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Impact of long-lasting insecticide treated bednets with and without piperonyl butoxide (PBO) on malaria indicators in Uganda

Submission date
20/01/2017

Recruitment status
No longer recruiting

Registration date
14/02/2017

Overall study status
Completed

Last Edited
25/06/2024

Condition category
Infections and Infestations

[X] Prospectively registered

[X] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol

Background and study aims

Malaria is an infectious disease which is common in tropical and subtropical countries, caused by a microscopic parasite which is spread from person to person by mosquitos. Every year, millions of people become infected with malaria parasites and hundreds of thousands of people die from the infection. Many of these infectious bites happen at night, when people are sleeping inside their homes. Over the last 15 years, malaria control programs have been scaled-up dramatically across Africa, resulting in an estimated 40% decrease in the incidence of disease between 2000 and 2015. 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. 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 using two or more drugs with different modes of action (artemisinin-based combination therapy; ACTs), has increased substantially. However, overall progress toward control of malaria in Uganda has been slow, and recent evidence suggests that gains may be fragile in high transmission areas, if effective control measures are not sustained. LLINs have been shown to be an effective malaria prevention strategy, however they are not always effective as many mosquitos are resistant to the insecticide (pyrethroid insecticide) that the nets are treated with. One possible approach to resolving this problem is to use a combination of chemicals to treat nets. The aim of this study is to compare four nets that are given out by the Ministry of Health to find out which type of net works the best.

Who can participate?

Households with at least one adult resident and one child aged 2-10 years.

What does the study involve?

Nets are 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. In each area, households receive one of four long-lasting insecticide-treated bed nets that have been

approved by the World Health Organisation. To find out how well the mosquito nets work and how they are being used, surveys are carried out before and after the nets are given out.

What are the possible benefits and risks of participating?
There are no notable benefits or risks involved with participating.

Where is the study run from?
The study is run from Infectious Diseases Research Collaboration and takes place withing 48 districts in Eastern and Western Uganda.

When is study starting and how long is it expected to run for?
January 2017 to December 2020 (updated 12/05/2020, previously: September 2020; updated 22 /10/2019, previously: December 2019)

Who is funding the study?
Against Malaria Foundation (UK)

Who is the main contact?
Professor Martin Donnelly
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Contact information

Type(s)
Public

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
PBO-Ug1

Study information

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

Acronym
Uganda PBO Net Study

Study objectives
The aim of this study is to determine whether 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) in Uganda.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Makerere University, School of Health Sciences Research and Ethical Committee, 20/12/2016, ref: 2016-133
2. Liverpool School of Tropical Medicine: Research Ethics Committee, 08/02/2017, ref 16-072
3. London School of Hygiene & Tropical Medicine: Observational/Interventions Research Ethics Committee, 20/2/2017, ref:12019

Amendments:
1. SOM-REC Uganda, 31/08/2017
2. London School of Hygiene and Tropical Medicine, 01/11/2017
3. Liverpool School of Tropical Medicine, 06/10/2017

Study design
Cluster randomized trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Malaria

Interventions
A total of 104 clusters (defined as a health sub-district) have been included in the study, covering 48 districts in Eastern and Western Uganda. Clusters are randomised by a member of the study team who is not based in Uganda, and who will not be directly involved in the field work to one of four groups, who receive different types of LLINs. Variation in the production capacity and the number of nets available for each manufacturer, is considered in the randomisation process, resulting in unequal numbers of clusters being allocated to each of the 4 study arms.

Group 1: PermaNet 2.0
Group 2: PermaNet 3.0
Group 3: Olyset Net
Group 4: Olyset Plus

The Ugandan National Malaria Control Programme and other stakeholders will take the lead on delivering the LLINs to health sub districts 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. Households in all intervention arms will receive 1 LLIN per 2 household members, rounded up in the case of an uneven number of household members. The bednets are deployed over the sleeping spaces in each household and are used to reduce the number of potentially malaria infectious bites received by household members whilst asleep. Social behaviour change communication (SBCC)/information, education, communication (IEC) will accompany net distribution to increase compliance. 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. 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.

