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The role of under-fives in pneumococcal transmission to newborn babies within households

Submission date	Recruitment status	[X] Prospectively registered
31/01/2023	No longer recruiting	[_] Protocol
Registration date	Overall study status	[_] Statistical analysis plan
09/02/2023	Ongoing	[_] Results
Last Edited	Condition category	[_] Individual participant data
03/02/2026	Infections and Infestations	[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Streptococcus pneumoniae (the pneumococcus) is a bacterium that lives harmlessly at the back of the nose but also causes serious infections, mostly in young children. African infants are vaccinated against the pneumococcus from about 2 months of age but are often exposed to the pneumococcus before they are fully protected. This study will use innovative technologies to study the importance of children less than 5 years old in the transmission of the pneumococcus to newborn infants living within the same household. The aim is to test whether a booster dose of the pneumococcal conjugate vaccine (PCV) given to children 1-5 years old reduces transmission and therefore protects babies living within the same household (cocooning).

Who can participate?
Mothers, their children and their household contacts who are 12-59 months old

What does the study involve?
The household contacts will be randomly allocated to receive the 13-valent PCV (PCV13) vaccine in the experimental group or the pentavalent vaccine in the control group. Pneumococcal carriage and transmission within the households will be assessed in their respiratory secretions (fluid).

What are the possible benefits and risks of participating?
This study will improve our understanding of how the pneumococcus is transmitted to infants in a household-setting and will providing information to improve current vaccination policies for children. It is possible that the household contacts 12-59 months old may directly benefit from receiving a booster dose of PCV13 or the pentavalent vaccine. However, it is not known for sure if and to what extent the booster doses will improve the protection of children from the infections targeted by the vaccines.
During participation in this study, participants may experience slight discomfort or some irritation from the collection of the samples from the front and back of the nose. In some rare instances, usually when a participant has certain conditions, the participant may briefly experience light bleeding from the sample collection.

Like most vaccines, PCV13 and the pentavalent vaccines can sometimes cause mild side effects. These include a slightly raised temperature, redness where the injection was given and hardness or swelling where the injection was given. Although very uncommon, a child may experience seizures after vaccination, usually from a high temperature. In extremely rare cases, anaphylaxis (severe allergic reaction) can occur in a child. If a child develops seizures or signs of anaphylaxis after being vaccinated, they should be taken to hospital immediately and if possible, inform the study team.
The study will contribute valuable scientific knowledge on how the pneumococcus is transmitted to babies in a household setting and will provide information to improve current vaccination policies for children.

Where is the study run from?
The study will be run from the Malawi Liverpool Wellcome Research Programme in Blantyre, Malawi. The study is sponsored by the Liverpool School of Tropical Medicine (UK).

When is the study starting and long is it expected to run for?
April 2022 to May 2027

Who is funding the study?
Wellcome Trust (UK)

Who is the main contact
Dr Brenda Anna Kwambana, Brenda.Kwambana@lstmed.ac.uk

Contact information

Type(s)
Principal investigator

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
2.0; LSTM: 22-022 Malawi: NHSRC7217; 224354/Z/21/Z

Study information

Scientific Title
A pneumococcal conjugate vaccine (PCV) probe study to define the role of under-fives in within-household transmission of Streptococcus pneumoniae to infants in high disease burden settings (PNEUMOCOCOON)

Acronym
PneumoCocoon

Study objectives
It is hypothesised that under-fives are the primary source of VT transmission to infants living within the same household, hence, giving them a single PCV-booster will interrupt within-household VT transmission and significantly reduce residual VT carriage among PCV-age-ineligible infants, so-called “cocooning”. Cocooning is a targeted vaccination strategy in which individuals at substantial risk of infection are indirectly protected by immunising those individuals most likely to transmit the pathogen.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval pending:
1. National Health Sciences Research (NHSRC) Committee (Ministry Of Health, P.O. Box 30377, Lilongwe 3, Malawi), ref: 22/09/3067
2. Research Ethics Committee, Liverpool School of Tropical Medicine (w-2037, 2nd Floor, Wolfson, Liverpool, UK), ref: 22-022

