Pyrethroid		PBO	Design and weight
	Insecticide	Concentration	Concentration	
PermaNet® 2.0	Deltamethrin	55 mg/m^2	—	Polyester net (75 or 100 denier)
PermaNet® 3.0	Deltamethrin	Top panel:~180mg/m^2 (4g/kg) Side panels:~118mg/m^2 (2.8g/kg)	25 g/kg (~1.1g/m^2)	Top panel: polyethylene (100 denier), deltamethrin + PBO; Side panels: multifilament polyester (75 denier) with a strengthened border, deltamethrin only
Olyset® Net	Permethrin	2% w/w, ~1000mg/m^2	—	Polyethylene net (150 denier)
Olyset® Plus	Permethrin	2% w/w, ~800mg/m^2	10g/kg (~400mg/m^2)	Whole net: polyethylene (150 denier); permethrin + PBO

A recent study conducted in four sites across Uganda evaluated three of these nets, including Olyset Net, PermaNet 2.0, and PermaNet 3.0 [18]. In this study, conventional LLINs (without PBO) failed to achieve desired killing of *A. gambiae* mosquitoes, with mortality rates as low as 45.8% [18]. The PermaNet 3.0 (with PBO) showed the highest bio-efficacy of all the nets, with mortality rates reaching 100%, suggesting that the introduction of LLINs containing PBO may have a greater impact than use of conventional LLINs in Uganda. There have been no published controlled trials on the efficacy of PBO LLINs versus conventional LLINs in areas with pyrethroid resistance. The WHO recommends 'exploratory' introduction of PBO LLINs accompanied by robust evaluation. Uganda, with its persistently high burden of malaria transmission and widespread pyrethroid resistance, is an optimal setting to undertake this evaluation.

2 Rationale

Evidence of the impact of combination LLINs (with PBO) is urgently needed. The Uganda National Malaria Control Program (NMCP) and implementing partners are planning to carry out a universal LLIN campaign in 2016-17, supported by generous contributions from international donors, including The Against Malaria Foundation, The Global Fund to Fight AIDS, Tuberculosis and Malaria, the US President's Malaria Initiative, The AIDS Support Organisation (TASO), and the UK's Department for International Development. LLINs will be distributed at no cost to all Ugandan households through a mass-distribution campaign. LLINs with, and without, PBO will be distributed, which presents an opportunity to rigorously evaluate and compare the performance of combination LLINs (with PBO) and conventional LLINs (without PBO) on a wide-scale in Uganda, across a variety of malaria transmission intensities, vector ecologies, and insecticide resistance patterns. Following WHO guidance for robust evaluation of PBO nets, we propose to carry out a cluster-randomised trial to compare the impact of LLINs with, and without, PBO in Uganda.

3 Study objectives

We propose to address the following research question: *Are combination LLINs (with PBO) more effective than conventional LLINs (without PBO) for malaria control in Uganda, particularly in areas with high-level insecticide resistance?*

The primary objective of the study is: *To evaluate the impact of combination LLINs (with PBO), as compared to conventional LLINs (without PBO), on parasite prevalence, in Eastern and Western Uganda.* We will test the hypothesis that parasite prevalence will be lower in intervention clusters (health sub-districts randomised to receive PBO nets), than in control clusters (health sub-districts randomised to conventional nets) overall, and plan a sub-group analysis stratified by region (Eastern and Western regions).

In addition, the following secondary objectives will be addressed:

1 *To evaluate the impact of PermaNet 3.0 (with PBO), as compared to PermaNet 2.0 (without PBO), on parasite prevalence.* We will test the hypothesis that parasite prevalence will be lower in intervention clusters (PermaNet 3.0 nets), than in control clusters (PermaNet 2.0 nets).

2 *To evaluate the impact of Olyset Plus (with PBO), as compared to Olyset Net (without PBO), on parasite prevalence.* We will test the hypothesis that parasite prevalence will be lower in intervention clusters (Olyset Plus nets), than in control health clusters (Olyset Nets).

3 *To determine the factors associated with effectiveness of combination LLINs (with PBO), as compared to conventional LLINs (without PBO), with a focus on the level of insecticide resistance.* We will test the hypothesis that LLINs with PBO will be more effective than LLINs without PBO in settings with higher-level insecticide resistance.

4 *To assess net durability, bio-efficacy, survivorship and use in Uganda.* We will conduct cross-sectional surveys to determine net survivorship and use, and to measure attrition, and will supplement these with laboratory assessments of net durability and bio-efficacy.

4 Study design & methods

4.1 Overview

We propose to conduct a rigorous, cluster-randomised trial to evaluate the impact of LLINs distributed in Uganda through a national universal coverage campaign in 2017-18. A cluster has been defined as a health sub-district (HSD). A total of 104 clusters have been included in the study, covering 48 districts in Eastern and Western Uganda. Clusters have been randomised to receive one of 4 types of LLINs: (1) PermaNet 2.0 [n=37], (2) PermaNet 3.0 [n=32], (3) Olyset Net [n=15], and (4) Olyset Plus [n=20]. Variation in the production capacity and the number of nets available for each manufacturer, was considered in the randomisation process, resulting in unequal numbers of clusters allocated to each of the 4 study arms. The intervention, including delivery of the LLINs and behaviour change communication (BCC), will be led by the Ugandan National Malaria Control Programme (NMCP) and other stakeholders. The evaluation will include repeated cross-sectional community surveys to gather information on net survivorship and use, and parasite prevalence in children 2-10 years of age, entomological surveillance for insecticide resistance monitoring, and assessment of net durability and efficacy at 12 and 24-30 months. The primary outcome of the trial will be parasite prevalence as measured by microscopy in the cross-sectional surveys. The study will be conducted over 2-3 years (24-36 months) targeting Jan 2017 to June 2020, depending on available funding. The field work in Uganda will be led by IDRC, with oversight from the Liverpool School of Tropical Medicine (LSTM), and support from the London School of Hygiene & Tropical Medicine (LSHTM), and the University of California, San Francisco (UCSF).

4.2 Study site

The NMCP and supporting partners will distribute LLINs to 104 HSDs in Eastern and Western Uganda (Figure 5). This area represents approximately half of Uganda, and covers a wide range of epidemiological settings with varying levels of malaria transmission and insecticide resistance.

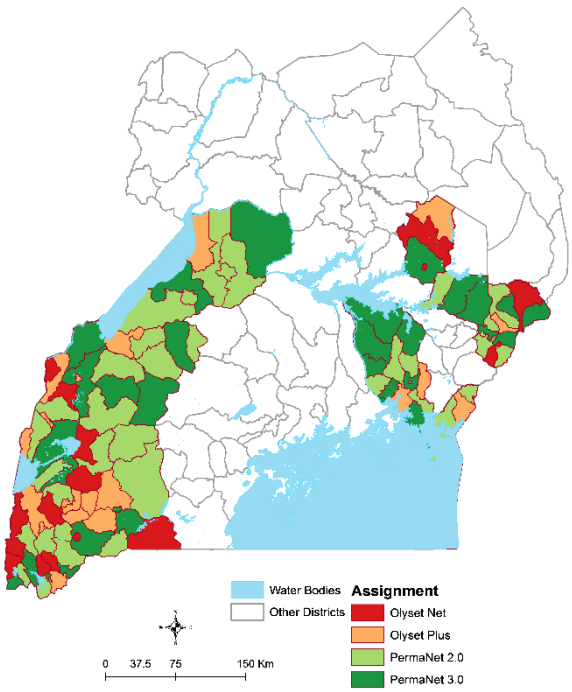

Figure 5. Randomised allocation of LLINs in selected health sub-districts in Uganda

4.3 Randomisation

4.3.1 Original randomisation

The randomisation was carried out by a member of the study team who is not based in Uganda, and who will not be directly involved in the field work. The unit of randomisation (cluster) was at the level of the HSD (N=104). HSDs scheduled to receive IRS with pirimiphos-methyl (Actellic) were excluded from the study. The total number of LLINs available for the 4 types of nets (corresponding to the 4 study arms) and the estimated number of LLINs needed for each HSD were established prior to the randomisation (Table 2).

Given the restriction on the number of nets to be distributed in each study arm, adaptive randomisation was applied using the following steps: (1) A random number was generated for each HSD using STATA (StataCorp, Texas, USA). (2) Cumulative probability ranges were generated for each of the 4 types of bednets based on the targeted number of each individual type of net / targeted number of total nets. (3) The first HSD was assigned to their intervention based on which cumulative probability range the

corresponding random number fell into. (4) Step 2 above was repeated after removing the number of targeted bednets assigned to the HSD for the corresponding type of net and the total number of nets. (5) The next HSD was assigned to their intervention based on which revised cumulative probability range the corresponding random number fell into. (6) This process was repeated until all HSDs were allocated to an intervention. The process was stratified by region, with 66 HSDs in the Western regions, and 38 HSDs in the Eastern regions, because of vectors and suspected differences in insecticide resistance patterns (Figure 5). The total number of HSDs originally allocated to the 4 study arms is shown in Table 2 below.

Table 2. Study interventions, target number of nets, and final number of clusters allocated

Type of bednet	Targeted total number of nets for distribution	Cumulative number of nets allocated	Number of health sub-districts allocated		
			Total	Western region	Eastern region
PermaNet 2.0	3,217,360	3,220,280	37	24	13
PermaNet 3.0 (contains PBO)	4,100,000	4,101,840	44	28	16
Olyset	650,000	651,240	9	5	4
Olyset Plus (contains PBO)	1,000,000	994,000	14	9	5
Total	**8,967,360**	**8,967,360**	**104**	**66**	**38**

4.3.2 Re-randomisation and final net allocation

Nets were scheduled to be distributed in the PBO study area in Waves 2, 3 and 4 of the Universal Coverage Campaign (UCC) led by the Ministry of Health (MOH). Distribution in the 44 HSDs in Waves 2 and 3 was completed as scheduled, with nets distributed in 24 PBO and 20 non-PBO clusters. However, the number of nets distributed in Waves 2 & 3 was greater than expected, resulting in a deficit of nets available for distribution in Wave 4. This gap was primarily due to projected shortages in PermaNet 3.0 (~ 1 million LLINs). The shortage of PermaNet 3.0 nets was addressed by increasing the number of the other three types of LLINs. After determining the total number of nets available, the 60 HSDs in Wave 4 were re-randomised, using the same process of adaptive randomisation described above, such that the number of clusters assigned to the two study arms (PBO vs non-PBO) balanced, with clusters assigned to the two study arms in a 1:1 ratio (52 clusters in each arm). The final treatment allocations are summarized in Table 2a, and the full intervention allocation list is provided in Appendix A.

Table 2a. Revised study interventions, target number of nets, and final number of clusters allocated

Type of bednet	Targeted total number of nets for distribution in Wave 4	Cumulative number of nets allocated in Wave 4	Number of health sub-districts allocated				
			Wave 4	Waves 2 & 3	Western region	Eastern region	Total
PermaNet 2.0	2,344,008	2,346,240	21	16	24	13	37
PermaNet 3.0 (contains PBO)	1,597,359	1,591,600	14	18	16	16	32
Olyset	1,004,621	971,000	11	4	11	4	15
Olyset Plus (contains PBO)	1,090,332	1,127,480	14	6	15	5	20
Total	**6,036,320**	**6,036,320**	**60**	**44**	**66**	**38**	**104**

4.4 Sensitisation

Prior to starting the study, we plan to build awareness, secure commitment, and encourage participation from stakeholders at the national and local levels. We will engage with members of the Ugandan Ministry of Health in Kampala, and other key stakeholders including representatives from the US President's Malaria Initiative (PMI), the World Health Organisation (WHO), and the UK's Department for International Development (DFID). We will also engage with key stakeholders and opinion leaders at the district and community level in participating districts, including the District Health Officers and Malaria Focal Persons, local council chairmen (LCIs), village health team (VHT) members, health care workers and religious leaders. Study personnel will use a standard information sheet (Appendix B) to help guide sensitisation discussions.

5 Intervention

The NMCP and other stakeholders will take the lead on delivering the LLINs to HSDs in Uganda. Here, the plans for the net distribution campaign are described to provide background information on the intervention. The research team will only be responsible for carrying out the evaluation.

5.1 Overview

The LLINs will be distributed according to detailed national guidelines, which build on prior experience from a similar net distribution campaign carried out in 2013-2014 [19]. The overall goal the 2016-2017 mass LLIN distribution campaign is to reduce malaria morbidity and mortality in Uganda by achieving universal coverage with LLINs, aiming to ensure that: (1) 85% of the targeted population has access to a LLIN, and (2) 85% of LLINs distributed are utilised. Members of the research team will engage with Uganda's national committees that are coordinating the LLIN universal coverage campaign, including the National Coordination Committee (NCC), which will be responsible for overall coordination and oversight of campaign planning and implementation and engagement with political and traditional authorities, the Operations Sub-committee (OSC), the Logistics Sub-committee (LSC) and the Advocacy, Communication and Social Mobilisation Sub-committee (ACSMSC). All LLINs procured for the campaign will be stored centrally in Kampala, and will be distributed across the country in waves. The 48 districts selected for this study are currently included in Waves 2-6, and are scheduled to receive nets in Feb-March 2017. The research team will work closely with the NCC and other partners to ensure that the nets are allocated per the randomisation scheme.

5.2 Household registration

A key aspect of the distribution will be to ensure that the community members receive the correct number of LLINs. To establish net need, household-level registration data will be collected prior to the LLIN distribution. The registration will be carried out by VHTs and community owned resource persons (CORPs) door-to-door at the village level [19]. The VHTs/CORPs will record the name of the household head, number of residents, and the telephone number of someone within the household (if available). Once completed, the VHTs/CORPs will present their registration lists to the local council chairman of the village (LC1), who will review and endorse the list. Once verified by the LC1, the lists will be taken to sub-county supervisor for a second round of verification, and will then be submitted to the district biostatistician for data entry. To ensure data quality, two rounds of data collection are planned. In the first round, 100% of households will be approached by data collectors. In the second round, a random selection of 5% of the households in each village will be re-registered by the parish chief (or representative) with no knowledge of the results from the first round, and the results will be compared to the first round. If discrepancies are identified, possible solutions will include: (1) re-registering inaccurately registered households, or (2) re-registering entire villages where multiple discrepancies exist. Once data have been cleared by the sub-county technical team, including 3 data managers per sub-county, data will be transported to the district data management team for final validation and entry. Data will be entered only once onto a read-only data screen, and will then be automatically transferred centrally to the MOH Resource Centre and the NMCP. The final electronic data will be encrypted and stored at the MOH Resource Centre.

5.3 LLIN distribution

The LLINs will be stored centrally in Kampala, and then transferred from the central location to sub-county stores, and then onward to the distribution points. LLINs will be distributed by sub-county teams, led by the sub-county campaign coordinator, working at the district level with the district technical teams and data managers. Using the household registration data, the district data team will apply an allocation formula

(total number of people in the household, divided by 2, and rounded up in the case of an uneven number of household members), and an electronic version of the registration forms will be produced [19]. Each district will produce a master allocation list by sub-county, parish, and village that will be reviewed by the Logistics Sub-committee, which will be responsible for ensuring that the LLINs are transported to the district, and the sub-county stores. Distribution of the LLINs will be overseen by LC1s, parish chiefs, and sub-county and district supervisors. In rural areas, LLINs will be distributed at the village level from fixed distribution points by the VHTs / CORPs supported by the LC1s. In more populated and urban areas, at least 5 people will be stationed at each distribution point, including one distribution site supervisor, 2-3 security personnel (crowd controllers), 2 LLIN distributors, and one health education. Community members will be mobilised and informed in advance of the distribution.

5.4 Communication

The NMCP and other stakeholders will take the lead on social behaviour change communication (SBCC)/information, education, communication (IEC). At each LLIN distribution point, a demonstration area will be set up to show how to correctly hang LLINs and to disseminate key messages about malaria, use of LLINs, and the importance of caring for the nets correctly [19]. SBCC and health education sessions will focus on correct care and maintenance of LLINs, including washing, repair of holes and tears, and avoidance of sun when washing and drying nets.

6 Cross-sectional surveys

6.1 Overview

We propose to conduct cross-sectional community surveys repeatedly, including at baseline (prior to distribution of the nets) and up to 4 times after nets are distributed (at 6, 12, 18 and 24-30 months after distribution) for up to 5 rounds of surveys. Households will be randomly selected from each of the 104 clusters and screened until 50 households with at least one child aged 2-10 years are enrolled (total 5,200 households). Random selection of households for screening and enrolment will be repeated with replacement for each cross-sectional survey. The cross-sectional community surveys will include two components: (1) a household survey targeting heads of households, and (2) a clinical survey of children aged 2-10 years. The clinical surveys will include a finger-prick blood sample for thick blood smear, measurement of haemoglobin (in children < 5 years), and filter paper blood sample. The primary outcome of the cross-sectional surveys will be parasite prevalence as measured by microscopy.