The evaluation will include repeated cross-sectional community surveys to gather information on net survivorship and use, and parasite prevalence in children over 5 years of age, entomological surveillance for insecticide resistance monitoring, and assessment of net durability and bio-efficacy at 12 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 years (24 months).

Intervention Type
Other

Primary outcome(s)
Parasite prevalence (defined as the proportion of thick blood smears that are positive for asexual parasites) in children aged 2-10 years is assessed using cross-sectional surveys at baseline (prior to distribution of the nets) and up to 3 times after nets are distributed, 6, 12 and 18-24 months after distribution.

Key secondary outcome(s))
1. Prevalence of anaemia and mean haemoglobin in children aged 2-10 years. Anaemia will be defined as a haemoglobin concentration (g/dl) less than 11 in children 24-59 months and less than 11.5 in child 5-10 years. Haemoglobin concentration will be measured on site using a drop of blood collected from a finger-prick. The test will be conducted during the cross-sectional surveys using a battery-operated portable HemoCue analyzer (HemoCue, Anglom, Sweden) at baseline (prior to distribution of the nets) and up to 3 times after nets are distributed, 6, 12 and 18-24 months after distribution
2. Frequency of molecular markers associated with insecticide resistance in the primary malaria vector will be conducted on DNA extracted from mosquitoes collected in each of the study clusters during the cross-sectional surveys and will utilise PCR and rtPCR approaches at baseline (prior to distribution of the nets) and up to 3 times after nets are distributed, 6, 12 and 18-24 months after distribution
3. Prevalence of phenotypic insecticide resistance in 12 study clusters will be assessed using standard World Health Organization (WHO) tests of insecticide resistance performed during the

cross-sectional surveys at baseline (prior to distribution of the nets) and up to 3 times after nets are distributed, 6, 12 and 18-24 months after distribution
4. LLIN survivorship, durability and bio-efficacy will be assessed during a cross-sectional survey conducted 12 months after distribution. The tests will follow WHO guidelines: survivorship defined as the presence or absence of a LLIN in a survey household; durability is defined based on the number and area of holes in the LLIN; bio-efficacy is defined based the proportion of known susceptible mosquitoes surviving exposure to the LLIN netting.

Completion date
31/12/2020

Eligibility

Key inclusion criteria
Household inclusion criteria:
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

Children inclusion criteria:
1. Child aged 5 years and over
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

Participant type(s)
Other

Healthy volunteers allowed
No

Age group
Child

Lower age limit
2 years

Sex
All

Total final enrolment
38751

Key exclusion criteria
Household exclusion criteria:
1. Dwelling destroyed or not found
2. Household vacant
3. No adult resident home on more than 3 occasions

Children exclusion criteria:
Child not home on day of survey

Date of first enrolment
16/03/2017

Date of final enrolment
30/04/2020

Locations

Countries of recruitment
Uganda

Study participating centre
Infectious Diseases Research Collaboration
Plot 2C Nakasero Hill Road
Kampala
Uganda
none

Sponsor information

Organisation
Liverpool School of Tropical Medicine

ROR
https://ror.org/03svjbs84

Funder(s)

Funder type
Charity

Funder Name
Against Malaria Foundation

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Professor Sarah Staedke (sarah.staedke@lshtm.ac.uk)

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	baseline results	13/11/2018		Yes	No
Results article	baseline results	12/03/2019	15/03/2019	Yes	No
Results article	provisional results	24/06/2019	22/10/2019	Yes	No
Results article	results	18/04/2020	21/04/2020	Yes	No
Results article	final results	26/09/2022	30/09/2022	Yes	No
Results article		24/06/2024	25/06/2024	Yes	No
Protocol article	protocol	03/06/2019	05/06/2019	Yes	No
Participant information sheet	version V2	01/02/2017	21/02/2017	No	Yes
Preprint (other)	Plasmodium infection prevalence and genotypic markers of insecticide resistance in Anopheles vectors from 48 districts of Uganda	05/08/2023	14/08/2023	No	No