ISRCTN16218936 https://doi.org/10.1186/ISRCTN16218936

The enhanced antenatal care bundle to improve maternal and newborn outcomes in Malawi and Zambia: a multi-country, parallel cluster-randomized trial

Submission date
03/03/2025

Recruitment status
Recruiting

Registration date
13/03/2025

Overall study status
Ongoing

Last Edited
08/07/2025

Condition category
Pregnancy and Childbirth

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

Plain English summary of protocol

Background and study aims

Even though many pregnant women in Malawi and Zambia receive regular healthcare during pregnancy and give birth in health centres, there are still many women who die from complications during childbirth. We have reliable evidence that these maternal deaths can be prevented with good quality healthcare that follows the guidance of the World Health Organisation (WHO). The WHO recommend that all pregnant women have regular health visits during pregnancy; the WHO also recommends that healthcare staff perform specific checks during each pregnancy visit so that any problems during pregnancy are found and treated before they become life-threatening to women or their babies.

This study will look at the healthcare pregnant women receive during their pregnancy and when they give birth in primary health centres in Malawi and Zambia. The researchers will compare important events during pregnancy and birth in facilities where staff provide women with standard pregnancy care versus those same important events in facilities where staff deliver an improved pregnancy healthcare service. The improved pregnancy health services include training for staff and pregnant women and supplies for health facilities.

Who can participate?

This study will include health facilities rather than individuals. The health centres will have 700 - 2000 visits per year from pregnant women. The health centres will also be able to provide emergency pregnancy care, provide services for free to pregnant women, and complete an assessment process to ensure that the site is ready for the trial.

What does the study involve?

The study will start with a baseline phase, where the researchers will measure key events during pregnancy and childbirth. Next, the facilities will be randomly assigned to either continue providing their standard pregnancy care with basic supplies or to deliver the study intervention to improve pregnancy care, with training for staff and pregnant women and with basic supplies.

What are the possible benefits of participating?
The researchers expect that the health centres receiving the study intervention to improve pregnancy will be better able to provide care that meets WHO standards. They expect these health facilities to have better results for women and babies in terms of avoiding complications during pregnancy that lead to preventable deaths amongst women.

Where is the study run from?
This study is run from the Malawi Liverpool Wellcome Institute in Blantyre (Malawi) and from Lusaka Apex Medical University in Lusaka (Zambia). The study teams also have support from the University of Liverpool (UK).

When is the study starting and how long will it run for?
August 2022 to July 2026

Who is funding the study?
National Institute for Health and Social Care Research (UK)

Who is the main contact?
safemotherhood@liverpool.ac.uk

Contact information

Type(s)
Principal investigator

Contact name
Prof David Lissauer

ORCID ID
https://orcid.org/0000-0002-7878-2327

Contact details
Liverpool Women's Hospital - First Floor
University of Liverpool Dept. of Women's and Children's Health
Crown Street
Liverpool
United Kingdom
L8 7SS
+44 (0)1517942064
david.lissauer@liverpool.ac.uk

Type(s)
Scientific

Contact name
Prof Alinane Nyondo Mipando

ORCID ID
https://orcid.org/0000-0002-3572-3810

Contact details

Private Bag 360
Chichiri
Blantyre
Malawi
BT3
+265 (0)1810911
lmipando@kuhes.ac.mw

Type(s)
Public

Contact name
Ms Nancy Medley

Contact details
Liverpool Women's Hospital
University of Liverpool Dept. of Women's and Children's Health
Crown Street
Liverpool
United Kingdom
L8 7SS
+44 (0)1517942064
nmedley2@liverpool.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
University of Liverpool Sponsor UoL001883

Study information

Scientific Title
The enhanced antenatal care bundle to improve maternal and newborn outcomes in pregnant women attending maternity health services in Malawi and Zambia: a multi-country, parallel cluster-randomised trial

Acronym
ENHANCE

Study objectives
ENHANCE will provide a comprehensive bundle of measures carefully developed for primary health centres in resource-limited settings, to support the consistent and comprehensive delivery of all aspects of antenatal care according to WHO guidelines. ENHANCE includes tools, leadership, mentorship, task shifting and basic antenatal care supplies.