6.2 Definitions

- **Household:** A household will be defined as any single permanent or semi-permanent dwelling structure acting as the primary residence for a person or group of people that generally cook and eat together. Some households may include members who sleep in other dwelling structures within the same compound, if the members are still dependent on the head of household in the main household.
- **Head of household:** The head of household is an adult person or persons who primarily make decisions for the general household (e.g. decisions on healthcare, income, etc.), including emancipated minors.
- **Household resident:** A resident within each household will be defined as a person who intends to have a sleeping place primarily at that location for a period of the next 6 months. This may include people who sleep in a separate house within the same compound, if they are still dependent on the head of household for decisions on finances and health care.

6.3 Household survey

6.3.1 Selection of households

A sample of 50 households from each of the 104 clusters will be randomly selected using a two-stage cluster sampling procedure, which has been used previously for large surveys in Uganda [20, 21]. Specifically, the primary sampling unit will be the enumeration areas identified in the 2014 national census. Ten enumeration areas will be randomly selected in each of the HSDs using probability proportionate to size (PPS) sampling. Within each sampled enumeration area, households will be randomly sampled from either a list of households generated by the Uganda Bureau of Statistics, or a list of households enumerated by the study team, until 5 households are enrolled, for a total of 50 households sampled per cluster.

6.3.2 Screening

When a household is identified, study personnel will briefly describe the purpose of the study to the head of the household (or their designate) in the appropriate language, and screen for eligibility (Appendix C).

The inclusion criteria are:

1 At least one household resident between 2-10 years of age present (with an adult caregiver willing to provide informed consent for the clinical survey)
2 At least one adult aged 18 years or older present
3 Adult is a usual resident who slept in the sampled household on the night before the survey

4 Agreement of the adult resident to provide informed consent for the household survey

The exclusion criteria are:

1 Dwelling destroyed or not found
2 Household vacant
3 No adult resident home on more than 3 occasions

6.3.3 Informed consent

A detailed description of the informed consent procedures is provided in section 13.2. Briefly, study personnel will carry out the informed consent discussion with the head of the household (or their designate) in the appropriate language, and a translator will be used if necessary. The information sheets and consent forms will be available in English and the appropriate local languages. Following the consent discussion, the respondent will be asked by the study personnel to sign a written consent form to participate in a research study (Appendix D). If the respondent is unable to read or write, their fingerprint will substitute for a signature, and a signature from an impartial witness to the process will be obtained.

6.3.4 Household survey questionnaire

The household questionnaire (Appendix E) will be administered to the head of the household (or their designate), after obtaining their consent using a hand-held tablet computer. Information will be gathered on the characteristics of households and residents, proxy indicators of wealth including ownership of assets, and ownership and use of LLINs in the households, specifically focusing the nets distributed in the 2016-2017 universal LLIN campaign. The household survey questionnaire has been adapted from prior cross-sectional community surveys conducted in Uganda, including the national Malaria Indicator Survey [21-24]. Household locations will be mapped, using hand-held GPS receivers. Readings will be taken from the door of the household, if possible, or from a point that is most representative of the household. At each household, three readings will be taken and the most consistent will be recorded in degrees/minutes (longitude and latitude) and feet (elevation).

6.4 Clinical survey

6.4.1 Recruitment of participants

All children aged 2-10 years from enrolled households who are present will be eligible for participation in the clinical survey. Children will be identified from the household survey questionnaires.

6.4.2 Screening of participants

At the end of the household questionnaire, study personnel will discuss the clinical survey with the head of the household (or their designate). Study personnel will briefly describe the purpose of the clinical survey in the appropriate language and will screen for eligibility criteria (Appendix F).

The inclusion criteria are:

1 Child aged 2-10 years
2 Usual resident who was present in the sampled household on the night before the survey
3 Agreement of parent/guardian to provide informed consent
4 Agreement of child aged 8 years or older to provide assent

The exclusion criterion is:

1 Child not home on day of survey

6.4.3 Informed consent

A detailed description of the informed consent procedures is provided in section 13.2. Briefly, study personnel will carry out the informed consent discussion with the parent(s) or guardian(s) of children.

Informed consent will be conducted in the appropriate language and a translator will be used if necessary. Consent forms will be available in English and the local languages. Following the informed consent discussion, parents/guardians will be asked by the study personnel to sign a written consent form for their child(ren) to participate in a research study (Appendix G) and a second approved consent form for the future use of biological specimens obtained during the study (Appendix H). Written assent to participate in the study will also be obtained from children aged 8 years and older at the time of screening (Appendix I). If an adult respondent or parent/guardian is unable to read or write, their fingerprint will substitute for a signature, and a signature from a witness to the informed consent procedures will be obtained.

6.4.4 Clinical survey procedures

The clinical surveys will include measurement of temperature, subjective fever and a finger-prick blood sample for measurement of thick blood smear and haemoglobin (in children < 5 years), and filter paper blood sample (Appendix J).

6.4.5 Management of ill participants

Participants who have a temperature of $\geq$ 38.0^{o}C, or who report fever in the past 48 hours, will have an RDT performed. Febrile participants will be treated with paracetamol as appropriate. Participants with a positive RDT and no evidence of severe malaria will be treated with artemether-lumefantrine (AL), which is the first-line recommended treatment for uncomplicated malaria in Uganda. Participants with a positive RDT and evidence of danger signs of severe disease will be referred for further evaluation and treatment. Any participant with other concerning clinical symptoms will also be referred to an appropriate health care facility at the discretion of the study personnel.

6.4.6 Number and timing of surveys

We anticipate carrying out at least 2 rounds of surveys (the 6- and 12-month post-distribution surveys at a minimum) and up to 5 rounds of surveys (including the baseline and 18/24-month post-distribution surveys). The final decision about the total of number of cross-sectional surveys, and the timing of the surveys, will depend on timelines of the national net distribution campaign, and available resources.

7 Entomology surveys for insecticide resistance monitoring

7.1 Overview

Entomology surveys will be carried out to collect mosquito specimens for the insecticide resistance monitoring. Collections for genotypic monitoring will be carried out concurrently with the cross-sectional community surveys. Mosquitoes will be collected from a sub-set of households enrolled in the cross-sectional community survey. For the genotypic monitoring, mosquitoes will be collected from up to 10 randomly selected households in each of the 104 clusters using prokopack aspirators, aiming to collect 30-50 mosquitoes per cluster. For the phenotypic monitoring, mosquitoes will be collected from approximately 10-15 purposely selected households from 12 sentinel site clusters shortly after the cross-sectional survey. Female anopheles mosquitoes will be identified, and will be stored with silica gel in the field sites, prior to shipment to Kampala and onto LSTM for further analysis.

7.2 Genotypic monitoring

7.2.1 Recruitment and screening

In each cluster, up to ten households will be selected randomly for the entomology survey from the list of 50 households enrolled into the cross-sectional surveys. Study personnel will re-visit households on the list of randomly selected households to carry out the recruitment for the entomology survey. When a household on the selection list is identified, study personnel will briefly describe the purpose of the study in the appropriate language with the head of household (or their designate), and proceed with screening (Appendix K).

The inclusion criteria are:

1 At least one adult aged 18 years or older present
2 Adult is a usual resident who slept in the sampled household on the night before the survey
3 Agreement of the adult resident to provide informed consent for the entomology survey

The exclusion criteria are:

1 Dwelling destroyed or not found
2 Household vacant
3 No adult resident home on more than 3 occasions

7.2.2 Informed consent

A detailed description of the informed consent procedures is provided in section 13.2. Briefly, study personnel will conduct the informed consent discussion with the head of household (or their designate). Informed consent will be conducted in the appropriate language and a translator will be used if necessary. Consent forms will be available in English and the local languages (Appendix L). Following the informed consent discussion, the head of household (or their designate) will be asked to sign a written consent form for their household to participate in the entomological survey. If the head of household (or their designate) is unable to read or write, their fingerprint will substitute for a signature, and a signature from a witness to the informed consent procedure~~s~~ will be obtained.

7.2.3 Entomology survey

Mosquitoes will be sampled using prokopack aspirators. Study personnel will enter selected households after obtaining consent and will use the aspirators to collect mosquitos resting indoors on walls. A brief questionnaire will also be administered to gather information on household characteristics and use of malaria prevention measures (Appendix M).

7.2.4 Processing of mosquito specimens

Female anopheles mosquitoes will be identified, and will be stored and refrigerated in the regional field sites, prior to shipment to Kampala and onto Liverpool for further analysis.

7.3 Phenotypic monitoring

7.3.1 Sentinel sites

Resistance phenotyping will be conducted on mosquito samples collected from a sub-set of households located in up to 12 sentinel site clusters (Table 3), which were purposely selected based on the likelihood of collecting large numbers of mosquitoes, supported by baseline entomology data, and by proximity to the regional entomology labs where the assays will be performed. Six clusters were proposed ~~selected~~ from each region (East and West), aiming to balance the net allocation assignments in each region (Table 3). The final selection of clusters to serve as sentinel sites will be made based on the number of mosquitoes collected in the follow-up entomology surveys and may include clusters not on the originally proposed list (Table 3).

Table 3. Proposed sentinel sites for phenotypic monitoring of insecticide resistance

Cluster	Health Sub-District	District	Net allocation	Region
2	Bughendera	Bundibugyo	Olyset Plus	West
3	Bwamba	Bundibugyo	Olyset Net	West
9	Kibanda	Kiryandongo	PermaNet 3.0	West
22	Bujenje	Masindi	PermaNet 2.0	West
51	Bugangaizi East	Kibaale	PermaNet 2.0	West
52	Bugangaizi West	Kibaale	PermaNet 3.0	West
67	Amuria	Amuria	Olyset Net	East
68	Kapelebyong	Amuria	Olyset Plus	East
74	Kagoma	Jinja	PermaNet 2.0	East
76	Buzaaya	Kamuli	PermaNet 3.0	East
84	Luuka	Luuka	PermaNet 2.0	East
92	Bunya South	Mayuge	PermaNet 3.0	East

7.3.2 Survey procedures

In each cluster, approximately 10-15 households will be selected purposely for mosquito collections, or approximately 120-180 households in total, per survey. The same procedures described above will be followed for recruitment, screening, consenting, surveying, and mosquito collection, with one exception; households may be visited more than once for mosquito collections, as described in the consent form (Appendix N).

8 LLIN survivorship, durability and bio-efficacy

8.1 Overview

To assess survivorship of LLINs, information will be captured in each round of the cross-sectional surveys on household ownership and use of LLINs, specifically focusing the nets distributed in the 2016-2017 universal LLIN campaign, as described above. Durability and efficacy of the LLINs will be assessed one year after distribution of nets, concurrently with the 12-month, and 24-30 month, cross-sectional surveys. We will quantify net durability using the WHO Vector Control Working Group methodology, and will use HPLC to analyse the nets for chemical composition at the 12-month, and 24-30 month timepoints. Standard WHO cone bioassays on nets collected from the community will be carried out at the 12-month timepoint.

8.2 Definitions

- **Survivorship:** the proportion of LLINs distributed that are still available for use as intended in the households to which they were given after a defined period.
- **Attrition:** (opposite of survivorship): the proportion of nets no longer in use as intended after a defined period after their distribution to households. Attrition can be categorized by the main reasons why a net is no longer used, namely decay (e.g. destroyed, so torn and worn out that it is considered useless for protection against mosquitoes), absence (e.g. stolen, given away, moved) or used for other purposes.
- **Durability:** reflects the number, location, size, and type of holes in each net.
- **Bio-efficacy:** the degree of knock-down, mortality or inhibition of blood-feeding induced in susceptible mosquitoes, as determined by standard WHO test procedures and criteria (i.e. cone bioassay).
- Chemical composition: the amount of permethrin, deltamethrin and PBO insecticide contained in the LLIN as measured by High Performance Liquid Chromatography (HPLC) analysis

8.3 Durability

To assess durability, a sub-set of nets distributed during the 2017-2018 universal LLIN campaign will be withdrawn (and replaced) from households during the 12-month, and 24-30 month, cross-sectional surveys. We propose to sample 400 nets (100 per study arm) from randomly selected households in the 104 clusters for the durability assessment, using the list of households selected using the two-stage cluster sampling for the cross-sectional community surveys. During the cross-sectional survey, availability of nets distributed during the universal LLIN campaign will be assessed in selected households. If nets are available in the household, one net per household will be withdrawn (and replaced) for the durability assessment. We will quantify durability of the net using the methodology developed by the WHO Vector Control Working Group [25]. LLINs will be fitted over a frame, and subjected to a detailed visual examination. Net integrity will be assessed by measuring the number and size (length) of observed holes, including tears in the netting and spilt seams.

Holes will be classified into standardized categories:

- smaller than a thumb (0.5–2 cm)
- larger than a thumb but smaller than a fist (2–10 cm)
- larger than a fist but smaller than a head (10–25 cm)
- larger than a head (> 25 cm)

The integrity of nets shall be quantified based on the proportion of LLINs with any hole, and the proportionate holes index (pHI) for each net [25]. Using the pHI, the condition of the nets will be categorised as: (1) good, (2) serviceable (repairable), or (3) in need of replacement.

8.4 Bio-efficacy

To assess bio-efficacy, a sub-set of nets distributed during the universal LLIN campaign will be withdrawn (and replaced) from households during the 12-month cross-sectional survey. We propose to sample 400 nets (100 per study arm) from randomly selected households in the 104 clusters for the bio-efficacy assessment, using the list of households selected using the two-stage cluster sampling for the cross-sectional community surveys. During the cross-sectional survey, availability of nets distributed during the 2016-2017 universal LLIN campaign will be assessed in selected households. If nets are available in the household, one net per household will be withdrawn (and replaced) for the bio-efficacy assessment. These nets will be taken to our central insectary facility in Nagongera, Tororo where we will conduct standard WHO cone bioassays on each net [26]. We will used a standard lab strain of *A.gambiae* from Kisumu, western Kenya which is fully susceptible to both permethrin and deltamethrin in WHO discriminant dose tests. In brief, 5 unfed 3 to 5 day old will be exposed for 3 minutes to a net sample taken from the top of each net. The rationale being that this is the first point of contact for a mosquito taking a blood meal and ensures that we sample the dual treated surface on both types of PBO net [27, 28]. Knockdown will be recorded 60 minutes post-exposure and mortality after. Two cone tests will be conducted per net together with appropriate negative controls. For a subset of 20 nets of each type we will use the same protocol but with a Ugandan pyrethroid resistant strain which exhibits P450 mediated resistance to test for the durability of PBO treatment on the dual-treatment nets.

8.5 Chemical composition

To assess the chemical composition of the LLINs a sub-set of the nets withdrawn (and replaced) during the 12-month, and 24-30 month, surveys will be assayed using HPLC. Samples of nets will be taken from the top surface of the LLIN, the rationale being that this is the first point of contact for a mosquito taking a blood meal and ensures that we sample the dual treated surface on both types of PBO net [27, 28], and stored individually in foil prior to shipment to Liverpool for further analysis using standard LSTM methods for LLIN chemical assessment. Results will be compared to that of control nets (unused nets from same distribution batch) to assess loss of insecticide with time.

9 Laboratory procedures

9.1 Microscopy

Thick blood smears will be prepared in the field for microscopy using blood samples obtained from a finger-prick. New glass slides, frosted at one end, will be used to make the thick blood smears. Before making the smears, a barcode label will be placed on the under-side of the glass slides at the frosted end linked to the appropriate cross-sectional community survey. Thick blood smears will be made by placing a drop of blood in middle of the slide. An applicator stick will be used to spread the blood into a spot of approximately 1 cm in diameter. The blood smear will be dried on a slide tray, in an ideally dust-free environment. Slides will be kept at the field site protected from excessive heat and light for no longer than 1 week to avoid auto-fixation. The slides will be kept in a slide box and stored in the coolest place possible. The blood slides for malaria will be periodically transported to the IDRC Molecular Research Laboratory (MOLAB) in Kampala for reading. At the MOLAB, thick blood smears will be stained with 2% Giemsa for 30 minutes, and will be evaluated for the presence of parasitaemia (asexual forms only). Parasite densities will be calculated from thick blood smears by counting the number of asexual parasites, respectively, per 200 leukocytes (or per 500, if the count is less than 10 parasites per 200 leukocytes), assuming a leukocyte count of 8,000/μl. A thick blood smear will be considered negative when the examination of 100 high power fields does not reveal asexual parasites. For quality control, all slides will be read by a second microscopist and a third reviewer will settle any discrepant readings.