Study design
Prospective observer-blinded two-arm randomized controlled trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Prevention of pneumococcal carriage and disease

Interventions
The researchers will conduct a prospective observer-blinded two-arm randomized controlled trial (RCT) testing a PCV13-cocooning strategy targeting children 12-59 months old. This vaccine probe approach employing state-of-the-art genomics provides a controlled environment to study complex within-household pneumococcal transmission with greater depth and precision. The RCT will leverage resources and infrastructure from an ongoing cluster-randomized evaluation of a PCV 3P+0 switch to 2P+1 infant vaccination schedule (PAVE) in Blantyre District,

Malawi (COMREC Ref No. P.05192680). Recruitment for this RCT will be from antenatal care (ANC) clinics outside of PAVE catchment areas to avoid mixing of participants.

784 mother-child dyads and their household contacts 12-59 months old will be recruited in Blantyre District, Malawi. Their household contacts will be randomized to receive the 13-valent PCV (PCV13) in the experimental arm or the pentavalent vaccine in the control arm. Pneumococcal carriage and transmission within the households will be assessed in respiratory secretions using molecular and next-generation sequencing methods.

Intervention Type
Biological/Vaccine

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
13-valent Pneumococcal Conjugate Vaccine

Primary outcome(s)
The impact of the PCV13-cocooning intervention on residual pneumococcal vaccine type (VT) carriage prevalence among unvaccinated 6-week-old infants comparing study arms, estimated by prevalence risk ratio (95% confidence interval [CI]). Pneumococcal carriage will be determined microbiologically from nasopharyngeal swabs (NPS) and vaccine serotypes will be confirmed by genomic sequencing at 6-week timepoint.

Key secondary outcome(s))
The impact of the PCV13-cocooning intervention comparing study arms on:
1. Fraction of VT carriage among 6-week-old infants attributed to transmission from children 12-59 months old, measured using culture and genomic sequencing at the 6-week timepoint
2. Frequency of within-household VT transmission events at each study visit. Transmission will be confirmed by sequencing the cultured pneumococci
3. VT carriage prevalence among mothers and children 12-59 months old at each study visit measured using culture and genomic sequencing
4. VT carriage prevalence among unvaccinated 1- and 4-week-old infants and vaccinated 5- and 9-month-old infants measured using culture and genomic sequencing at the 1- and 4-week timepoints
5. VT shedding prevalence among children 12-59 months old, mothers and infants at each study visit. Shedding will be determined by culturing pneumococci shed from the upper respiratory tract

Completion date
31/05/2027

Eligibility

Key inclusion criteria
Current key inclusion criteria as of 03/02/2026:
All participants:
1. Adult participants (>18 years old) with written informed consent and children with parental /legal guardian’s written informed consent
2. Residence in Blantyre District

Mothers:
1. >28 weeks gestation
2. Household contacts 12-59 months old (HHC)
3. 18-45 years old

HHC:
1. 12-59 months old at time of entry into the study
2. Record of PCV13 infant immunisation
3. Lives in the same household as study mothers

Infants
1. <14 days old at recruitment

Previous key inclusion criteria:
All participants:
1. Adult participants (>18 years old) with written informed consent and children with parental /legal guardian's written informed consent
2. Residence in Blantyre District

Mothers:
1. <32 weeks gestation
2. Household contacts 12-59 months old (HHC)
3. 18-45 years old

HHC:
1. 12-59 months old at time of entry into the study
2. Record of PCV13 infant immunisation
3. Lives in the same household as study mothers

