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Choice of anti-malarial drugs for chemoprevention

Submission date
15/07/2026

Recruitment status
Not yet recruiting

Registration date
28/08/2026

Overall study status
Ongoing

Last Edited
17/11/2026

Condition category
Infections and Infestations

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Malaria is a major health problem in Malawi and other parts of sub-Saharan Africa. Children under 5 years of age are especially at risk of becoming seriously ill or dying from the disease. Medicines can be given regularly to prevent malaria, but it is not yet clear which drugs work best in East and Southern Africa, where patterns of malaria transmission and drug resistance differ from other regions.

This study aims to find out whether three antimalarial medicines, hydroxychloroquine, amodiaquine and sulfadoxine-pyrimethamine, can safely and effectively prevent malaria in young children. The researchers will compare these medicines with placebo (dummy treatment) and assess whether they reduce malaria illness, malaria-related hospital admissions, and other health problems. The results will help guide future malaria prevention policies in Malawi and similar countries.

Who can participate?
Children aged 3 months to 59 months can take part if they:
• Live in the study area and are expected to remain there during the study period
• Have a parent or guardian who gives consent for participation
• Have a parent or guardian willing to follow the study requirements, including attending a designated health centre if the child develops malaria symptoms

Some children cannot participate, including those with known allergies to the study medicines, certain medical conditions, or specific medicines that could interact with the study treatments.

What does the study involve?
The study plans to enrol about 6,900 children in Mwanza District, Malawi.

Participants will be randomly assigned to receive one of several combinations of study medicines or matching placebos. Neither the families nor the study team will know which treatment a child receives during the study.

The study medicines will be taken by mouth once each month for 5 months. Some medicines will be given for 3 consecutive days each month, while others will be given as a single dose.

Children will attend scheduled study visits where researchers will monitor their health, record any illnesses, and measure growth. Blood samples will be collected to test for malaria infection, measure haemoglobin levels, assess drug levels in the body, and study markers of malaria drug resistance.

Researchers will follow participants during the treatment period and for several months afterwards to record malaria episodes, hospital admissions, and other health outcomes.

What are the possible benefits and risks of participating?
Children taking part may benefit from protection against malaria, although this cannot be guaranteed. Participants will receive regular health assessments, and any illnesses identified during the study can be assessed by the study team.

As with any medicine, there is a risk of side effects. Some children may experience adverse reactions to the study drugs, although participants will be monitored closely for safety throughout the study. There may also be some discomfort from blood sample collection.

The information gained from the study could help improve malaria prevention for children in Malawi and other countries in the future.

Where is the study run from?
The study is run by the Malawi Liverpool Wellcome Programme and the Liverpool School of Tropical Medicine.
Study activities will take place in Mwanza District, Malawi, including Mwanza District Hospital, Kunenekude Health Centre, Thambani Health Centre, and Tulonkhondo Health Centre.

When is the study starting and how long is it expected to run for?
The study is expected to begin enrolling participants in November 2026. The overall study is expected to run until December 2027.

Who is funding the study?
The study is funded by the GiveWell Community Foundation, United States of America.

Who is the main contact?
Dr Donnie Mategula
donnie.mategula@lstmed.ac.uk

Contact information

Type(s)
Principal investigator, Scientific, Public

Contact name
Dr Donnie Mategula

ORCID ID
https://orcid.org/0000-0001-7109-9042

Contact details
Malawi Liverpool Wellcome Programme, PO box 30096
Blantyre
Malawi
NA
+265 995415277
donnie.mategula@lstmed.ac.uk

Type(s)
Scientific, Principal investigator, Public

Contact name
Dr Lauren Cohee

ORCID ID
https://orcid.org/0000-0002-7575-630X

Contact details
Liverpool School of Tropical Medicine
Pembroke Place
Liverpool
United Kingdom
L3 5QA
+44 (0) 151 351 7674
Lauren.Cohee@lstmed.ac.uk

Type(s)
Public, Scientific

Contact name
Dr James Watson

ORCID ID
https://orcid.org/0000-0001-5524-0325

Contact details
Big Data Institute, Old Road Campus
Oxford
United Kingdom
OX3 7LF
+44 7424 972469
james.watson@ndm.ox.ac.uk