9.2 Haemoglobin measurement

Haemoglobin analysis will be carried out on site using a drop of blood collected from a finger-prick. The test will be conducted using a battery-operated portable HemoCue analyzer (HemoCue, Anglom, Sweden) which provides a result within one minute. The haemoglobin results will be provided to the caregiver of the participant verbally, and will be recorded on the appropriate case record form. Any participant who is found to have severe anaemia (Table 4) requiring treatment will be referred to an appropriate health care facility for further management.

9.3 Filter paper samples

9.3.1 Collection

Blood spots will be collected onto filter paper to store for future laboratory studies, which may include serologic response to malaria, Loop-Mediated Isothermal DNA Amplification (LAMP) for detection of *P. falciparum* parasites, testing for the presence and speciation of malaria parasites based on nested PCR of cytochrome b [29], analyses of polymorphisms in parasite and/or human genes for mutations that may impact on clinical malaria or other diseases, detection of HRP-2 deletions, and genotyping of malaria parasites. Filter paper (Whatman no 1, Whatman 3MM; Whatman, Maidstone, UK) will be pre-cut into individual squares and stapled to a thick card which will serve as its cover. Blood spots will be collected onto the filter paper in volumes of approximately 25 μl aliquots per blood spot (4 blood spots per sample). Filter paper samples labelled with the sample's bar codes on the covering cardboard, and will be allowed to dry at ambient temperature and relative humidity before closing the card over the filter paper (like closing a matchbook).

9.3.2 Storage

Filter paper samples will be transported from the field in a zip lock bag and will be placed into a stock card filter paper box for final storage with a dessicant. Filter paper samples will be stored initially in Kampala, at IDRC's Molecular Laboratory (MOLAB), in -20^{o}C freezers. Filter paper samples may be stored for up to 10

years, and ultimately will be destroyed using incineration. Future laboratory studies would be performed only for research purposes and will have no impact on the clinical management of study participants.

9.4 Rapid diagnostic tests

RDTs will be performed in the field on cross-sectional survey participants who are found to have a temperature of $\geq 38.0^{o}C$, or who report fever in the past 48 hours. RDTs will be performed according to the directions provided for the specific tests, using the blood transfer device and reagent provided by the manufacturer. Tests will be performed by study personnel, and results will be available within 15 minutes. The results of the RDT will be provided to the participant's caregiver verbally, and will be recorded on the appropriate case record form. Participants who test positive for malaria will be provided a full course of antimalarial treatment, and will also be counselled to go to the nearest health facility immediately if their condition worsens.

9.5 Insecticide resistance monitoring

Insecticide resistance monitoring will be led by LSTM. We will use a combination of standard WHO resistance phenotyping at 12 sentinel HSD sites, 6 per study area, together with genotyping using Ugandan specific molecular diagnostics.

9.5.1 Phenotyping

Resistance phenotyping will be conducted on mosquito samples collected during the entomology surveys carried out concurrently with the cross-sectional community surveys, using permethrin, deltamethrin, permethrin + PBO and deltamethrin + PBO. In line with newly developed WHO guidelines, we will combine standard WHO tube tests with intensity assays where indicated. Test mosquitoes will be 3-5 day old females raised from larval collections or, where necessary, mixed physiological age group females. All three primary vectors *Anopheles gambiae, An. arabiensis* and *An. funestsus* will be assessed. This resistance phenotyping will give us a broad overview of resistance patterns and likely causal mechanisms.

9.5.2 Genotyping

Our work in the Lake Victoria Basin has demonstrated how heterogeneous resistance can be on a fine spatial scale [30]. Therefore variations in insecticide resistance between clusters could be a major confounder of our primary endpoint. It is therefore important for us to obtain an HSD specific estimate of resistance. Our experience on the Implications of Insecticide Resistance project has shown us that phenotypic assays cannot be pushed reliably to such a scale and that standard phenotyping-based approaches are insufficiently sensitive to be used to monitor changes in resistance at fine spatial and temporal scales [31, 32]. We therefore propose to use a combination of Ugandan specific resistance markers which together explain about 50% of the variance in pyrethroid resistance to complement the focal resistance phenotyping. Female anopheles mosquitoes collected from the 104 clusters during the entomology surveys will be identified, and will be stored and refrigerated in the field sites, prior to shipment to Kampala and onto Liverpool for further analysis. Mosquitoes will be identified to species using standard PCR-based assays [33]. *A. gambiae* and *A. arabiensis* will be screened for key insecticide target sites (e.g. Vgsc) together with variants in metabolic resistance genes (e.g. Gste4, Cyp4j5, and Coeae1d) [32]. Mosquito DNA samples will be destroyed by autoclaving followed by incineration in accordance with LSTM standard safety procedures.

9.6 Chemical analysis of LLINs

HPLC will be conducted on samples of nets taken from the top surface of the LLINs withdrawn at 12-month and 24-30-month timepoints. The insecticides permethrin and deltamethrin, and the synergist PBO, will be extracted from the net samples using standard solvent extraction protocols employed at LSTM. The

chemicals extracted from the net will then be filtered to remove impurities before quantitative analysis performed via HPLC using controls of known insecticide concentration. This will allow the total concentration of insecticide and or synergist remaining on each net to be measured. Comparison to results of HPLC analysis on unused nets from the same distribution batch will allow the chemical degradation of the nets at 12 month, and 24-30 months to be determined.

10 Data management

10.1 Cross-sectional community surveys and entomology surveys

All data will be collected by survey teams using hand-held tablet computers. Prior to conducting the surveys information from the questionnaires and fields for entering results of biomarker testing will be programmed into the tablet computers. Programming will include range checks, structure checks and internal consistency checks. Before leaving the household, an inventory will be made of the completed questionnaires and blood samples collected; both will be checked to make sure they are labelled correctly. The completed questionnaires will be checked for mistakes and completeness. Data from these devices will be transferred at the end of every day to our data core facilities in Kampala and stored on a secure server. The data file will be kept on a separate network so that only authorized survey staff will have access to the data during collection and processing phase. The file with data from the questionnaires will be merged with results from reading the malaria slides at the laboratory, using the unique bar codes. All filter paper samples and blood slides will be returned to the IDRC offices in Kampala.

10.2 Laboratory data

Laboratory data, including results of microscopy, will be recorded by study personnel on standardized data forms. Data entered onto paper record forms will be entered into a computerised database (Microsoft Access) by a data entry clerk and will be double-entered to verify accuracy. An audit trail of the date and time of data entry, and a record of any changes made, will be kept in compliance with Good Clinical Practice (GCP).

10.3 Quality assurance & quality control

All members of the study personnel will be trained in the project objectives, methods of effective communication with study participants, collection of high quality data and principles of ethical research practice. Study personnel members will receive additional training specific to the tasks they will perform within the project including interviewing techniques, administration of surveys, completing questionnaires, and use of tablet devices. Standard Operating Procedures (SOPs) will be written for all project activities and booklets of all relevant documents provided to each member of the project team. Frequent study group meetings will be conducted by the investigators and study coordinators to assess progress of the study, address any difficulties, and provide performance feedback to the members of the study group.

10.4 Records & storage

Records for this study will be maintained and stored in compliance with the principles of GCP and regulatory and institutional requirements, and in compliance of the requirements for the protection of confidentiality of participants. Only study personnel members will have access to these records. All forms with participant names will be kept in a locked cabinet, when not in use. Participants will be identified by their study ID number, and participant names will not be included in databases used for analysis. Authorised representatives of the sponsor, the ethics committee(s) or regulatory bodies may inspect all documents and records required to be maintained by the investigators. The investigators will allow all requested monitoring visits, audits or reviews. Data will be stored for at least 10 years. Anonymized data collected in this study may also be shared with other investigators and/or placed into the public domain via a data repository.

11 Statistical issues

11.1 Outcome measures

The primary and secondary outcomes outlined in Table 4, and the criteria for diagnosing anaemia are outlined in Table 5.

Table 4. Outcome measure definitions

Community survey	***Indicator definition***
Prevalence of parasitaemia	Proportion of thick blood smears that are positive for asexual parasites
Prevalence of anaemia	Proportion of haemoglobin measurements categorised as anaemia as per WHO age-stratified guidelines (Table 5)
LLIN coverage	Proportion of households owning at least one net
	Proportion of households owning at least one LLIN
	Average number of nets per household
	Average number of LLINs per household
	Proportion of households with one LLIN for every 2 residents
	Proportion of children who slept under an LLIN the prior night
	Proportion of pregnant women who slept under an LLIN the prior night
Insecticide resistance	***Indicator definition***
Phenotyping	Prevalence of phenotypic insecticide resistance.
Genotyping	Prevalence of molecular markers associated with insecticide resistance
LLINs	***Indicator definition***
Survivorship	Proportion of households owning at least one 2016-17 campaign net
	Proportion of households using at least one 2016-17 campaign net the prior night
Durability	Proportionate Hole Index (PHI)
	(1) good, (2) serviceable (repairable), or (3) in need of replacement
Bio-efficacy	Knock-down rate at 60 minutes of mosquitoes tested
	Mortality rate of mosquitoes tested
Chemical composition	Proportion of insecticide and synergist remaining

Table 5. Haemoglobin levels to diagnose anaemia (g/dL)[34]

Population	**No anaemia**	**Anaemia**		
		Mild	**Moderate**	**Severe**
Children 6-59 months	$\geq$ 11.0	10.0 – 10.9	7.0 – 9.9	< 7.0
Children 5-11 years	$\geq$ 11.5	11.0 – 11.4	8.0 – 10.9	< 8.0

11.2 Sample size calculations

11.2.1 Cross-sectional community surveys

The study sample size (number of clusters, and allocation of interventions) was set by the number of different types of LLINs available and the estimated number of LLINs need per cluster. We will sample all eligible children aged 2-10 years from 50 households in the 104 clusters in each round of surveys, aiming to maximising the potential prevalence ratio detectable in the intervention arm, as well as the cost/value of the trial. Assuming an average of 2 children aged 2-10 years per households, we estimate that we will survey 10,400 children from 5,200 households, which would allow us to detect a maximum parasite prevalence of 33% in the intervention arm, assuming parasite prevalence in the control arm of 40% [22], a power of 80%, a two-sided significance level of 0.05, and coefficient of variation between clusters of 0.3

(derived from the ongoing trial in Tanzania, https://clinicaltrials.gov/ct2/show/NCT02288637?term=rowland+tanzania&rank=2), which would correspond to a prevalence ratio (parasite prevalence in the intervention [PBO net] arm / parasite prevalence in the control arm [conventional net]) of 83%.

11.2.2 Entomology surveys for insecticide resistance monitoring.

Mosquitoes will be collected from up to 10 randomly selected households in each of the 104 clusters, aiming to collect 30-50 mosquitoes per cluster. Data from Nagongera district in Uganda, which were included in the Phase 1 of the Anopheles gambiae 1000 genomes project, together with earlier studies from East Africa, show no evidence for population structuring at or below the village level, and indeed only minimal levels of differentiation on a continental scale. Therefore, a sample from 5-10 houses should provide an unbiased estimate of village level genomic diversity. Locus specific selection could result if interventions were unevenly distributed throughout the study area, (eg resistance mutations may be at higher frequency in houses with LLINs vs houses without) however universal coverage should result in relatively even selection pressure across the cluster. The sample sizes were chosen based upon the expected frequency of the known resistance associated variants in eastern Uganda (Figure 4). The two resistance associated mutations in COE an Cyp4j5 occur at a frequency of approximately 50 to 60%; therefore, a relatively small sample size is required for an accurate estimate of resistance marker frequency. However, we are aware that resistance is a highly dynamic system and that we may need to increase the number of mosquitoes analysed in certain clusters if resistance marker frequencies change dramatically. All anopheles that are collected will be stored so we will have more than 50 mosquitoes per collection time-point resistance surfaces.

11.3 Analytical plan

All data will be analysed on the basis of intention-to-treat and per-protocol analyses. Intention-to-treat analyses will include the assigned treatment arms and results from all clusters. Per-protocol analyses will only include results from geographic areas within each cluster that received the type of LLINs from their assigned treatment arm. The primary outcome will be the prevalence of asexual parasitaemia from the cross-sectional surveys. An individual-level approach to the analysis will be used due to the large number of clusters per arm. For comparison of the primary outcome between treatment arms, generalized linear Poisson models with log link function will be used to allow for within-cluster correlations. The effect of the intervention will be quantified by calculation of a prevalence ratio. Separate analyses will be performed using data from the post-distribution cross-sectional surveys (performed at 6, 12, 18 and 24-30 months after the delivery of the nets). Stratified subgroup analyses will be performed at the level of the region (Western or Eastern) and net manufacturer (PermaNet or Olyset). Adjusted analyses will be performed if imbalances exist in the prevalence of asexual parasitaemia at baseline, or in the level of insecticide resistance. Spatial autocorrelation in insecticide resistance will also be explored to interpolate resistance patterns collected at the household level.

12 Ethical considerations

12.1 Institutional review boards

This protocol and the informed consent documents and any subsequent amendments or modifications will be reviewed and approved by all institutional review boards (IRBs) before the study begins, including: (1) Makerere University School of Medicine Sciences Research and Ethical Committee; (2) Uganda National Council of Science and Technology; (3) Liverpool School of Tropical Medicine; (4) London School of Hygiene & Tropical Medicine Ethics Committee; and (5) UCSF Committee for Human Research.

12.2 Informed consent process

Approval from local leaders will be sought before beginning activities in the project area. All informed consent discussion will be conducted in the appropriate language and a translator will be used if necessary. Information sheets and consent forms will be available in English and appropriate local languages, describing the purpose of the project and the procedures to be followed, and the risks and benefits of participation. During the consent discussions, each section of the consent form will be read exactly as it is written either by study personnel or by the translator, and then further explained to the respondent (participant or parent/guardian) if necessary. The translator will also assist with the discussion and assessment of comprehension. All participants and parents/guardians will be informed that participation in the study is completely voluntary and that they may withdraw from the study at any time.

Written consent to participate in the research study will be documented on the appropriate form for participation in the community surveys and entomology surveys. In all cases involving participation of children aged 8 years or older, written assent will also be obtained from the child. Written consent for future use of biological specimens will also be obtained for the community surveys. If the person asked to provide consent is unable to read or write, their fingerprint will substitute for a signature, and a signature from a witness to the informed consent procedures will be obtained.

12.3 Risks and discomforts

12.3.1 Randomisation

In this cluster-randomised trial, clusters will be randomly assigned to receive 4 different types of LLINs. The combination LLINs (with PBO) may prove to be more, or less efficacious, and/or more, or less well-tolerated than conventional nets (without PBO). Thus, there is the risk that clusters will be randomised to receive a less efficacious and/or less well-tolerated LLIN. However, the risks associated with randomisation in this study are likely to be low.

12.3.2 Blood draws

The potential risks of drawing blood from a finger-prick include temporary discomfort, pain, transient bleeding, bruising, skin infection, and fainting. The volumes of blood taken will be too small to produce any adverse effects from the blood drawing, and overall the risks associated with blood draws are likely to be low. To reduce the potential risks, study staff will be trained in the proper conduct of a finger-prick according to standard operating procedures to minimize the risk of discomfort and infection.

12.3.3 Positive malaria tests

Results of blood slides collected in the community surveys will not be returned to participants. RDTs will be performed on participants with temperature of $\geq 38.0^{o}$C, or who report fever in the past 48 hours in the community surveys. RDT results will be provided to participants and treatment will be offered if RDT results are positive. Participants with positive tests will be told to seek care at the health facility if their illness worsens. It is possible that for some cases in the community surveys, the RDT will be negative, but

microscopy will be positive. This most commonly occurs when parasitaemia is very low, below the level of detection for RDTs. The risk of developing symptomatic or severe illness is very low from a presumably low parasitaemia in an RDT-negative asymptomatic individual. Of note, RDTs are used nationally at the point of care in health facilities, with treatment based on the result of the RDT, without confirming the RDT result by microscopy.

12.3.4 Entomology surveys

Potential risks and discomforts to participating households include loss of privacy, but this will likely be minimal. Care will be taken to protect the privacy of participating households, as described in this protocol. However, there is a risk that others may inadvertently see participants' information, and thus their privacy compromised. Intrusion by the study staff into the household, and discomforts related to the study procedures, are other concerns. Study personnel will be instructed to interact with the households in a courteous and respectful manner in order to limit this possible discomfort. All field workers will obtain training in confidentiality and gender sensitivity before working in the households.