Infants
1. <14 days old at recruitment

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
Yes

Age group
Adult

Lower age limit
18 years

Upper age limit
45 years

Sex
All

Total final enrolment
2588

Key exclusion criteria
Previous key exclusion criteria:
Mothers and household contacts 12-59 months old (HHC):
1. Ongoing antibiotic treatment
2. Ongoing TB treatment, including isoniazid prophylaxis
3. Immunosuppressive illnesses, e.g., HIV infection not on ART
4. Immunosuppressive treatment, e.g., steroids
5. Women with prior PCV vaccination
6. Women with the following comorbidities: a hypertensive disorder (including pre-eclampsia and eclampsia), diabetes (including gestational diabetes), a previous history of preterm delivery, incompetent cervix/cervical cerclage placement, or multiple gestations (twins or more babies)
7. Residence in a PAVE 2+1 catchment area

HHC:
1. Previous severe adverse reaction to PCV13 or the pentavalent vaccine
2. Known hypersensitivity to any components of the Prevnar 13 or the pentavalent combination vaccine, or a severe reaction to a previous dose of either vaccine or any of its constituents.
3. <2 or >4 doses of PCV

Infants:
1. Preterm birth (<37 weeks)
2. Congenital abnormalities of the upper airways

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1. Preterm birth (<37 weeks)
2. Congenital abnormalities of the upper airways

Date of first enrolment
01/03/2023

Date of final enrolment
27/01/2026

Locations

Countries of recruitment
Malawi

Study participating centre
Malawi Liverpool Wellcome Research Programme
Queen Elizabeth Central Hospital
College of Medicine
Chichiri
Blantyre
Malawi
PO BOX 30096

Sponsor information

Organisation
Liverpool School of Tropical Medicine

ROR
https://ror.org/03svjbs84

Funder(s)

Funder type
Charity

Funder Name
Wellcome Trust

Alternative Name(s)
Wellcome, WT

Funding Body Type
Private sector organisation

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

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

Datasets that support research findings will be made publicly available at the point of publication to allow validation by others in compliance with the Wellcome Trust's open-access policy with the approval of the ethics committee. Only anonymised datasets will be made publicly available to protect the confidentiality of participants. All digital data will be made available within 12 months of completing the study. Anonymisation will be performed in accordance with LSTM guidelines. Interim and final analyses will be shared with the Malawi Ministry of Health, and other agencies. Partial and final findings will be presented at local and international meetings. During the study, digital outputs will be held securely on password-protected databases and backed-up on-site and off-site according to standard operating procedures at MLW. Secure file-sharing systems will be used to transfer anonymised files to provide access to third parties where necessary. All protocol and research articles will be published in open-access journals to maximise accessibility.

As clinical samples are limited and depletable, access will be carefully controlled. The quantities of samples provided will be judged against the potential benefits of the proposed research project. Nucleic acid specimens and bacterial strains will be shipped to the UK for further genetic analysis. Likewise, the respiratory specimens and saliva samples may be sent to the UK or other countries for further testing such as immunology analysis.

The researchers will avoid placing restrictions on sharing outputs including specimens and data with bona fide health-related research from across the spectrum of institutions and locations. However, prior to gaining access to these outputs, researchers will be required to complete data and or material request forms in which they will outline the intended purpose. Researchers wishing to access data and samples will be required to adhere to ethics guidelines and seek necessary approvals before accessing the outputs. If the research complies with the objectives set out in this study, the researchers will be asked to sign Data and/or Materials Transfer Agreements and other necessary paperwork. Researchers wishing to access data and samples will be required to adhere to ethics guidelines and seek necessary approvals before accessing the data and samples. Researchers that fulfil these conditions will be provided aliquots of the samples and/or a digital copy of the data as requested.

The data can be requested by contacting the PI of the study, Dr Brenda Kwambana (bkwambana@mlw.mw or crsu@mwl.mw). Dates of availability: from 31/12/2026.

IPD sharing plan summary

Available on request, Published as a supplement to the results publication, Stored in non-publicly available repository