Additional identifiers

Study information

Scientific Title

Drug choice for malaria chemoprevention: comparison of hydroxychloroquine or amodiaquine with or without sulfadoxine-pyrimethamine in Malawi - a factorial, individually randomised, double blind, placebo controlled trial

Acronym
CHAMP Drug

Study objectives
Primary objectives:
Randomisation 1 : To evaluate the effect of amodiaquine and hydroxychloroquine each compared to placebo on the prevention of hospitalization due to malaria during the intervention period (day 0-150).
Randomisation 1 : To evaluate the effect of amodiaquine and hydroxychloroquine each compared to placebo on the incidence of uncomplicated clinical malaria in children under five years of age during the intervention period (day 0-150).

Randomisation 2 : To evaluate the efficacy of SP versus placebo on the prevention of uncomplicated clinical malaria during the intervention period (day 0-150).

Secondary objectives:
Randomisation 1: Comparison of hydroxychloroquine or amodiaquine versus placebo
1.1 To evaluate the effect of hydroxychloroquine or amodiaquine, compared with placebo, on all-cause hospital admission during the intervention period (days 0-150)
1.2 To evaluate the effect of hydroxychloroquine or amodiaquine, compared with placebo, on all-cause mortality during the intervention period (days 0-150)
1.3 To evaluate the effect of hydroxychloroquine or amodiaquine, compared with placebo, on the incidence of severe malaria, as defined by WHO criteria, during the intervention period (days 0-150)
1.4 To assess the impact of hydroxychloroquine or amodiaquine, compared with placebo, on malaria transmission potential, using gametocytaemia as a proxy indicator, during the intervention period (days 0-150)
1.5 To assess the impact of hydroxychloroquine or amodiaquine, compared with placebo, on the number of hospitalisation events due to malaria during the post-intervention period (days 150-365)
1.6 To assess the impact of hydroxychloroquine or amodiaquine, compared with placebo, on the number of uncomplicated clinical malaria events, defined as RDT positive with fever or a history of fever, during the post-intervention period (days 150-365)

Randomisation 2: Comparison of sulfadoxine-pyrimethamine versus placebo
2.1 To evaluate the effect of sulfadoxine-pyrimethamine, compared with placebo, on non-malaria outcomes, including:
2.1.1 All-cause hospital admission during the intervention period (days 0-150) and the post-intervention period (days 150-365)
2.1.2 All-cause mortality during the intervention period (days 0-150) and the post-intervention period (days 150-365)
2.1.3 Number of infections requiring antibacterial or antimalarial treatment during the intervention period (days 0-150)
2.1.4 Change in haemoglobin concentration during the intervention period (days 0-150)
2.1.5 Changes in weight, height, and weight-for-height z-scores during the intervention period (days 0-150)

These apply to both randomizations:
3.1 To characterise the pharmacometric relationship between antimalarial drug exposure, including parent drug and relevant metabolites, and prevention of blood-stage infection
3.2 To assess the safety and tolerability of chemoprevention regimens during the intervention period (days 0-150)
3.3 To investigate the relationship between molecular markers of antimalarial drug resistance and the efficacy of chemoprevention regimens

Ethics approval required
Ethics approval required

Ethics approval(s)
1. Approved 09/10/2025, National Health Sciences Research Committee (C/O Ministry of Health, Research Unit P.O. Box 30377 Capital City, Lilongwe, -, Malawi; +265 1 789 321; reseearch@mail.gov.mw), ref: 25/02/4580

2. Approved 08/03/2026, Liverpool School of Tropical Medicine (Pembroke Place, Liverpool, L3 5QA, United Kingdom; +44 (0)151 705 3100; lstmgov@lstmed.ac.uk), ref: 0348

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Placebo

Assignment
Factorial

Purpose
Prevention

Study type(s)

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

Interventions
This is a factorial, individually randomised, double-blind, placebo-controlled trial with six treatment arms arising from two independent randomisations administered concurrently. All study drugs are given orally at monthly intervals for five months (~days 0, 30, 60, 90, and 120).