12.3.5 Confidentiality

Participation in a research study may involve a loss of privacy, but successful implementation of the study will require that the confidentiality of all study participants be strictly maintained. The risks associated with loss of privacy in this study are likely to be low. To ensure confidentiality is maintained, all information gathered will be treated as private by the study personnel, and records will be kept securely in locked filing cabinets and offices. For all data collected as part of the study, participants will be assigned a unique identification number. No personal identification information such as names will be used in any reports arising out of this research. All project staff will be trained on procedures for maintaining confidentiality.

12.4 Compensation

Participants will not be paid for taking part in this study. If study participants are referred by study personnel to a health facility for further assessment, transportation may be facilitated by the project on a case to case basis. Participants diagnosed with uncomplicated malaria during our study by RDT will be treated as per the national treatment guidelines; participants in the community surveys with uncomplicated malaria will be treated with AL, and participants with severe malaria and other illnesses will be referred to the appropriate health facility for further management.

13 Proposed timeline

PBO study activites & timelines	Year 1 (2017)				Year 2 (2018)				Year 3 (2019)				Year 4 (2020)	
	Jan-Mar17	Apr-Jun17	July-Sept17	Oct-Dec17	Jan-Mar18	Apr-Jun18	July-Sept18	Oct-Dec18	Jan-Mar19	Apr-Jun19	July-Sept19	Oct-Dec19	Jan-Mar20	Apr-Jun20
Baseline surveys														
–Community & entomology surveys														
Intervention														
–LLIN distribution	Wave 2	Wave 3	Wave 4a		Wave 4b									
Follow-up surveys														
–Community & entomology surveys (6-month)														
–Community & entomology surveys (12-month)														
–Community & entomology surveys (18-month)														
–Community & entomology surveys (24+ month)														
Net assessments														
–Durability & bioefficacy														
Analysis & dissemination														
–Analysis of trial data & preparation of manuscripts														
–Dissemination to local & national stakeholders														

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Appendix A: Intervention allocation list

Wave	Cluster	Region	District	Health sub-district	Net allocation
2	67	Eastern	Amuria District	Amuria	Olyset Net
2	68	Eastern	Amuria District	Kapelebyong	Olyset Plus
2	70	Eastern	Soroti District	Soroti	PermaNet 3.0
2	71	Eastern	Soroti District	Soroti Municipality	Olyset Net
2	85	Eastern	Kumi District	Kumi	PermaNet 3.0
2	86	Eastern	Ngora District	Ngora	PermaNet 2.0
2	87	Eastern	Sironko District	Budadiri East	Olyset Plus
2	88	Eastern	Sironko District	Budadri West	PermaNet 2.0
2	95	Eastern	Bulambuli District	Bulambuli	PermaNet 2.0
2	100	Eastern	Bukedea District	Bukedea	PermaNet 3.0
2	101	Eastern	Manafwa District	Bubulo East	PermaNet 2.0
2	102	Eastern	Manafwa District	Bubulo West	Olyset Net
2	103	Eastern	Bududa District	Manjia	PermaNet 3.0
3	4	Western	Buliisa District	Buliisa	Olyset Plus
3	9	Western	Kiryandongo District	Kibanda	PermaNet 3.0
3	22	Western	Masindi District	Bujenje	PermaNet 2.0
3	23	Western	Masindi District	Buruli	PermaNet 2.0
3	24	Western	Masindi District	Masindi Municipality	PermaNet 2.0
3	43	Western	Ntoroko District	Ntoroko	PermaNet 3.0
3	69	Eastern	Namayingo District	Bukooli South	PermaNet 2.0
3	72	Eastern	Jinja District	Butembe	PermaNet 3.0
3	73	Eastern	Jinja District	Jinja Municipal	PermaNet 3.0
3	74	Eastern	Jinja District	Kagoma	PermaNet 2.0
3	75	Eastern	Kamuli District	Bugabula	PermaNet 3.0
3	76	Eastern	Kamuli District	Buzaaya	PermaNet 3.0
3	77	Eastern	Busia District	Busia Municipality	PermaNet 3.0
3	78	Eastern	Busia District	Samia Bugwe South	PermaNet 2.0
3	79	Eastern	Busia District	Samia Bugwe North	Olyset Plus
3	80	Eastern	Iganga District	Bugweri	Olyset Plus
3	81	Eastern	Iganga District	Iganga Municipality	PermaNet 2.0
3	82	Eastern	Iganga District	Kigulu South	PermaNet 2.0
3	83	Eastern	Iganga District	Kigulu North	PermaNet 3.0
3	84	Eastern	Luuka District	Luuka	PermaNet 2.0
3	89	Eastern	Kapchorwa District	Tingey	PermaNet 3.0
3	90	Eastern	Kween District	Kween	Olyset Net
3	91	Eastern	Mayuge District	Bunya West	PermaNet 2.0
3	92	Eastern	Mayuge District	Bunya East	PermaNet 3.0
3	93	Eastern	Mayuge District	Bunya South	Olyset Plus
3	94	Eastern	Kaliro District	Bulamogi	PermaNet 3.0
3	96	Eastern	Bukwo District	Kongasis	PermaNet 3.0
3	97	Eastern	Mbale District	Bungokho North	PermaNet 3.0
3	98	Eastern	Mbale District	Bungokho South	PermaNet 2.0
3	99	Eastern	Mbale District	Mbale Municipality	PermaNet 2.0
3	104	Eastern	Buyende District	Budiope	PermaNet 3.0
4	1	Western	Ibanda District	Ibanda	PermaNet 2.0
4	2	Western	Bundibugyo District	Bughendera	Olyset Plus

Appendix A: Intervention allocation list

4	3	Western	Bundibugyo District	Bwamba	Olyset Net
4	5	Western	Isingiro District	Bukanga	Olyset Net
4	6	Western	Isingiro District	Isingiro North	PermaNet 3.0
4	7	Western	Isingiro District	Isingiro South	PermaNet 2.0
4	8	Western	Mitooma District	Ruhinda	Olyset Net
4	10	Western	Kiruhura District	Kazo	PermaNet 2.0
4	11	Western	Kiruhura District	Nyabushozi	PermaNet 2.0
4	12	Western	Sheema District	Sheema South	Olyset Plus
4	13	Western	Sheema District	Sheema North	Olyset Plus
4	14	Western	Rubirizi District	Bunyaruguru	PermaNet 3.0
4	15	Western	Rubirizi District	Katerera	PermaNet 2.0
4	16	Western	Kamwenge District	Kibaale	PermaNet 2.0
4	17	Western	Kamwenge District	Kitagwenda	Olyset Net
4	18	Western	Ntungamo District	Kajara	PermaNet 2.0
4	19	Western	Ntungamo District	Ntungamo Municipality	Olyset Net
4	20	Western	Ntungamo District	Ruhaama	PermaNet 3.0
4	21	Western	Ntungamo District	Rushenyi	PermaNet 2.0
4	25	Western	Kasese District	Bukonzo West	Olyset Plus
4	26	Western	Kasese District	Bukonzo East	PermaNet 2.0
4	27	Western	Kasese District	Busongora South	PermaNet 3.0
4	28	Western	Kasese District	Busongora North	PermaNet 2.0
4	29	Western	Kasese District	Kasese Municipality	Olyset Plus
4	30	Western	Hoima District	Bugahya	PermaNet 3.0
4	31	Western	Hoima District	Buhaguzi	PermaNet 2.0
4	32	Western	Hoima District	Hoima Municipality	PermaNet 2.0
4	33	Western	Bushenyi District	Bushenyi-Ishaka Municipality	Olyset Plus
4	34	Western	Bushenyi District	Igara West	PermaNet 2.0
4	35	Western	Bushenyi District	Igara East	Olyset Plus
4	36	Western	Kyegegwa District	Kyaka	PermaNet 3.0
4	37	Western	Kabarole District	Buyangabu	Olyset Net
4	38	Western	Kabarole District	Burahya	PermaNet 3.0
4	39	Western	Kabarole District	Fort-Portal Municipality	Olyset Plus
4	40	Western	Rukungiri District	Rubabo	PermaNet 2.0
4	41	Western	Rukungiri District	Rujumbura	Olyset Plus
4	42	Western	Rukungiri District	Rukungiri Municipality	Olyset Plus
4	44	Western	Kyenjojo District	Mwenge North	PermaNet 2.0
4	45	Western	Kyenjojo District	Mwenge South	PermaNet 3.0
4	46	Western	Kanungu District	Kinkizi East	PermaNet 2.0
4	47	Western	Kanungu District	Kinkizi West	Olyset Net
4	48	Western	Mbarara District	Kashari	Olyset Plus
4	49	Western	Mbarara District	Mbarara Municipality	PermaNet 3.0
4	50	Western	Mbarara District	Rwampara	Olyset Plus
4	51	Western	Kibaale District	Bugangaizi West	PermaNet 3.0
4	52	Western	Kibaale District	Bugangaizi East	PermaNet 2.0
4	53	Western	Kibaale District	Buyaga West	Olyset Plus
4	54	Western	Kibaale District	Buyaga East	PermaNet 2.0
4	55	Western	Kibaale District	Buyanja	PermaNet 2.0

Appendix A: Intervention allocation list

4	56	Western	Buhweju District	Buhweju	Olyset Net
4	57	Western	Kisoro District	Bufumbira East	PermaNet 2.0
4	58	Western	Kisoro District	Bufumbira North	Olyset Net
4	59	Western	Kisoro District	Bufumbira South	PermaNet 3.0
4	60	Western	Kabale District	Kabale Municipality	PermaNet 3.0
4	61	Western	Kabale District	Ndorwa East	Olyset Plus
4	62	Western	Kabale District	Ndorwa West	PermaNet 2.0
4	63	Western	Kabale District	Rubanda East	Olyset Net
4	64	Western	Kabale District	Rubanda West	PermaNet 3.0
4	65	Western	Kabale District	Rukiga South	PermaNet 3.0
4	66	Western	Kabale District	Rukiga North	Olyset Net

APPENDIX B: INFORMATION SHEET
PBO Net Study Sensitisation

Why is this study being done?

Sleeping under a mosquito net is one of the most important ways to prevent malaria. In 2016-2017, the Ugandan Ministry of Health will be leading a campaign to give out mosquito nets around the country. Prof Janet Hemingway from the Liverpool School of Tropical Medicine, and colleagues from the Infectious Diseases Research Collaboration, Ugandan Ministry of Health, London School of Hygiene & Tropical Medicine, and University of California, San Francisco, are carrying out a research study. We are doing this study to find out if the mosquito nets given out by the Ministry of Health are working, and which type of net works the best.

Why are we talking to you today?

Your area has been chosen to take part in the study. Today, we would like to explain the purpose of the study and how it will be done. You are free to ask questions at any time.

How will this study be done?

Nets will be given out across the entire country, but only certain areas have been selected to take part in this study. In all, 104 health sub-districts in 48 districts in Eastern and Western Uganda have been chosen to take part. These areas have been assigned to receive one of four types of mosquito nets. Assignment to the four groups has been determined by a lottery. The nets that will be given out by the Ugandan Ministry of Health are long-lasting insecticide-treated bed nets that have been approved by the World Health Organisation, including: (1) PermaNet 2.0, (2) PermaNet 3.0, (3) Olyset Net, and (4) Olyset Plus.

To find out how well the mosquito nets work, we will carry out surveys before and after the nets are given out. We will also collect mosquitoes from the area. We will survey households to learn more about them. We will also review the health of children aged 2-10 years. Up to four rounds of surveys will be done over two years. In each round, only 50 households from each area will be surveyed, and mosquitoes will be collected from about 10 houses. Houses will be chosen for these surveys by a lottery. Different households will be chosen to take part in each round of surveys. We will talk to the head of household (or another adult resident in the household) about this study, and they will be asked to sign a form if they wish to take part, before carrying out any surveys.

What risks and benefits can be expected from this study?

Taking part in research may involve a loss of privacy, but information about households and children will be handled as confidentially as possible. The knowledge gained from this study will help researchers and policy-makers understand how best to control malaria in Uganda and elsewhere in Africa.

Who can answer questions about the study?

You can talk to the researchers about any questions or concerns you have about these study activities. Contact Prof Sarah Staedke (the PI in Uganda) or other members of staff working on this study on telephone number +256 (0) 312 281479. If you have any questions or concerns about the study, first talk to the researchers. If for any reason, you do not wish to do this or you still have concerns, you may contact Associate Prof Ponsiano Ocama, the Chair of the Makerere University, School of Medicine, Research and Ethics Committee at telephone number +256 (0) 772 421190.

APPENDIX C: CROSS-SECTIONAL COMMUNITY SURVEY

Household Screening Form

PART 1: Identification

SURVEY code	CLUSTER code	Enumeration area (EA) number
[_____]	[_____|_____|_____]	[_____|_____]

HOUSEHOLD number	Date adult resident FIRST interviewed
[_____|_____]	[_____|_____] / [_____|_____] / [_____|_____] *day* *month* *year*

PART 2: Locating household

Selection criteria	Include	Exclude
1. Dwelling destroyed or not found	[___] No	[___] Yes
2. Household vacant	[___] No	[___] Yes

If any answers are in the EXCLUDE column, exclude from the study. If not, proceed to the next section.

PART 3: Availability of adult resident

	DATE APPROACHED:	Adult available?		**IF YES,** go to Part 4. **IF NO,** GIVE REASON*	DATE TO RETURN:
1		1 = Yes	0 = No		
2		1 = Yes	0 = No		
3		1 = Yes	0 = No		
4		1 = Yes	0 = No		xxxxxxxxxxxxxxx

***1=Not at home, 2=Come back later, 3=Not Interested, 77=Other (Please Specify above)**

PART 4: Able to locate adult resident & consent discussion

Selection criteria	Include	Exclude
3. Able to locate adult	[___] Yes	[___] No
4. At least one household resident between 2-10 years of age present (with an adult caregiver willing to provide informed consent for the clinical survey)		
5. Adult aged 18 years or older	[___] Yes	[___] No
6. Adult is usual resident who was present in this household the previous night	[___] Yes	[___] No
7. Willingness of adult resident to provide informed consent?	[___] Yes	[___] No

If any answers are in the EXCLUDE column, exclude from the study. If not, proceed to the next section.

PART 4: CLOSING OUT THE SCREENING FORM

All criteria for study inclusion met?	Date enrolled
If no, exclude from the study [___] Yes [___] No	[_____|_____]/[_____|_____]/[_____|_____] day month year

PART 5: Assigning Community Survey ID

SURVEY code (as above)	CLUSTER code (as above)	HOUSEHOLD ID number
[_____]	[_____|_____|_____]	[_____|_____]

Staff ID: [_____|_____] **Data entrant (1st):** [_____|_____] **Data entrant (2nd):** [_____|_____]

[_____] [_____|_____|_____] [_____|_____] [_____|_____]____]

Survey code **Cluster code** **Enumeration area (EA) number** **Household ID number**

APPENDIX D. CROSS-SECTIONAL COMMUNITY SURVEY
Household informed consent form

Protocol Title:	Uganda PBO Net Study: Impact of long-lasting insecticide treated bednets with and without piperonyl butoxide (PBO) on malaria indicators in Uganda: a cluster-randomised trial
Site of Research:	Eastern and Western Uganda
Principal Investigator:	Prof Janet Hemingway (Prof Sarah Staedke in Uganda)
Version Date:	V4.0, 1 December 2018

Why is this study being done?

Sleeping under a mosquito net is one of the most important ways to prevent malaria. In 2016-2017, the Ugandan Ministry of Health will be leading a campaign to give out mosquito nets around the country. Prof Janet Hemingway from the Liverpool School of Tropical Medicine, and colleagues from the Infectious Diseases Research Collaboration, Ugandan Ministry of Health, London School of Hygiene & Tropical Medicine, and University of California, San Francisco, are carrying out a research study. We are doing this study to find out if the mosquito nets given out by the Ministry of Health are working, and which type of net works the best.

How will this study be done?

Nets will be given out across the entire country, but only certain areas have been selected to take part in this study. In all, 104 health sub-districts in 48 districts in Eastern and Western Uganda have been chosen to take part. These areas have been assigned to receive one of four types of mosquito nets. Assignment to the four groups has been determined by a lottery. The nets that will be given out by the Ugandan Ministry of Health are long-lasting insecticide-treated bed nets that have been approved by the World Health Organisation. To find out how well the mosquito nets work, we will carry out surveys before and after the nets are given out. We will also collect mosquitoes from the area.

Why are we talking to you today?