This study will determine whether an ENHANCE strategy compared with standard antenatal care is acceptable to pregnant women and healthcare staff; whether ENHANCE improves the implementation of antenatal care services according to WHO guidance; and whether ENHANCE improves both the quality of antenatal care and the maternal and neonatal clinical outcomes for women and babies who receive the intervention.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. approved 24/02/2025, The University of Liverpool Ethics Committee (Foundation Building, Liverpool, L69 7ZX, United Kingdom; +44 (0)151 794 2000; research.ethics@liverpool.ac.uk), ref: 15682

2. approved 05/12/2024, College of Medicine Research Ethics Committee (Private Bag 360 Chichiri, Blantyre, 3, Malawi; +265 (0)1874377; comrec@medcol.mw), ref: P.10/24-1155

3. approved 25/10/2024, Lusaka Apex Medical University Biomedical Research Ethics Committee (Foxdale Campus Plot No. 3073, Lusaka, PO Box 31909, Zambia; +260 (0)979452488; lamubrec@lamu.edu.zm), ref: 0294/25/10/2024

4. approved 23/01/2025, National Health Research Authority (Lot No. 18961/M off Kasama Rd, Chalala Lusaka, PO Box 30075, Zambia; +260 (0)211250309; znhrasec@nhra.org.zm), ref: NHRA-1849/09/01/2025

Study design
Parallel cluster-randomized trial

Primary study design
Interventional

Study type(s)
Prevention, Treatment

Health condition(s) or problem(s) studied
Delivery of antenatal care services

Interventions
The study will implement a package designed to improve the quality and content of antenatal care delivered in resource-limited settings and compare this with the standard antenatal care offered to pregnant women in Malawi and Zambia.

This is a multi-country, parallel cluster-randomised controlled trial with a baseline period. There is an integrated implementation evaluation and health economic evaluation. The trial will include primary healthcare centres in Malawi and Zambia as clusters. During the first 3 months each cluster will provide standard care to establish weekly rates of maternal and newborn outcomes. After the baseline, the clusters will be randomly allocated in a 1:1 ratio to ENHANCE or standard care with the provision of basic ANC supplies, using a minimisation algorithm to account for the imbalance in location, hospital deliveries volume and distance to referral facility. Both quantitative and qualitative approaches will gather the data required to meet the

objectives. The researchers will conduct an intention-to-treat analysis of the composite primary outcome. Descriptive statistics for continuous (mean and standard deviations), discrete (median and range or interquartile range) and categorical (frequency counts and percentages) variables will summarize baseline characteristics (demographic and clinical data) and outcome variables. Process evaluation surveys will be summarised using descriptive statistics as appropriate, and responses compared across PHCs and countries. Interviews will be analysed using combined deductive framework and inductive thematic analysis.

Intervention Type
Mixed

Primary outcome(s)
1. Maternal mortality:
1.1. Maternal deaths
2. Newborn mortality:
2.1. Stillbirths
2.2. Neonatal deaths
3. Maternal morbidity:
3.1. (Pre)-eclampsia
3.2. Uterine rupture
3.3. Antepartum haemorrhage
3.4. Postpartum haemorrhage
3.5. Maternal sepsis
4. Newborn morbidity:
4.1. Birth asphyxia
4.2. Prematurity (born before 37 weeks gestation)
4.3. Low birthweight (weight less than 2500 g)
5. Emergency obstetric referrals
6. Appropriate emergency referrals

Measured by monthly collection of routine health facility records for maternity ward records from the baseline phase to the end of cluster participation.

In addition to the primary and secondary outcomes listed here, the researchers may evaluate general process outcomes as described in the protocol attached.