Randomisation 1 allocates participants in a 1:1:1 ratio to:
- Hydroxychloroquine: 154 mg base per day (children aged over 12 months) or 77 mg base per day (children aged under 12 months) for 3 consecutive days per monthly cycle
- Amodiaquine: 153 mg base per day (children aged over 12 months) or 76.5 mg base per day

(children aged under 12 months) for 3 consecutive days per monthly cycle
- Matching placebo: identical in appearance to active drug, for 3 consecutive days per monthly cycle

Randomisation 2 allocates participants within each Randomisation 1 arm in a 1:1 ratio to:
- Sulfadoxine-pyrimethamine (SP): 500 mg/25 mg (children aged over 12 months) or 250 mg/12.5 mg (children aged under 12 months) as a single dose per monthly cycle
- Matching placebo: single dose per monthly cycle

This produces six treatment combinations: HCQ+SP, HCQ+placebo, AQ+SP, AQ+placebo, placebo+SP, and double placebo.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Hydroxychloroquine, amodiaquine, sulfadoxine-pyrimethamine

Primary outcome(s)
1. Number of hospitalisation events due to malaria measured using clinical diagnosis of malaria, malaria rapid diagnostic test (RDT), and hospital inpatient admission registers at during the intervention period (days 0-150)

2. Number of uncomplicated clinical malaria events measured using Malaria rapid diagnostic test (RDT) and clinical assessment for fever or history of fever at during the intervention period (days 0-150)

Key secondary outcome(s)
1. Number of all-cause hospital admissions measured using hospital inpatient admission registers and discharge summaries at Mwanza District Hospital and study health centres, supplemented by caregiver-reported admissions captured on electronic case report forms (eCRFs) at during the intervention period (days 0-150)

2. Number of all-cause hospital admissions measured using hospital inpatient admission registers and discharge summaries at Mwanza District Hospital and study health centres, supplemented by caregiver-reported admissions captured on electronic case report forms (eCRFs) at during the post-intervention period (days 150-365)

3. All-cause mortality measured using death notification via community health workers and caregiver report, with review of health facility death registers and verbal autopsy for deaths occurring outside hospital at during the intervention period (days 0-150)

4. All-cause mortality measured using death notification via community health workers and caregiver report, with review of health facility death registers and verbal autopsy for deaths occurring outside hospital at during the post-intervention period (days 150-365)

5. Incidence of severe malaria measured using clinical assessment and laboratory investigations according to WHO criteria for severe malaria at during the intervention period (days 0-150)

6. Gametocytaemia prevalence measured using blood film microscopy and PCR at during the intervention period (days 0-150)

7. Number of malaria hospitalisation events measured using clinical diagnosis of malaria, malaria rapid diagnostic test (RDT), and review of hospital inpatient admission registers and discharge summaries at Mwanza District Hospital and study health centres at during the post-intervention period (days 150-365)

8. Number of uncomplicated clinical malaria events measured using malaria rapid diagnostic test (RDT) and clinical assessment for fever or history of fever at during the post-intervention period (days 150-365)

9. Number of infections requiring antibacterial or antimalarial treatment measured using review of electronic case report forms (eCRFs) documenting clinician-prescribed antibacterial or antimalarial treatments recorded at scheduled and unscheduled study visits at during the intervention period (days 0-150)

10. Change in haemoglobin concentration measured using point-of-care haemoglobin measurement (HemoCue) at during the intervention period (change in concentration between the days 0 and 150

11. Pharmacometric relationship between drug exposure and prevention of blood-stage infection measured using drug concentration measurement from dried blood spots and parasite detection by microscopy and PCR at during the intervention period (days 0-150)

12. Molecular markers of antimalarial drug resistance in P. falciparum measured using quantitative PCR (qPCR) genotyping of blood samples collected during the intervention period (days 0-150) and at clinical episodes at during the intervention period (days 0-150) and at clinical episodes

13. Adverse events and serious adverse events measured using clinical assessment and structured adverse event reporting at during the intervention period (days 0-150)

14. Changes in weight, height, and weight-for-height z-scores measured using standardised anthropometric assessment at during the intervention period (measured at baseline, days 0 and day 150)