Your household has been selected to take part in a community survey. Today, we would like to explain the purpose of the study, how the community survey will be done, and what will be expected of you. You are free to ask questions at any time.

After this consent form is read to you, and your questions have been answered, we will ask you if you want to take part in the survey. You may talk about taking part in the survey with other people, including family and friends. If you agree to take part, we will ask you to sign this consent form. You will get a copy of this form to keep.

What will happen if my household takes part in this survey?

- We will ask you questions about the people who live here, and your household.
- We will ask you questions about the mosquito nets you own (if any), and will ask if we can see the nets to find out the brand of the net.
- We will then request for permission to review the health of children in this household.

How will my information be used?

The information you share will help us to find out how well the mosquito nets work. Your information will be recorded and will be used to write reports. Information gathered in this study may also be shared, or stored in a data repository, without names, so that other researchers may use it. Anyone assigned to review this study, to check that the study is being done correctly and that the information collected is accurate, will be granted direct access to your information, if needed.

How long will these activities last?

This household survey will take about 45 minutes.

Can I stop being in the survey?

You can decide to stop taking part at any time. Just tell our study personnel right away if you wish to stop the activities.

What risks can I expect if my household takes part in this survey?

Participation in any research study may involve a loss of privacy, but this will likely be very small.

Are there benefits to taking part in this survey?

There will be no direct benefit to you from taking part in this community survey. However, the knowledge gained from this survey will help researchers and policy-makers understand how best to control malaria in Uganda and elsewhere in Africa.

What other choices do I have if I do not to let my household take part in this survey?

You are free to choose not to allow your household to take part in this survey. If you decide you do not want your household to take part or decide to stop being in the study at any time and for any reason, there will be no penalty to you or your household members.

Will my household's information be kept private?

Information you provide will be recorded, but your name will not be used in any reports. The information obtained from these survey activities will be locked up at our project offices. All personal information will be stored electronically in a secure, password protected database to ensure privacy.

What are the costs of taking part in this survey? Will I be paid for letting my household take part?

You will not be charged for your household to take part in this survey. You will not be paid if your household takes part in this survey.

What are my rights if I allow my household to take part in this survey?

Taking part in this survey is your choice. You may choose either to allow your household to take part or not to take part. If you decide to allow your household to take part in this survey, you may change your mind at any time. No matter what decision you take, there will be no penalty to you or your household members in any way.

What if me or a member of my household is harmed as result of being in this survey?

We do not anticipate any harm resulting from taking part in this survey. If you are harmed or injured due to taking part in this survey, or if you have questions, please contact Dr. Samuel Gonahasa (the Study Coordinator), Prof Sarah Staedke (the Principal Investigator in Uganda) or other members of staff working on this study on telephone number +256 (0) 707 710720. The sponsoring organisations do not have a program to cover your costs if you are hurt or have other bad results.

Who can answer questions about the study?

You can talk to the researchers about any questions or concerns you have about these study activities. Contact Dr. Samuel Gonahasa (the Study Coordinator), Prof Sarah Staedke (the Principal Investigator in Uganda) or other members of staff working on this study on telephone number +256 (0) 707 710720. If you have any questions, comments or concerns about the study, first talk to the researchers. If for any reason, you do not wish to do this or you still have concerns, you may contact Associate Prof Ponsiano Ocama, the chair of the Makerere University, School of Medicine, Research and Ethics Committee at telephone number +256 (0) 772 421190.

Dissemination of results:

Information on the progress and findings of this study will be shared with the National Malaria Control Division at the Uganda Ministry of Health, and with other key stakeholders.

WHAT YOUR SIGNATURE OR THUMBPRINT MEANS
Your signature or thumbprint below means that you understand the information given to you in this consent form about your household's participation in the survey and agree with the following statements: • I have read the consent form concerning this survey (or have understood the verbal explanation of the consent form) and I understand what will be required of me if I take part in it. • My questions concerning this survey have been answered by the person who signed below. • I understand that at any time, I may withdraw from this survey without giving a reason and without affecting my household member's normal health care and management. • I agree that my household will take part in this survey.
If you wish to participate in this survey, you should sign or place your thumbprint below **WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM**

Name of head of household/another adult resident (printed)

Signature or Fingerprint * of head of household/another adult resident Date

Name of Study Personnel Administering Consent (printed) Position/Title

Signature of Study Personnel Administering Consent Date

Name of Translator (printed)

Signature of Translator Date

* If the head of household (or another adult resident) is unable to read and/or write, an impartial witness should be present during the informed consent discussion. After the written informed consent form is read and explained to the head of household (or another adult resident), and after they have orally consented to their household's participation in the trial, and have either signed the consent form or provided their fingerprint, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by the head of household (or another adult resident), and that informed consent was freely given by the head of household (or another adult resident).

Name of Person Witnessing Consent (printed)

Signature of Person Witnessing Consent Date

Appendix E: Cross-sectional Community Survey Household Questionnaire

Variable Name	Question	Variable Type	Variable Codes	Accepted Values	Skip	Comments
Section 1: Identification						
intnum	Interviewer's Number	Numeric		(10-50)		Each census worker will be assigned a unique ID
starttime	Date/time of start of interview	DateTime				Datetime stamp - automatically generated
survey	Survey round	Numeric	1 – Baseline 2 – 6-month 3 – 12-month 4 – 18-24 months			automatically generated
cluster	Health sub-district number	Numeric	Drop down list from allocation list	(001 - 104)		HSD = clusters
eanum	Enumeration number	Numeric	1 to 10	(01-10)		10 EAs to be randomly selected per cluster
hhnum	Household number	Numeric	1 to 25	(01-25)		5 Households to be enrolled per EA
hhid	Household ID	Numeric				8-digit number generated at the time of the first HH visit, composed of the following: Survey: 1 digit Cluster: 3 digits [001-104] EA number: 2 digits [01-10] Household number: 2 digits [01-25]
hhid2	Household ID	Numeric				Have RA enter the HHID to make sure it matches
gps	GPS coordinates of household	String				
enrolled	Household enrolled in the survey?	Numeric	1 - Yes 0 - No			All criteria for enrollment met? If yes, skip next question. If no, proceed to next question.
conducting_survey		Numeric				Used for programing logic, can be ignored for analysis
exclreason	If not enrolled, reason for exclusion?	Numeric	1 - Dwelling destroyed or not found 2 - Household vacant 3 - Unable to locate adult 4 - No household resident between 2-10 years of age present (with an adult caregiver willing to provide informed consent for the clinical survey) 5 - No adult aged 18 years or older 6 - Adult was not usual resident who was present in this household the previous night 7 - Adult resident not willing to provide informed consent	as per variable codes	preskip: if enrolled = 1, skip to swater postskip: skip to totvisit	From screening form
Section 2: Household Characteristics						
swater	What is the main source of drinking water for members of your household?	Numeric	10 - borehole 11 - pipe into dwelling 12 - piped into yard/compound 13 - public tap 21 - open well in yard/compound 22 - open public well 31 - protected well in yard/compound 32 - protected public well 41 - protected spring 42 - unprotected spring 43 - river/stream 44 - pond/lake 45 - dam 51 - rainwater 61 - water truck 71 - bottled water	as per variable codes	postskip: if swater <> 96, skip to tfaclty	
otherscs	Specify other source of water	String				
tfaclty	What kind of toilet facility do members of your household usually use?	Numeric	1 - flush toilet 2 - vip latrine 3 - covered pit latrine no slab 4 - covered pit latrine w/slab 5 - uncovered pit latrine no slab 6 - uncovered pit latrine w/slab 7 - composting toilet 8 - no facility/bush/field 96 - other	as per variable codes	postskip: if tfaclty <> 96, skip to fueltype	
otherfcy	Specify other kind of toilet facilities	String				
fueltype	What type of fuel does your household mainly use for cooking?	Numeric	1 - electricity 2 - lpg/natural gas 3 - biogas 4 - paraffin/kerosene 5 - charcoal 6 - firewood 7 - straw/shrubs/grass 8 - animal dung 95 - no food cooked in household 96 - other	as per variable codes	postskip: if fueltype <> 96, skip to senergy	
otherfuel	Specify other type of fuel used	String				
senergy	What is the main source of energy for lighting in the household?	Numeric	1 - electricity 2 - solar 3 - gas 4 - paraffin - hurricane lamp 5 - paraffin - pressure lamp 6 - paraffin - wick lamp 7 - firewood 8 - candles 9 - torch/battery powered lamp 96 - other	as per variable codes	postskip: if senergy <> 96, skip to mmfloor	
othereng	Specify other source of energy for lighting	String				
mmfloor	MAIN MATERIAL OF THE FLOOR RECORD OBSERVATION.	Numeric	11 - earth or sand 12 - earth and dung 31 - parquet or polished wood 33 - mosaic or tiles 34 - bricks 35 - cement/concrete 36 - stones 96 - other	as per variable codes	postskip: if mmfloor <> 96, skip to mmroof	
othermmf	Specify other material of the floor	String				

Appendix E: Cross-sectional Community Survey Household Questionnaire

Variable Name	Question	Variable Type	Variable Codes	Accepted Values	Skip	Comments
mmroof	MAIN MATERIAL OF THE ROOF. RECORD OBSERVATION.	Numeric	11 - thatched (including papyrus) 12 - mud 21 - wood/planks 22 - iron sheets 23 - asbestos 24 - tiles 25 - tin 26 - cement 96 - other	as per variable codes	postskip: if mmroof <> 96, skip to mmewalls	
othermmr	Specify other material of the roof	String				
mmewalls	MAIN MATERIAL OF THE EXTERIOR WALLS. RECORD OBSERVATION.	Numeric	11 - thatched/straw 21 - mud and poles 22 - un-burnt bricks 23 - un-burnt bricks with plaster/cement 24 - burnt bricks with mud 31 - cement blocks 32 - stone 33 - timber 34 - burnt bricks with plaster/cement 35 - iron sheets 96 - other -9: Skipped	as per variable codes	postskip: if mmewalls <> 96, skip to eaves	
othermme	Specify other material of the exterior walls	String				
eaves	Does the household have eaves?	Numeric	1 - Yes 0 - No			
eavetype	TYPE OF EAVES. RECORD OBSERVATION.	Numeric	1 - Open 2 - Closed			
windows	Does the household have windows?		1 - Yes 0 - No		postskip: if windows = 0, skip to hhrooms	
covered	Are any of the windows covered? Glass, screening, other material, etc.		1 - Yes 0 - No			
screened	Are any of the windows screened?		1 - Yes 0 - No			
hhrooms	How many rooms in your household are used for sleeping? (INCLUDING ROOMS OUTSIDE THE MAIN DWELLING) If there are 15 or more rooms, enter 15	Numeric	-7: Don't know -8: Refused to answer	1 - 15, -7, -8		
hhspaces	How many sleeping spaces like mats, mattresses, or beds are available in your household? If there are 25 or more sleeping places, enter 25	Numeric	-7: Don't know -8: Refused to answer	1 - 25, -8		cannot be less than hhrooms
electricity	Does your household have... ...Electricity?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes		
radio	...Radio?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes		
cassette	...Cassette player?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes		
tv	...Television?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes		
fridge	...Refrigerator?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes		
tble	...Table?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes		
chair	...Chairs?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes		
sofa	...Sofa set?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes		
bed	...Bed?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes		
cupboard	...Cupboard?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes		
clock	...Clock?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes		

Appendix E: Cross-sectional Community Survey Household Questionnaire

Variable Name	Question	Variable Type	Variable Codes	Accepted Values	Skip	Comments
mobile	Does any member of your household own or have... ...Mobile phone?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes		
watch	...A watch?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes		
bicycle	....A bicycle?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes		
scooter	...A motorcycle or motor scooter?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes		
car	...A car or truck?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes		
mboat	...A boat with a motor?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes		
nomboat	...A boat without a motor?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes		
bankacco	...A bank account?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes		
internet	...A device that can be used to access the internet?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes	postskip: if internet <> 1, skip to numaland	
device	...If yes, what type of device?	String	1 – Smartphone 2 – Tablet 3 – Laptop computer 4 – Desktop computer -7: Don't know			Multiple response question; Comma separated list of each item selected For example if 'Tablet' and 'Laptop computer' were both selected, the response would be: "2,3"
smartphone	...Smartphone	Numeric	1 - Yes 0 - No	as per variable codes		Individual responses for the 'decice' question. For example, if 'Tablet' and 'Laptop computer' were both selected, the responses would be: smartphone = 0 tablet = 1 laptop = 1 desktop = 0
tablet	...Tablet	Numeric	1 - Yes 0 - No	as per variable codes		
laptop	...laptop	Numeric	1 - Yes 0 - No	as per variable codes		
desktop	...desktop	Numeric	1 - Yes 0 - No	as per variable codes		
numaland	How many acres of agricultural land do members of this household own? IF NONE, ENTER '0' IF 10,000 OR MORE, ENTER 10,000	Decimal	-7: Don't know -8: Refused to answer	0.0 - 10,000; -7, -8		
dmarkt	How far is it to the nearest market place?	Decimal	-7: Don't know -8: Refused to answer	0.0 - 100, -7, -8		
hhmeals	Now I would like to ask you about the food your household eats. How many meals does your household usually have per day?	Numeric	-8: Refused to answer	1 - 8, -8		
hhnumt	In the past week, on how many days did the household eat meat?	Numeric	-8: Refused to answer	0 - 7, -8		
hhpsf	How often in the last year did you have problems in satisfying the food needs of the household?	Numeric	1 - never 2 - seldom 3 - sometimes 4 - often 5 - always -7: Don't know -8: Refused to answer	as per variable codes		
dhfcty	How far is it to the nearest health facility? If less than 1 km, enter 0 If more than 100 km, enter 100	Decimal	-7: Don't know -8: Refused to answer	0 - 100, -7, -8		
mthfcty	If you were to go this facility,how would you <u>most likely</u> go there?	Numeric	1 - car/motorcycle 2 - public transport(bus,taxi) 3 - animal/animal cart 4 - walking 5 - bicycle 7 - boat 96 - other -7: Don't know -8: Refused to answer	as per variable codes	postskip: if mthfcty <> 96, skip to pspray	
othermth	Specify other means of transport to the health facility	String				
Spraying						

Appendix E: Cross-sectional Community Survey Household Questionnaire

Variable Name	Question	Variable Type	Variable Codes	Accepted Values	Skip	Comments
pspray	At any time in the past 12 months, has anyone asked permission to come into your dwelling to spray the interior walls against mosquitoes?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes	postskip: if pspray <> 1, skip to ahwker	
gpspray	Did you grant them permission to spray the interior walls of your dwelling?	Numeric	1 - Yes 0 - No	as per variable codes	postskip: if gpspray = 1, skip to tspray	
rgspray	What was the primary reason that you did not grant permission to spray the interior walls of your dwelling against mosquitoes? DO NOT PROMPT.	Numeric	1 - had a sick person/baby 2 - spraying not effective against mosquitoes 3 - spraying chemicals are harmful 4 - someone in the house was pregnant 96 - other -7: Don't know	as per variable codes	postskip: if rgspray <> 96, skip to ahwker	
otherrgs	Specify other reasons for not granting permission to spray the interior walls of your dwelling against mosquitoes	String			postskip: skip to ahwker	
tspray	How many months ago was the dwelling last sprayed? If less than 1 month, enter 0	Numeric	-8: Refused to answer	0 - 12, -8		
CHW						
ahwker	Is there a community health worker (community medicine distributor/CMD, village health team/VHT, community own resource person/CORP) who distributes malaria medicines in your village or community?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes	if ahwker <> 1, skip to havenets	
amchwker	Does the community health worker currently have malaria medicines available?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes		
havenets	Does your household have any mosquito nets that can be used while sleeping?	Numeric	1 - Yes 0 - No	as per variable codes		
netsinhouse		Numeric				Used for programing logic, can be ignored for analysis
UCCnets	Did you receive one or more bednets in the recent net campaign (Universal Coverage Campaign) led by the Ministry of Health?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes	If UCCnets <>1, skip to whynoUCCnets	
numUCCnets	How many nets did you receive in the UCC campaign?	Numeric	[___|___]			
typeUCCnets	Do you know what type of nets you received?		1 - PermaNet 2.0 2 - PermaNet 3.0 3 - Olyset Net 4 - Olyset Plus -7 - Don't know -8 - Refused to answer			
adequate	Do you feel that this number of nets was adequate for this household?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes	If adequate <>1, skip to useUCCnets	
notadeqate	If the number of UCC nets received was not adequate, why?	Numeric	1 - Not enough nets to cover all sleeping spaces 2 - Not enough nets to cover all household residents 3 - Need nets for children at boarding school 4 - Net nets for other purposes (gardens, fishing, shower curtains) 5 - Other			
useUCCnets	Did you ever hang (or use) at least one of the nets?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes		
haveUCCnets	Do you still have all the nets you received in the campaign?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes		
whereUCCnet1	Where is the net now?	Numeric	1 – Hung in the house 2 – In the house, but not hung 3 – Used as a fishing net 4 – Used as a garden cover 5 – Used as a shower curtain 6 – Used for other household purpose 7 – Given to a child to take to boarding school 8 – Given away 9 – Sold 10 – Stolen 11 – Lost 12 - Other -7: Don't know -8: Refused to answer	as per variable codes		Record for each net received in the campaign - number consecutively starting with 1 (whereUCCnet1, whereUCCnet2, etc); total number of nets recorded should equal total number of nets received
whynoUCCnets	Why did you not receive nets during the UCC campaign?	Numeric	1 – No nets were delivered to this area (village, parish, HSD) 2 – No nets were delivered to this house 3 – We were never told to collect nets 4 – We were told our household did not need nets 5 – We were away when the nets were distributed 6 – They ran out of nets in our area 7 – Our local leaders refused to accept the nets 8 – We refused to accept the nets 9 – We had no transport to go collect the nets 10 - Other -7: Don't know -8: Refused to answer	as per variable codes		