Key secondary outcome(s))
1. Proportion of women with the following obstetric complications:
1.1. (Pre)-eclampsia
1.2. Anaemia (Hb less than 7g/dl)
1.3. Syphilis
2. Proportion of women referred out for any cause, or due to pre/eclampsia, anaemia and risk for obstruction of labour
3. Proportion of newborns with the following complications: neonatal sepsis
4. Proportion of neonatal unit (NNU) admission for any cause
5. Proportion of newborn breastfeeding initiated within 60 minutes of birth
6. Proportion Kangaroo Mother Care (KMC) admissions
7. Proportion of newborns resuscitated
8. Proportion of newborns received antibiotics
9. Proportion of women starting antenatal care (ANC) visit in the first trimester (<12 weeks)
10. Average total ANC visits per woman

11. Proportion of women who received required doses of the following (data from registers):
11.1. Tetanus toxoid vaccination (TTV) (≥2 doses)
11.2. Sulphadoxine-pyrimethamine (SP) (≥3 doses)

Measured by monthly collection of routine health facility maternity and neonatal records and cohort records (6 months prior to reporting month) for ANC data records, from the baseline to the end of cluster participation.

In addition to the primary and secondary outcomes listed here, the researchers may evaluate general process outcomes as described in the protocol attached.

Completion date
31/07/2026

Eligibility

Key inclusion criteria
Clusters:
Primary Health Centre facilities offering maternity care will be included as a cluster following the completion of a successful feasibility report with the minimum prerequisites of:
1. A minimum of 700 ANC initial visits to a maximum of 2000 per year
2. Providers of basic emergency obstetric care
3. Public primary facility
4. Completed the site readiness assessment process

Participants: clients (in process evaluation interviews and survey):
1. ≤ 20 weeks of gestation at the initial visit to ANC
2. Able to provide informed consent
3. Willing to participate in the study
4. Aged 18 years and above

Participants: HCWs (in process evaluation interviews and survey):
1. Healthcare workers responsible for the care of women during pregnancy
2. Willing to participate in the study
3. Able to provide informed consent

Participant type(s)
Patient, Health professional

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
100 years

Sex
All

Key exclusion criteria
Clusters:
1. PHC with less than 700 initial ANC visits per year
2. PHCs with more than 2000 initial ANC visits per year-outliers to other facilities
3. PHCs not willing to participate in the study
4. High risk of contamination (geographically close to another participating centre or site where similar interventions are already taking place)

Participants: clients (in process evaluation - interviews and survey):
1. >20 weeks of gestation at the initial visit to ANC
2. Unable to provide informed consent
3. Medical and obstetric complications on the initial visit
4. Aged less than 18 years

Participants: HCWs (in process evaluation - interviews and survey):
1. Not willing to participate in process evaluation
2. Unable to provide informed consent

Date of first enrolment
01/08/2025

Date of final enrolment
31/05/2026

Locations

Countries of recruitment
Malawi

Zambia

Study participating centre
Katchale, Ming'ongo, Chimbalanga, Matapila, Chadza, Ndaula, Malembo, Diamphwe, Maluwa, Chiunjiza, Mbang'ombe2, Mbabzi, Ngoni, Chiwamba, Chiwoza, Nthondo, Nsara, Kang'oma and Khongoni
Lilongwe District Health Centres
Lilongwe
Malawi
207201

Study participating centre
Phirilongwe, Malukula, Namkumba, Chilonga, Kukalanga, Namwera, Mkumba, Malombe, Mtimabii, Lungwena, Chilipa, Nangalamu, Jalasi and Makanjira
Mangochi District Health Centres

Mangochi
Malawi
301400

Study participating centre
Chipapa and Chinyanya Health Centres
Kafue District Health Centres
Kafue
Zambia
None

Study participating centre
Kanakantapa Health Centre
Chongwe District
Chongwe Lusaka
Zambia
None

Study participating centre
Malombe and Chisamba Health Centres
Chisamba District Health Centres
Chisamba
Zambia
None

Study participating centre
Lungobe, Myooye and Kamilambo Health Centres
Mumbwa District Health Centres
Mumbwa
Zambia
None

Sponsor information

Organisation
University of Liverpool

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date. The researchers expect the data sets generated from this study to be available upon request.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 2.0	12/11/2024	12/03/2025	No	No