Completion date
31/12/2027

Eligibility

Key inclusion criteria
1. Children who will be between 3-59 months at the time of planned first study drug administration
2. Resident in the study area with plans to remain for the duration of the study
3. Consent to participate in the study obtained
4. Willingness and ability of the child’s guardians to comply with the study protocol for the duration of the study including attending a designated health centre if their child has malaria symptoms during the data collection period

Healthy volunteers allowed
Yes

Age group
Child

Lower age limit
3 Months

Upper age limit
59 Months

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Known allergy or history of severe adverse reactions to any study drugs provided (SP, HCQ or AQ)
2. Receiving a sulfa-based medication for long-term treatment or prophylaxis, including co-trimoxazole (trimethoprim–sulfamethoxazole).
3. Children with HIV taking efavirenz
4. Children with epilepsy or psoriasis

Date of first enrolment
23/11/2027

Date of final enrolment
19/12/2027

Locations

Countries of recruitment
Malawi

Study participating centre
Malawi Liverpool Wellcome Programme
Malawi Liverpool Wellcome Programme, Chipatala Avenue, PO Box 30096
Blantyre
Malawi

Study participating centre

Mwanza District Hospital, Mwanza District, Malawi
Mwanda District Hospital, PO Box 80, Mwanza
Mwanza
Malawi

Study participating centre
Kunenekude Health Centre, Mwanza District, Malawi
Mwanza
Malawi

Study participating centre
Thambani Health Centre, Mwanza District, Malawi
Mwanza
Malawi

Study participating centre
Tulonkhondo Health Centre, Mwanza District, Malawi
Mwanza
Malawi

Sponsor information

Organisation
Liverpool School of Tropical Medicine

ROR
https://ror.org/03svjbs84

Funder(s)

Funder type

Funder Name
GiveWell Community Foundation

Alternative Name(s)
GIVEWELL COMMUNITY FOUNDATION, INC., Givewell Community Foundation Inc, GWCF

Funding Body Type
Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be deposited in a controlled-access repository following completion of the study. Details of the specific repository will be confirmed and updated at a later date.

Type of data: Pseudonymised individual participant data (IPD) including clinical outcomes (malaria-related hospitalisation, clinical malaria episodes, adverse events), laboratory results (blood slides, filter paper analyses, plasma), sociodemographic data, drug exposure measures, and molecular markers of antimalarial resistance. Direct identifiers (name, date of birth, household GPS coordinates, and mobile phone numbers) are stored separately from analysis datasets and will not be shared.

When available and for how long: Pseudonymised datasets will be made available following publication of the primary trial results. Data will remain available for the duration of the study's 25-year retention period, in accordance with clinical trial regulatory requirements.

Access criteria and with whom: Data will be shared with qualified researchers who submit a scientifically sound research proposal, subject to approval by the study team and relevant ethics and data governance bodies. Access will be governed through the repository's access management system and formal data-sharing agreements.
Types of analyses: Secondary analyses consistent with the study objectives, including epidemiological analyses, drug efficacy modelling, resistance marker analyses, and health outcomes research.

Mechanism: Researchers will submit access requests through the designated repository platform. Approved requestors will receive pseudonymised datasets under a signed data-sharing agreement specifying permitted uses, security obligations, and conditions of publication.

Consent: Written informed consent will be obtained from the caregiver of each participant prior to enrolment. Participants will be informed of the possibility of pseudonymised data being shared with collaborating institutions for approved research purposes.

Data anonymisation: All datasets for sharing will be pseudonymised prior to transfer, with direct identifiers removed and stored separately under restricted access at MLW. Re-identification is not possible without the linking code held securely at MLW.

Ethical and legal restrictions: Data sharing is subject to compliance with Malawi National Health Sciences Research Committee ethical approval and relevant data protection regulations,

including those applicable to LSTM as joint data controller. Shared data may not be used for purposes beyond those specified in the approved data-sharing agreement.

Other comments: Data will be collected using ODK eCRFs on secure encrypted Android tablets, transmitted to the MLW ODK Central server, and protected by multi-layered access controls at device, form, and server levels. Biological samples transferred to MORU/University of Oxford for approved analyses are governed by a material transfer and data-sharing agreement between the institutions.

IPD sharing plan summary

Stored in non-publicly available repository