Appendix E: Cross-sectional Community Survey Household Questionnaire

Variable Name	Question	Variable Type	Variable Codes	Accepted Values	Skip	Comments
Section 3: Household Members - this section will be repeated for each household member						
linenum	Household member's line number (head of household=1)	Numeric				Consecutive number starting with 1 and continuing for all household members. Will be used to generating a unique HH member ID number
participantsname	Household member name?	String				Grant thinks we should collect. Note that I've shortened the variable name to 'name'
gender	Gender of [[participantsname]]?	Numeric	1 - Male 2 - Female	as per variable codes		Note that I've changed this variable name from 'sex' to 'gender'
hoh		Numeric				Used for programing logic, can be ignored for analysis
lessthantwo	Is [[participantsname]] less than 2 years old?	Numeric	1 - Yes 0 - No -9: Skipped (fof HoH)	as per variable codes	postskip: if lessthantwo = 1, then skip to agemonths	
age	If 2 years or older, record age in years	Numeric	-9 skipped	2 - 110; -9 (18 - 110 for Head of household)	postskip: skip to relation	
agemonths	If less than 2 years, record age in months	Numeric	-9 skipped	0-24		
relation	What is [[participantsname]]'s relationship to the household head?	Numeric	0: Self (household head) 1: husband/wife 2: son/daughter 3: father/mother 4: grandson/granddaughter/great-grandson/great-granddaughter 5: grandmother/grandfather/great-grandmother/great-grandfather 6: Brother/Sister 7: Aunt/Uncle 8: Cousin 9: Niece/Nephew 10: Stepchild 11: Foster child 12: Girlfriend 13: Boyfriend 14: House helper 15: Employee 16: Renter 17: Student-boarder 18: Other	as per variable codes	postskip: if relation <> 18, then skip to inclusion_criteria	
relation_oth	Enter [[participantsname]]'s relationship to the household head	String				
inclusion_criteria	Is participant eligible for Clinical Survey	Numeric	1 - Yes 0 - No	as per variable codes		automatically generated - Yes, if ageyears is 2 to 10
Section 4: Bednets All questions in this section will be repeated for each mosquito net in the household						
netnum	Net Number	Numeric				Consecutive number starting with 1 and continuing for all nets in the house
obs	May I have a look at net number [[netnum]] to establish the brand?	Numeric	1 - Observed 0 - Not observed -9: Skipped	as per variable codes		
howoldnet	How many months ago did your household obtain net number [[netnum]]? IF LESS THAN ONE MONTH, WRITE '0'. IF MORE THAN 36 MONTHS AGO RECORD 37	Numeric	-7: Don't know	0 - 37, -7		
wherenet	Where did you get net [[netnum]] from?	Numeric	0 – MOH net distribution campaign (2017) 1 – Gov't hospital 2 – Gov't health center 3 – Private hospital/clinic 4 – Private pharmacy 5 – Shop 6 – Open market 7 – Hawker 8 – Project/NGO 9 – Campaign/VHT (Community, school, etc.) 10 – Church 11 – Friend/Relative 96 – Other	as per variable codes	if wherenet <> 96, skip to free	Added in option '0' for the MOH UCC, and deleted option '12' for village leader
spcfro	Specify other source of net [[netnum]]	String				
free	Was net number [[netnum]] given to you free of charge? Or did you or someone in your household pay for this net?	Numeric	1 – Free 2 – Paid for -7: Don't know -8: Refused to answer			

Appendix E: Cross-sectional Community Survey Household Questionnaire

Variable Name	Question	Variable Type	Variable Codes	Accepted Values	Skip	Comments
brandnet	What is the brand of net number [[netnum]]?	Numeric	1 - PermaNet 2.0 2 - PermaNet 3.0 3 - Olyset Net 4 - Olyset Plus 5 - Duranet 6 - Interceptor 7 - Netprotect 10 - KO net 11 - Kooper net 12 - Iconet 13 - Safi net 14 - B52 15 - Bamboo hut 16 - Century 17 - Lucky net 18 - Victoria 19 - Homemade net 96 - Other -7: Don't know brand	as per variable codes	postskip: if brandnet = 1, skip to slpnet postskip: if brandnet = 2, skip to slpnet postskip: if brandnet = 3, skip to slpnet postskip: if brandnet = 4, skip to slpnet postskip: if brandnet = 5, skip to slpnet postskip: if brandnet = 6, skip to slpnet postskip: if brandnet = 7, skip to slpnet	
otherb	Specify other brands or types of mosquito net	String			preskip: if brandnet <> 96, skip to smnet	
smnet	Since you got net number [[netnum]], was it ever soaked or dipped in a liquid to repel mosquitoes or bugs?	Numeric	1 - Yes 0 - No -7: Don't know -9: Skipped	as per variable codes	postskip: if smnet <> 1, skip to slpnet	
tsmnet1	How many months ago was net number [[netnum]] last soaked or dipped? IF LESS THAN 1 MONTH, RECORD '0'. IF MORE THAN 25 MONTHS AGO, RECORD 26	Numeric	95 - More than 25 months ago -7: Don't know -9: Skipped	0 - 26, -7		
slpnet	Did anyone sleep under net number [[netnum]] last night?	Numeric	1 - Yes 0 - No -7: Don't know -8: Refused to answer	as per variable codes	postskip: if slpnet = 1, skip to sleptun1 postskip: if slpnet = -7, go to the next net postskip: if slpnet = -8, go to the next net	
Net not used						
whynotused	What are some of the reasons why net number [[netnum]] was not used? Mark all that apply	String	1 - Too hot 2 - Don't like smell 3 - No mosquitoes 4 - Net too old/too many holes 5 - Net not hung 6 - Net too dirty 7 - Net no longer kill insects 96 - Other -7: Don't know			Multiple response question; Comma separated list of each item selected For example if 'No mosquitoes' and 'Net too dirty' were both selected, the response would be: "3,6"
nutoohot	...Too hot	Numeric	1 - Yes 0 - No	as per variable codes		Individual responses for the 'decice' question. For example, if 'No mosquitoes' and 'Net too dirty' were both selected, the response would be: nutoohot = 0 nusmell = 0 nunomos = 1 nuold = 0 nunothung = 0 nudirty = 1 nunotkillins = 0 nuother = 0
nusmell	...Don't like smell	Numeric	1 - Yes 0 - No	as per variable codes		
nunomos	...No mosquitoes	Numeric	1 - Yes 0 - No	as per variable codes		
nuold	...Net too old/too many holes	Numeric	1 - Yes 0 - No	as per variable codes		
nunothung	...Net not hung	Numeric	1 - Yes 0 - No	as per variable codes		
nudirty	...Net too dirty	Numeric	1 - Yes 0 - No	as per variable codes		
nunotkillins	...Net no longer kill insects	Numeric	1 - Yes 0 - No	as per variable codes		
nuother	...Other	Numeric	1 - Yes 0 - No	as per variable codes		
othrnt	Specify other reason why net number [[netnum]] was not used.	String			preskip: if whynotused 'does not contain' 96, skip to nthung	
nthung	If not hung, why not? PROBE FOR THE MAIN REASON. SELECT ONLY ONE.	Numeric	1 - Nowhere to hang 2 - Don't know how to hang net 3 - No tools to hang net 4 - Shape did not fit 5 - Size did not fit 6 - Don't want to hang 7 - Extra net/Used for Visitor/ Owner not home 96 - other -7: Don't know -8: Refused to answer	as per variable codes	preskip: if whynotused 'does not contain' 5, repeat section 4 if there are still more nets in the house	
Who slept under net						
sleptunder	Who slept under net number [[netnum]] last night?	Numeric	-6: N/A		preskip: if any1 <> 1, repeat Section 4 if there are still more nets in the house	Multiple response question; Comma separated list of each linenum of the people who slept under the net Logic check: Person cannot sleep under more than 1 net
Section 5: Interviewer Details						
totvisit	How many visits have you made to this household?	Numeric		1 - 3		
stoptime	End time of interview	DateTime				automatically generated

APPENDIX F: COMMUNITY SURVEY – Clinical Survey Screening Form

PART 1: Identification

SURVEY code	CLUSTER code	Enumeration Area (EA) number
[_____]	[_____|_____|_____]	[_____|_____]

Household ID number	Resident line number	Date parent/guardian FIRST interviewed
[_____|_____]	[_____|_____]	[_____|_____] / [_____|_____] / [_____|_____] day month year

Age	Gender *(1=male, 2 = female)*	Date of birth
[_____|_____]	[_____]	[_____|_____] / [_____|_____] / [_____|_____] day month year

PART 1: Consent discussion with parent/guardian

Selection criteria	Include	Exclude
1. Child aged 2-10 years	[___] Yes	[___] No
2. Child is usual resident who was present in this household the previous night	[___] Yes	[___] No
3. Willingness of adult resident to provide informed consent?	[___] Yes	[___] No

If any answers are in the EXCLUDE column, exclude from the study. If not, proceed to the next section.

PART 2: Able to locate child & assent discussion

Selection criteria	Include	Exclude
4. Able to locate child	[___] Yes	[___] No
5. Willingness of child aged ≥ 8 years to provide assent?	[___] Yes	[___] No

If any answers are in the EXCLUDE column, exclude from the study. If not, proceed to the next section.

PART 3: CLOSING OUT THE SCREENING FORM

All criteria for study inclusion met?	Date enrolled
If no, exclude from the study [___] Yes [___] No	[_____|_____]/[_____|_____]/[_____|_____] *day month year*

PART 4: Assigning Community Clinical Survey ID

SURVEY code	CLUSTER code	HOUSEHOLD number	CCS number
[_____]	[_____|_____|_____]	[_____|_____]	[_____|_____|_____]

Staff ID: [_____|_____] **Data entrant (1st):** [_____|_____] **Data entrant (2nd):** [_____|_____]

[_____] [_____|_____|_____] [_____|_____] [_____|_____]____] [_____|_____]

Survey code | Cluster code | EA number | Household ID number | Resident line number

APPENDIX G. COMMUNITY CLINICAL SURVEY

Research Participant Informed Consent form (CHILD) for Parents/Guardians

Protocol Title:	Uganda PBO Net Study: Impact of long-lasting insecticide treated bednets with and without piperonyl butoxide (PBO) on malaria indicators in Uganda: a cluster-randomised trial
Site of Research:	Eastern and Western Uganda
Principal Investigator:	Prof Janet Hemingway (Prof Sarah Staedke in Uganda)
Version Date:	V4.0, 1 December 2018

Why is this study being done?

Sleeping under a mosquito net is one of the most important ways to prevent malaria. In 2016-2017, the Ugandan Ministry of Health will be leading a campaign to give out mosquito nets around the country. Prof Janet Hemingway from the Liverpool School of Tropical Medicine, and colleagues from the Infectious Diseases Research Collaboration, Ugandan Ministry of Health, London School of Hygiene & Tropical Medicine, and University of California, San Francisco, are carrying out a research study. We are doing this study to find out if the mosquito nets given out by the Ministry of Health are working, and which type of net works the best.

How will this study be done?

Nets will be given out across the entire country, but only certain areas have been selected to take part in this study. In all, 104 health sub-districts in 48 districts in Eastern and Western Uganda have been chosen to take part. These areas have been assigned to receive one of four types of mosquito nets. Assignment to the four groups has been determined by a lottery. The nets that will be given out by the Ugandan Ministry of Health are long-lasting insecticide-treated bed nets that have been approved by the World Health Organisation. To find out how well the mosquito nets work, we will carry out surveys before and after the nets are given out. We will also collect mosquitoes from the area.

Why are we talking to you today?

Your household has been selected to take part in a community survey. As part of these surveys, we would like to review the health of children aged 2-10 years. Today, we would like to explain the purpose of the clinical survey, how it will be done, and what will be expected of you and your child. You are free to ask questions at any time.

What will happen if my child takes part in this survey?

If you agree to let your child participate in this survey, the following will happen today:

- We will ask some questions about your child, their health, and whether (s/he sleeps under a bednet, and we will briefly examine your child.
- We will take a blood sample from your child's finger to examine for malaria parasites and to measure your child's blood counts.
- We will use a sterile needle to make the prick on your child's finger, and the total amount of blood taken will the less than half a teaspoon (2ml).
- We will collect one drop of blood to measure the amount of haemoglobin (blood count) in a machine (only in children < 5 years).
- Small drops of blood will also be put on a glass slide and onto filter paper to look for malaria parasites
- If your child had a fever in the last 48 hours (2 days) or has a high temperature, we will do a rapid test to look for malaria.
- If the rapid test is positive, we will give your child malaria treatment with artemether-lumefantrine, which is the first-line recommended treatment for simple malaria in Uganda.
- If your child has a low blood count, or has signs of severe malaria or another serious illness, we will refer your child to an appropriate health center or to hospital for further care.

How will my child's information be used?

The information we gather in this study will help us to find out how well the mosquito nets work. Your child's information will be recorded and will be used to write reports. Information gathered in this study may also be shared, or stored in a data repository, without names, so that other researchers may use it. Anyone assigned to review this study, to check that the study is being done correctly and that the information collected is accurate, will be granted direct access to your child's information, if needed.

How long will these activities last?

Today the survey activities, including questions, examination, and blood tests will take about 1 hour.

Can I stop my child from being in the survey?

You can decide to stop taking part at any time. Just tell our study personnel right away if you wish to stop the activities.

What risks can I expect if my child takes part in the survey?

- **Loss of Privacy:** Participation in any research study may involve a loss of privacy, but this will likely be very small.
- **Blood draws:** The risks of drawing blood from a finger prick include temporary discomfort from the needle stick, bruising, skin infection, and fainting. The amount of blood removed will be too small to affect your child's health.

Are there benefits to letting my child take part in the survey?

As part of this survey, we will test your child's blood counts, and will test your child for malaria if your child has fever. If we do a malaria test, and it is positive, we will give your child malaria treatment. In addition, the knowledge gained from this survey will help researchers and policy-makers understand how best to control malaria in Uganda and elsewhere in Africa.

What other choices do I have if I do not allow my child to take part in the survey?

You are free to choose not to allow your child to take part in this survey. If you decide you do not want your child to take part or decide to stop your child from being in the study at any time and for any reason, there will be no penalty to you or your child.

Will my child's information be kept private?

Your child's samples will be labeled using an identification number so that your child's name cannot be readily identified. Information we gather about your child will be recorded, but no names will be used in any reports. The information obtained from these survey activities will be locked up at our project offices. All personal information will be stored electronically in a secure, password protected database to ensure privacy.

What are the costs of taking part in this survey? Will I be paid for letting my child take part?

You and your child will not be charged for any of the treatments or procedures we perform today. However, if we refer your child for further evaluation and health care, you will be responsible for all costs for your child's health care. You and your child will not be paid for participation in the survey.

What are my rights if I allow my child to take part in the survey?

Taking part in this survey is your choice. You may choose either to allow your child to take part or not to take part. If you decide to allow your child to take part in this survey, you may change your mind at any time. No matter what decision you take, there will be no penalty to you or your child in any way.

What if me or a member of my household is harmed as result of being in this survey?

We do not anticipate any harm resulting from taking part in this survey. If you are harmed or injured due to taking part in this survey, or if you have questions, please contact Dr. Samuel Gonahasa (the Study Coordinator), Prof Sarah Staedke (the Principal Investigator in Uganda) or other members of staff working on this study on telephone number +256 (0) 707 710720. The sponsoring organisations do not have a program to cover your costs if you are hurt or have other bad results.

Who can answer questions about the study?

You can talk to the researchers about any questions or concerns you have about these study activities. Contact Dr. Samuel Gonahasa (the Study Coordinator), Prof Sarah Staedke (the Principal Investigator in Uganda) or other members of staff working on this study on telephone number +256 (0) 707 710720. If you have any questions, comments or concerns about the study, first talk to the researchers. If for any reason, you do not wish to do this or you still have concerns, you may contact Associate Prof Ponsiano

Ocama, the chair of the Makerere University, School of Medicine, Research and Ethics Committee at telephone number +256 (0) 772 421190.

Dissemination of results:

Information on the progress and findings of this study will be shared with the National Malaria Control Division at the Uganda Ministry of Health, and with other key stakeholders.

WHAT YOUR SIGNATURE OR THUMBPRINT MEANS
Your signature or thumbprint below means that you understand the information given to you in this consent form about your child's participation in the survey and agree with the following statements: • I have read the consent form concerning this survey (or have understood the verbal explanation of the consent form) and I understand what will be required of me and my child if my child takes part in it. • My questions concerning this survey have been answered by the person who signed below. • I understand that at any time, I may withdraw my child from this survey without giving a reason and without affecting my child's normal health care and management. • I agree that the child under my care will take part in this survey.
If you wish for your child to take part in this survey, you should sign or place your thumbprint below. You will also be asked to sign another informed consent form for the use of stored specimens. **WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM**

Name of Participant (printed)

Name of Parent/Guardian (printed)

Signature or Fingerprint * of Parent/Guardian Date

Name of Study Personnel Administering Consent (printed) Position/Title

Signature of Study Personnel Administering Consent Date

Name of Translator (printed)

Signature of Translator Date

* If the head of household (or another adult resident) is unable to read and/or write, an impartial witness should be present during the informed consent discussion. After the written informed consent form is read and explained to the head of household (or another adult resident), and after they have orally consented to their household's participation in the trial, and have either signed the consent form or provided their fingerprint, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by the head of household (or another adult resident), and that informed consent was freely given by the head of household (or another adult resident).

Name of Person Witnessing Consent (printed)

Signature of Person Witnessing Consent Date

[_____] [_____|_____|_____] [_____|_____] [_____|_____]____] [_____|_____]

Survey code | Cluster code | EA number | Household ID number | Resident line number

APPENDIX H. COMMUNITY CLINICAL SURVEY

Informed consent for future use of biological specimens (CHILD) for Parents/Guardians

Protocol Title:	Uganda PBO Net Study: Impact of long-lasting insecticide treated bednets with and without piperonyl butoxide (PBO) on malaria indicators in Uganda: a cluster-randomised trial
Site of Research:	Eastern and Western Uganda
Principal Investigator:	Prof Janet Hemingway (Prof Sarah Staedke in Uganda)
Version Date:	V4.0, 1 December 2018

Introduction

While your child or the child under your care is in this study, there may be blood samples taken from them that may be useful for future research. These filter-paper samples will be stored in what is called a "specimen bank". The samples will be stored long-term in Uganda at the Infectious Diseases Research Collaboration. Samples may also be shared with investigators at other institutions. Future research must be approved by the appropriate ethics committee or Institutional Review Board.

What samples will be used for

Your child's blood and the malaria parasites in it will be used to study malaria and the response of this disease to treatment. Results of these studies will not affect your child's care.

1. These samples will be used for future research to learn more about malaria and other diseases.
2. Your child's samples will be used only for research and will not be sold or used to produce commercial products.
3. Genetic research may be performed on samples. This may include the testing your child's genetic material to look for changes that may influence your child's risk of malaria and response to malaria treatment. However, no genetic information obtained from this research will be placed in your child's medical records. These samples will be identified only by codes so that they cannot be readily identified with your child.

What risks can I expect if my child's samples are used for future research?

There are few risks to your child from future use of their samples. A potential risk might be the release of information from your child's health or study records. Reports about research done with your child's

samples will not be put in their health record, but will be kept with the study records. The study records will be kept confidential as far as possible.

Are there benefits to letting my child's samples be used for future research?

There will be no direct benefit to your child. From studying your child's samples we may learn more about malaria or other diseases: how to prevent them, how to treat them, how to cure them.

What other choices do I have if I do not allow my child's samples to be used for future research?

You are free to choose not to allow your child's samples to be used for future research. If you choose not to let your child's samples be used for future research, no additional samples will be collected from them. Your child will still be eligible to participate in this survey and can still get medical care from health facilities around. No matter what decision you take, there will be no penalty to you in any way.

Will my child's information be kept private?

All personal information will be stored electronically in a secure, password protected database to ensure privacy. Your child's samples will be coded so that your child's name cannot be readily identified. Reports from future research done with your child's samples will not be given to you or your child's doctor. These reports will not be put in your child's medical record and will be kept confidential to the best of our ability. Results from future research using your child's samples may be included in reports but no names will be used. In the future, researchers studying your child's samples may need to know more about your child, such as their age, gender, and race. If this information is already available, it may be provided to the researcher. Your child's name or anything that might identify them personally will not be provided. You will not be asked to provide additional consent.

What are the costs of letting my child's samples be used for future research? Will I be paid for letting my child's samples be used for future research?

You will not be charged or paid for letting your child's samples be used for future research. If the data or any new products, tests or discoveries that result from this research have potential commercial value, you will not share in any financial benefits.

Who can answer questions about the study?

You can talk to the researchers about any questions or concerns you have about these study activities. Contact Dr. Samuel Gonahasa (the Study Coordinator), Prof Sarah Staedke (the Principal Investigator in Uganda) or other members of staff working on this study on telephone number +256 (0) 707 710720. If you have any questions, comments or concerns about the study, first talk to the researchers. If for any reason, you do not wish to do this or you still have concerns, you may contact Associate Prof Ponsiano Ocama, the chair of the Makerere University, School of Medicine, Research and Ethics Committee at telephone number +256 (0) 772 421190.

Freedom to refuse

You can change your mind at any time about allowing your child's samples to be used for future research. Just contact the telephone number above and ask that your child's samples be destroyed. Whether you allow us to use your child's samples in future research will not have any effect on your child's participation in this study or future participation in other studies.

Dissemination of results:

Information on the progress and findings of this study will be shared with the National Malaria Control Division at the Uganda Ministry of Health, and with other key stakeholders.

WHAT YOUR SIGNATURE OR THUMBPRINT MEANS

Your signature or thumbprint below means that you understand the information given to you in this consent form about your child's participation in the survey and agree with the following statements:

- I have read the consent form concerning this survey (or have understood the verbal explanation of the consent form) and I understand what will be required of me and my child if my child takes part in it.
- My questions concerning this survey have been answered by the person who signed below.
- I understand that at any time, I may withdraw my child from this survey without giving a reason and without affecting my child's normal health care and management.
- I agree that the child under my care will take part in this survey.

If you wish for your child to take part in this survey, you should sign or place your thumbprint below.
You will also be asked to sign another informed consent form for the use of stored specimens.

WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM

Name of Participant (printed)

Name of Parent/Guardian (printed)

Signature or Fingerprint * of Parent/Guardian Date

Name of Study Personnel Administering Consent (printed) Position/Title

Signature of Study Personnel Administering Consent Date

Name of Translator (printed)

Signature of Translator Date

* If the head of household (or another adult resident) is unable to read and/or write, an impartial witness should be present during the informed consent discussion. After the written informed consent form is read and explained to the head of household (or another adult resident), and after they have orally consented to their household's participation in the trial, and have either signed the consent form or provided their fingerprint, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by the head of household (or another adult resident), and that informed consent was freely given by the head of household (or another adult resident).

Name of Person Witnessing Consent (printed)

Signature of Person Witnessing Consent Date

[_____] [_____|_____|_____] [_____|_____] [_____|_____]____] [_____|_____]

Survey code **Cluster code** **EA number** **Household ID number** **Resident line number**

APPENDIX I. COMMUNITY CLINICAL SURVEY
Assent Form for Children

Protocol Title:	Uganda PBO Net Study: Impact of long-lasting insecticide treated bednets with and without piperonyl butoxide (PBO) on malaria indicators in Uganda: a cluster-randomised trial
Site of Research:	Eastern and Western Uganda
Principal Investigator:	Prof Janet Hemingway (Prof Sarah Staedke in Uganda)
Version Date:	V4.0, 1 December 2018

Why have we met you?

We want to tell you about a research study. A research study is when doctors collect information to learn more about something. After we tell you about it, we will ask if you'd like to be in this research study or not.

Why are we doing this study?

Sleeping under a mosquito net is one of the most important ways to prevent malaria. We are doing this study to find out if the mosquito nets given out by the Ministry of Health are working, and which type of net works the best.

What will happen if I agree to be in this study?

Only if you agree to be in this study, we will do the following;

- We will ask you some questions about you, your health, and whether you sleep under a bednet, and we will briefly examine you.
- We will take a blood sample from your finger to examine for malaria parasites. We will use a sterile needle to make the prick on your finger, and the total amount of blood taken will the less than half a teaspoon (2ml).
- Small drops of blood will also be put on a glass slide and onto filter paper to look for malaria parasites.
- We will collect one drop of blood to measure the amount of haemoglobin (blood count) in a machine (only in children < 5 years).
- If you had a fever in the last 48 hours (2 days) or have a high temperature, we will do a rapid test to look for malaria.
- If the rapid test is positive, we will give you malaria treatment with artemether-lumefantrine, which is the first-line recommended treatment for simple malaria in Uganda.

- If you have signs of severe malaria or another serious illness, we will refer you to an appropriate health center or to hospital for further care.

How long will these study activities last?
Today the study activities will take about 1 hour.

Can this study cause me harm?
You will feel some slight pain when the sample of blood is being removed from your finger, but it will stop quickly. The amount of blood removed will be too small to affect your health.

What will I gain from this study?
As part of this survey, we will test you for malaria if you have fever. If we do a malaria test, and it is positive, we will give you malaria treatment. In addition, the knowledge gained from this survey will help researchers and policy-makers understand how best to control malaria in Uganda, and in Africa.

Will my information be kept private?
We will not use your name. All personal information will be stored electronically in a secure, password protected database to ensure privacy.

Must I be in this study?
No one will force you to be in this study. If your parent/guardian agrees, you can be in this study, but you do not have to be in it if you do not want to. If you agree to be in this study now, you may change your mind at any time. No matter what you decide, no one will punish you or be annoyed with you. If you do not want to be in this study, just tell us.

Who can answer my questions about this study?
You may ask questions any time, you can talk to me or somebody else. You can also contact Dr. Samuel Gonahasa (the Study Coordinator), Prof Sarah Staedke (the Principal Investigator in Uganda) or other members of staff working on this study on telephone number +256 (0) 707 710720.

Dissemination of results:
Information on the progress and findings of this study will be shared with the National Malaria Control Division at the Uganda Ministry of Health, and with other key stakeholders.

ASSENT TO JOIN THE STUDY (We will give you a copy of this form to keep)
I have explained the study to: (print name of child here)
in a language he/she can understand and the child has agreed to be in the study

Signature or Fingerprint of Participant Date

Name of Person Conducting Assent Discussion (print)

Signature of Person Conducting Assent Discussion Date

Name of Translator (printed)

Signature of Translator Date

Appendix J. Cross-sectional Community Survey Clinical

Variable Name	Question	Variable Type	Variable Codes	Accepted Values	Skip	Comments
Section 1: Identification						
intnum	Interviewer's Number	Numeric		(10-50)		Each census worker will be assigned a unique ID
starttime	Date/time of start of interview	DateTime				Datetime stamp - automatically generated
hhid	Household ID number	Numeric				
linenum	Household member's line number (head of household=1)	Numeric				
participantsname	Household member name	String				
Section 2: Laboratory Testing						
consent	Does [[participantsname]] consent to laboratory testing? (Adult consents if it is a child)	Numeric	1 - Yes 0 - No 2 - Not at home	as per variable codes	postskip: if consnt <> 1, skip to stoptime	
fpbarcode1	Barcode for Filter paper	String	-9: Skipped			
fpbarcode2	Re-enter Barcode for Filter paper	String	-9: Skipped			Barcodes must be the same
bsbarcode1	Barcode for blood smear	String	-9: Skipped			
bsbarcode2	Re-enter Barcode for blood smear	String	-9: Skipped			Barcodes must be the same
hemocue	Result code of hemocue test.	Numeric	1 - Tested 2 - Not enough blood drawn 3 - Test Failed -9: Skipped		postskip: if hemocue <> 1, skip to fever	
hemoglobin	Record hemoglobin level	Numeric	-9: Skipped	1.0 - 20.0, -9		
fever	Did [[participantsname]] have a fever in the last 48 hours?	Numeric	1 - Yes 0 - No -7: Don't know	as per variable codes		
temperature	Temperature of [[participantsname]]?	Numeric	-8 Refused	30.0 - 45.0, -8		
rdtdone	RDT Done?	Numeric	1 - Yes 0 - No	as per variable codes	postskip: if rdtdone <> 1, skip to meds	
rdtrslt	Result of RDT	Numeric	1 - Positive 2 - Negative -9: Skipped	as per variable codes		
meds	Any medication prescribed to [[participantsname]]?	Numeric	1 - Yes 0 - No	as per variable codes	postskip: if meds = 0, skip to referred	
whichmeds	Which medication was prescribed?	String	1 - AL 2 - Panadol 9 - Other -9: Skipped	as per variable codes		Multiple response question; Comma separated list of each item selected For example if 'Panadol' and 'Other' were both selected, the response would be: "2,9"
al	...AL	Numeric	1 - Yes 0 - No	as per variable codes		Individual responses for the 'decice' question. For example, if 'Panadol' and 'Other' were both selected, the response would be: al = 0 panadol = 1 other = 1
panadol	...Panadol	Numeric	1 - Yes 0 - No	as per variable codes		
other	...Other	Numeric	1 - Yes 0 - No	as per variable codes		
descothermed	Which 'other' medication was used?	String			preskip: if whichmeds 'does not contain' 9, skip	
referred	Was [[participantsname]] referred for additional care?	Numeric	1 - Yes 0 - No	as per variable codes	if referred = 0, skip to stoptime	
whyreferred	Why was [[participantsname]] referred for additional care?	String				
stoptime	End time of interview	DateTime				automatically generated

APPENDIX K: ENTOMOLOGY SURVEY

Household Screening Form

PART 1: Identification

SURVEY code	CLUSTER code	Enumeration area (EA) number
[_____]	[_____|_____|_____]	[_____|_____]

HOUSEHOLD number	Date adult resident FIRST interviewed
[_____|_____]	[_____|_____] / [_____|_____] / [_____|_____] *day* *month* *year*

PART 2: Locating household

Selection criteria	Include	Exclude
1. Dwelling destroyed or not found	[___] No	[___] Yes
2. Household vacant	[___] No	[___] Yes

If any answers are in the EXCLUDE column, exclude from the study. If not, proceed to the next section.

PART 3: Availability of adult resident

	DATE APPROACHED:	Adult available?		IF YES, go to Part 4. IF NO, GIVE REASON*	DATE TO RETURN:
1		1 = Yes	0 = No		
2		1 = Yes	0 = No		
3		1 = Yes	0 = No		
4		1 = Yes	0 = No		xxxxxxxxxxxxxxxx

***1=Not at home, 2=Come back later, 3=Not Interested, 77=Other (Please Specify above)**

PART 4: Able to locate adult resident & consent discussion

Selection criteria	Include	Exclude
3. Able to locate adult	[___] Yes	[___] No
4. Adult is usual resident who was present in this household the previous night	[___] Yes	[___] No
5. Willingness of adult resident to provide informed consent?	[___] Yes	[___] No

If any answers are in the EXCLUDE column, exclude from the study. If not, proceed to the next section.

PART 4: CLOSING OUT THE SCREENING FORM

All criteria for study inclusion met?	Date enrolled
If no, exclude from the study [___] Yes [___] No	[_____|_____]/[_____|_____]/[_____|_____] day month year

PART 5: Assigning Entomology Survey ID

SURVEY code (as above)	CLUSTER code (as above)	Entomology ID number
[_____]	[_____|_____|_____]	[_____|_____]

Staff ID: [_____|_____] **Data entrant (1st):** [_____|_____] **Data entrant (2nd):** [_____|_____]

[_____] [_____|_____|_____] [_____|_____] [_____|_____]____]

Survey code **Cluster code** **Enumeration area (EA) number** **Household ID number**

APPENDIX L. ENTOMOLOGY SURVEY
Informed consent form

Protocol Title:	Uganda PBO Net Study: Impact of long-lasting insecticide treated bednets with and without piperonyl butoxide (PBO) on malaria indicators in Uganda: a cluster-randomised trial
Site of Research:	Eastern and Western Uganda
Principal Investigator:	Prof Janet Hemingway (Prof Sarah Staedke in Uganda)
Version Date:	V4.0, 1 December 2018

Why is this study being done?

Sleeping under a mosquito net is one of the most important ways to prevent malaria. In 2016-2017, the Ugandan Ministry of Health will be leading a campaign to give out mosquito nets around the country. Prof Janet Hemingway from the Liverpool School of Tropical Medicine, and colleagues from the Infectious Diseases Research Collaboration, Ugandan Ministry of Health, London School of Hygiene & Tropical Medicine, and University of California, San Francisco, are carrying out a research study. We are doing this study to find out if the mosquito nets given out by the Ministry of Health are working, and which type of net works the best.

How will this study be done?

Nets will be given out across the entire country, but only certain areas have been selected to take part in this study. In all, 104 health sub-districts in 48 districts in Eastern and Western Uganda have been chosen to take part. These areas have been assigned to receive one of four types of mosquito nets. Assignment to the four groups has been determined by a lottery. The nets that will be given out by the Ugandan Ministry of Health are long-lasting insecticide-treated bed nets that have been approved by the World Health Organisation. To find out how well the mosquito nets work, we will carry out surveys before and after the nets are given out. We will also collect mosquitoes from the area.

Why are we talking to you today?

Your household has been selected to take part in the entomology (mosquito) survey. Today, we would like to explain the purpose of the study, how the survey will be done, and what will be expected of you. You are free to ask questions at any time.

After this consent form is read to you, and your questions have been answered, we will ask you if you want to take part in the survey. You may talk about taking part in the survey with other people, including family and friends. If you agree to take part, we will ask you to sign this consent form. You will get a copy of this form to keep.

What will happen if my household takes part in this survey?

- We will ask you questions about your house, the people who sleep here, and mosquito nets.
- We will enter your house and use an aspirator to capture mosquitoes resting on the walls inside your house.
- We will only visit your house once.

How will my information be used?

The information you share will help us to find out how well the mosquito nets work. Your information will be recorded and will be used to write reports. Information gathered in this study may also be shared, or stored in a data repository, without names, so that other researchers may use it. Anyone assigned to review this study, to check that the study is being done correctly and that the information collected is accurate, will be granted direct access to your information, if needed.

How long will these activities last?

The survey and the mosquito collections will take about 1 hour.

Can I stop being in the survey?

You can decide to stop taking part at any time. Just tell our study personnel right away if you wish to stop the activities.

What risks can I expect if my household takes part in this survey?

Participation in any research study may involve a loss of privacy, but this will likely be very small.

Are there benefits to taking part in this survey?

Today we will remove mosquitos from your house, but there will be no other direct benefit to you from taking part in this survey. However, the knowledge gained from this survey will help researchers and policy-makers understand how best to control malaria in Uganda and elsewhere in Africa.

What other choices do I have if I do not to let my household take part in this survey?

You are free to choose not to allow your household to take part in this survey. If you decide you do not want your household to take part or decide to stop being in the study at any time and for any reason, there will be no penalty to you or your household members.

Will my household's information be kept private?

Information you provide will be recorded, but your name will not be used in any reports. The information obtained from these survey activities will be locked up at our project offices. All personal information will be stored electronically in a secure, password protected database to ensure privacy.

What are the costs of taking part in this survey? Will I be paid for letting my household take part?

You will not be charged for your household to take part in this survey. You will not be paid if your household takes part in this survey.

What are my rights if I allow my household to take part in this survey?

Taking part in this survey is your choice. You may choose either to allow your household to take part or not to take part. If you decide to allow your household to take part in this survey, you may change your mind at any time. No matter what decision you take, there will be no penalty to you or your household members in any way.

What if me or a member of my household is harmed as result of being in this survey?

We do not anticipate any harm resulting from taking part in this survey. If you are harmed or injured due to taking part in this survey, or if you have questions, please contact Dr. Samuel Gonahasa (the Study Coordinator), Prof Sarah Staedke (the Principal Investigator in Uganda) or other members of staff working on this study on telephone number +256 (0) 707 710720. The sponsoring organisations do not have a program to cover your costs if you are hurt or have other bad results.

Who can answer questions about the study?

You can talk to the researchers about any questions or concerns you have about these study activities. Contact Dr. Samuel Gonahasa (the Study Coordinator), Prof Sarah Staedke (the Principal Investigator in Uganda) or other members of staff working on this study on telephone number +256 (0) 707 710 720. If you have any questions, comments or concerns about the study, first talk to the researchers. If for any reason, you do not wish to do this or you still have concerns, you may contact Associate Prof Ponsiano Ocama, the chair of the Makerere University, School of Medicine, Research and Ethics Committee at telephone number +256 (0) 772 421190.

Dissemination of results:

Information on the progress and findings of this study will be shared with the National Malaria Control Division at the Uganda Ministry of Health, and with other key stakeholders.

WHAT YOUR SIGNATURE OR THUMBPRINT MEANS

Your signature or thumbprint below means that you understand the information given to you in this consent form about your household's participation in the survey and agree with the following statements:

- I have read the consent form concerning this survey (or have understood the verbal explanation of the consent form) and I understand what will be required of me if I take part in it.
- My questions concerning this survey have been answered by the person who signed below.
- I understand that at any time, I may withdraw from this survey without giving a reason and without affecting my household member's normal health care and management.
- I agree that my household will take part in this survey.

If you wish to participate in this survey, you should sign or place your thumbprint below

WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM

Name of head of household/another adult resident (printed)

Signature or Fingerprint * of head of household/another adult resident Date

Name of Study Personnel Administering Consent (printed) Position/Title

Signature of Study Personnel Administering Consent Date

Name of Translator (printed)

Signature of Translator Date

* If the head of household (or another adult resident) is unable to read and/or write, an impartial witness should be present during the informed consent discussion. After the written informed consent form is read and explained to the head of household (or another adult resident), and after they have orally consented to their household's participation in the trial, and have either signed the consent form or provided their fingerprint, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by the head of household (or another adult resident), and that informed consent was freely given by the head of household (or another adult resident).

Name of Person Witnessing Consent (printed)

Signature of Person Witnessing Consent Date

Appendix M. Entomology Survey Questionnaire

Entomology Questionaire						
Variable Name	**Question**	**Variable Type**	**Variable Codes**	**Accepted Values**	**Skip**	**Comments**
Part I: Identification						
survey	Survey round	Numeric	1 – Baseline 2 – 6-month 3 – 12-month 4 – 18-24 months	(1-4)		
cluster	Cluster Code	Numeric	Cluster codes	(001 - 104)		HSD = clusters
eanum	EA Number	Numeric	1 to 10	(01-10)		10 EAs to be randomly selected per cluster
hhnum	Household number	Numeric	1 to 999	(001-999)		1 Households to be enrolled per EA
ename	Entomology worker name	String				Entomology worker names
intdate	Date	DateTime				
hhid	Household ID number	Numeric				9 digit code -Survey,Cluster,EA number, HH number
Part II: Household characteristics						
burnyn	Did you burn anything to keep away mosquitoes in the house last night?	numeric	1 = Yes 2 = No 8 = Don't know 9 = Refused to answer - 9=Skipped	as per variable codes		
whatburn	If yes, specify	numeric	1 = Coil 2 = Herbs 3 = Other -9=Skipped	as per variable codes		
whatburnother	Describe other	string		-9 = Skipped		
spray	Did you spray any insecticide in the house last night?	numeric	1 = Yes 2 = No 8 = Don't know 9 = Refused to answer -9=Skipped	as per variable codes		
closewindow	Did you close the windows / doors to keep out mosquitoes last night	numeric	1 = Yes 2 = No 8 = Don't know 9 = Refused to answer -9=Skipped	as per variable codes		
closetime	If yes, at what time did you close the windows / doors?	DateTime		-9 = Skipped		
airbricks	Airbricks above windows?	numeric	1 = Yes 2 = No (if no skip to question 11) 8 = Don't know	as per variable codes	if airbricks=2 , skip to swindows	
scrairbricks	Screens over airbricks?	numeric	1 = Yes (all) 2 = No (or not all) 8 = Don't know	as per variable codes		

Appendix M. Entomology Survey Questionnaire

Variable Name	Question	Variable Type	Variable Codes	Accepted Values	Skip	Comments
sdoors	Screened external doors?	numeric	1 = Yes (all) 2 = No (or not all) 8 = Don't know	as per variable codes		
ceiling	A ceiling	numeric	1 = Yes (all) 2 = No (or not all) 8 = Don't know	as per variable codes		
result	**Result**	numeric	1 = Completed 2 = Not at home 3 = Refused to answer 4 = Incapacitated 5 = Other (specify)	as per variable codes		
otherresult	**Specify Other result**	string				
totvisit	**Total number of visits made to household**	numeric				
Data record of prokopak collections						
nonanophfem	Number of Female Non-Anopheline	numeric				
nonanophmal	Number of Male Non-Anopheline	numeric				
gambiaef	Number of female anopheles gambiae	numeric				
gambiaem	Number of male anopheles gambiae	numeric				
funestusf	Number of female Anopheles funestus	numeric				
funestusm	Number of male Anopheles funestus	numeric				
othanophfem	Number of female Anopheles -Other/Unidentified	numeric				
othanophmal	Number of male Anopheles -Other/Unidentified	numeric				
	Female Anopheles mosquitoes :this section will be repeated for each female anopheles mosquito					
idnumber	ID number of mosquito	numeric				
species	Species	string	GA = Anopheles gambiae FU = Anopheles funestus AO= Unknown/Other	as per variable codes		
bfstatus	Blood fed status	string	U = unfed HG = half gravid G = Gravid BF = blood fed	as per variable codes		

[_____] [_____|_____|_____] [_____|_____] [_____|_____]____]

Survey code **Cluster code** **Enumeration area (EA) number** **Household ID number**

APPENDIX N. ENTOMOLOGY SURVEY FOR PHENOTYPIC MONITORING
Informed consent form

Protocol Title:	Uganda PBO Net Study: Impact of long-lasting insecticide treated bednets with and without piperonyl butoxide (PBO) on malaria indicators in Uganda: a cluster-randomised trial
Site of Research:	Eastern and Western Uganda
Principal Investigator:	Prof Janet Hemingway (Prof Sarah Staedke in Uganda)
Version Date:	V2.0, 1 December 2018

Why is this study being done?

Sleeping under a mosquito net is one of the most important ways to prevent malaria. In 2016-2017, the Ugandan Ministry of Health will be leading a campaign to give out mosquito nets around the country. Prof Janet Hemingway from the Liverpool School of Tropical Medicine, and colleagues from the Infectious Diseases Research Collaboration, Ugandan Ministry of Health, London School of Hygiene & Tropical Medicine, and University of California, San Francisco, are carrying out a research study. We are doing this study to find out if the mosquito nets given out by the Ministry of Health are working, and which type of net works the best.

How will this study be done?

Nets will be given out across the entire country, but only certain areas have been selected to take part in this study. In all, 104 health sub-districts in 48 districts in Eastern and Western Uganda have been chosen to take part. These areas have been assigned to receive one of four types of mosquito nets. Assignment to the four groups has been determined by a lottery. The nets that will be given out by the Ugandan Ministry of Health are long-lasting insecticide-treated bed nets that have been approved by the World Health Organisation. To find out how well the mosquito nets work, we will carry out surveys before and after the nets are given out. We will also collect mosquitoes from the area.

Why are we talking to you today?

Your household has been selected to take part in the entomology (mosquito) survey. Today, we would like to explain the purpose of the study, how the survey will be done, and what will be expected of you. You are free to ask questions at any time.

After this consent form is read to you, and your questions have been answered, we will ask you if you want to take part in the survey. You may talk about taking part in the survey with other people, including family and friends. If you agree to take part, we will ask you to sign this consent form. You will get a copy of this form to keep.

What will happen if my household takes part in this survey?

- We will ask you questions about your house, the people who sleep here, and mosquito nets.
- We will enter your house and use an aspirator to capture mosquitoes resting on the walls inside your house.
- We may visit your house several times during the next few weeks.
- You may be asked to close the doors and windows before and during the collections.

How will my information be used?

The information you share will help us to find out how well the mosquito nets work. Your information will be recorded and will be used to write reports. Information gathered in this study may also be shared, or stored in a data repository, without names, so that other researchers may use it. Anyone assigned to review this study, to check that the study is being done correctly and that the information collected is accurate, will be granted direct access to your information, if needed.

How long will these activities last?

The mosquito collections will take about 15 minutes on each visit.

Can I stop being in the survey?

You can decide to stop taking part at any time. Just tell our study personnel right away if you wish to stop the activities.

What risks can I expect if my household takes part in this survey?

Participation in any research study may involve a loss of privacy, but this will likely be very small.

Are there benefits to taking part in this survey?

Today we will remove mosquitos from your house, but there will be no other direct benefit to you from taking part in this survey. However, the knowledge gained from this survey will help researchers and policy-makers understand how best to control malaria in Uganda and elsewhere in Africa.

What other choices do I have if I do not to let my household take part in this survey?

You are free to choose not to allow your household to take part in this survey. If you decide you do not want your household to take part or decide to stop being in the study at any time and for any reason, there will be no penalty to you or your household members.

Will my household's information be kept private?

Information you provide will be recorded, but your name will not be used in any reports. The information obtained from these survey activities will be locked up at our project offices. All personal information will be stored electronically in a secure, password protected database to ensure privacy.

What are the costs of taking part in this survey? Will I be paid for letting my household take part?
You will not be charged for your household to take part in this survey. You will not be paid if your household takes part in this survey.

What are my rights if I allow my household to take part in this survey?
Taking part in this survey is your choice. You may choose either to allow your household to take part or not to take part. If you decide to allow your household to take part in this survey, you may change your mind at any time. No matter what decision you take, there will be no penalty to you or your household members in any way.

What if me or a member of my household is harmed as result of being in this survey?
We do not anticipate any harm resulting from taking part in this survey. If you are harmed or injured due to taking part in this survey, or if you have questions, please contact Dr. Samuel Gonahasa (the Study Coordinator), Prof Sarah Staedke (the Principal Investigator in Uganda) or other members of staff working on this study on telephone number +256 (0) 707 710720. The sponsoring organisations do not have a program to cover your costs if you are hurt or have other bad results.

Who can answer questions about the study?
You can talk to the researchers about any questions or concerns you have about these study activities. Contact Dr. Samuel Gonahasa (the Study Coordinator), Prof Sarah Staedke (the Principal Investigator in Uganda) or other members of staff working on this study on telephone number +256 (0) 707 710720. If you have any questions, comments or concerns about the study, first talk to the researchers. If for any reason, you do not wish to do this or you still have concerns, you may contact Associate Prof Ponsiano Ocama, the chair of the Makerere University, School of Medicine, Research and Ethics Committee at telephone number +256 (0) 772 421190.

Dissemination of results:
Information on the progress and findings of this study will be shared with the National Malaria Control Division at the Uganda Ministry of Health, and with other key stakeholders.

WHAT YOUR SIGNATURE OR THUMBPRINT MEANS
Your signature or thumbprint below means that you understand the information given to you in this consent form about your household's participation in the survey and agree with the following statements: • I have read the consent form concerning this survey (or have understood the verbal explanation of the consent form) and I understand what will be required of me if I take part in it. • My questions concerning this survey have been answered by the person who signed below. • I understand that at any time, I may withdraw from this survey without giving a reason and without affecting my household member's normal health care and management. • I agree that my household will take part in this survey.
If you wish to participate in this survey, you should sign or place your thumbprint below **WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM**

Name of head of household/another adult resident (printed)

Signature or Fingerprint * of head of household/another adult resident Date

Name of Study Personnel Administering Consent (printed) Position/Title

Signature of Study Personnel Administering Consent Date

Name of Translator (printed)

Signature of Translator Date

* If the head of household (or another adult resident) is unable to read and/or write, an impartial witness should be present during the informed consent discussion. After the written informed consent form is read and explained to the head of household (or another adult resident), and after they have orally consented to their household's participation in the trial, and have either signed the consent form or provided their fingerprint, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by the head of household (or another adult resident), and that informed consent was freely given by the head of household (or another adult resident).

Name of Person Witnessing Consent (printed)

Signature of Person Witnessing Consent Date