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Measuring the change in genetic markers of antibiotic resistance carried in the nasopharynx of children with pneumonia in Blantyre, Malawi, and assessing whether this is associated with poor health outcomes

Submission date 12/08/2025	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 13/08/2025	**Overall study status** Ongoing	
Last Edited 13/08/2025	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims
Antimicrobial resistance (AMR) happens when bacteria become resistant to antibiotics, making infections harder to treat. This is a big problem worldwide, especially in Sub-Saharan Africa, where many children die from infections like pneumonia. However, there's not much data from this region to help us understand the issue.

This study is looking at how hospital stays and antibiotic treatment affect the bacteria and antibiotic resistance found in the nose and throat of young children in Malawi. Researchers want to find out if these changes in bacteria are linked to worse health outcomes, like needing to go back to hospital.

Who can participate?
The study will include 350 children aged 12 to 24 months from Blantyre, Malawi. Children will be grouped as follows:
-Healthy children from the community
-Children with pneumonia treated with antibiotics at home
-Children hospitalised with pneumonia
-Children who are re-hospitalised with pneumonia within 3 months of a previous hospital stay

What does the study involve?
Children will have a swab taken from their nose and throat, and a urine sample collected. These samples will help researchers study the bacteria and antibiotic resistance present. Some children will be followed up after hospital discharge or after 3 months, depending on their group.

The swabs will be tested using advanced lab techniques to identify bacteria and resistance genes. Researchers will also test for viruses like RSV and flu in children with pneumonia. Information about the child's health, any other illnesses, and antibiotic use will be recorded.

What are the possible benefits and risks of participating?
There are no direct benefits for children taking part, and they will receive the same medical care as other patients. However, the study may help improve how pneumonia is treated in the future.

Risks are minimal. In rare cases, a child might have a small nosebleed after the swab is taken, especially if they have a condition that makes them prone to bleeding.

Where is the study run from?
The study is being carried out by the Malawi Liverpool Wellcome Research Programme, in partnership with the Kamuzu University of Health Sciences in Malawi and the Liverpool School of Tropical Medicine in the UK.

When is the study starting and how long is it expected to run for?
April 2025 to February 2027

Who is funding the study?
Wellcome Trust (UK)

Who is the main contact?
Dr Lucy O'Connor, lucy.oconnor@lstmed.ac.uk

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)

Nil known

Protocol serial number
24-076

Study information

Scientific Title
Nasopharyngeal resistome evolution under selective pressure and association with adverse health outcomes in a paediatric population in Blantyre, Malawi

Acronym
NP Resistome

Study objectives
Our study aims to answer the following research question; does hospital admission and antibiotic treatment for pneumonia generate a persistent hospital-acquired nasopharyngeal resistome in Malawian children, and is this associated with adverse health outcomes in a resource limited setting? The primary objectives of this study are:
1. To measure how the diversity and relative abundance of the nasopharyngeal resistome of children hospitalised with pneumonia differs from the nasopharyngeal resistome of healthy children in the community.
2. To measure how the diversity and relative abundance of the nasopharyngeal resistome of children hospitalised with pneumonia differs from the nasopharyngeal resistome of children with pneumonia treated with antibiotics in the community.
3. To investigate whether there is measurable persistence of a hospital-acquired nasopharyngeal resistome post-discharge, and whether this is associated with adverse health outcomes, including recurrent hospitalisation.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. approved 01/07/2025, Liverpool School of Tropical Medicine Research Ethics Committee (Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, L3 5QA, United Kingdom; +44 (0)1517053100; lstmrec@lstmed.ac.uk), ref: Research Protocol (24-076)

2. approved 01/04/2025, Malawi College of Medicine Research & Ethics Committee (Room #822, Chimutu Building, Mahatma Gandhi Road, P/Bag 360 Chichiri, Blantyre, -, Malawi; (+265) 01 871 911/01 874 377; comrec@medcol.mw), ref: P.10/24-1200

Study design
Multi-site extended observational case-control study with a preliminary cohort component

Primary study design
Observational

Study type(s)
Other

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

Interventions
This observational study will recruit 350 children aged 12-24 months in four groups: healthy children in the community, children with pneumonia being treated with oral antibiotics in the community, children hospitalised with pneumonia and children re-hospitalised with pneumonia within 3-months of their previous admission. The study will be conducted at Ndirande community healthcare centre and Queen Elizabeth Central Hospital. Nasopharyngeal swabs (NPS) and urine samples will be taken at recruitment. NPS will also be taken at hospital discharge for children hospitalised with pneumonia, and at 3-month follow up study visits for children with pneumonia in the community and children hospitalised with pneumonia. NPS will undergo metagenomic sequencing to identify the nasopharyngeal microbiome (NPM) and nasopharyngeal resistome (NPR). NPS from participants with pneumonia will also be tested using a viral PCR for Respiratory Syncytial Virus (RSV), Influenza A and B. Urine samples will be used for an antibiotic bio-assay. Demographics, co-morbidities, health outcomes and antibiotic exposure will be recorded at recruitment for all participants, and subsequent study visits where applicable.

Intervention Type
Other

Primary outcome(s)
1. Diversity of antibiotic resistance genes (ARGs) in the nasopharyngeal resistome (NPR) of healthy children in Blantyre, children with pneumonia in the community and children hospitalised with pneumonia when measured using metagenomic sequencing of nasopharyngeal swabs (NPS), to assess whether there is a significant difference. The NPS will be taken at recruitment for healthy community participants, and 3-month follow up for participants with pneumonia.
2. Relative abundance of ARGs in the NPR of healthy children in Blantyre, children with pneumonia in the community and children hospitalised with pneumonia, as above.
3. Diversity of ARGs in the NPR of children hospitalised with pneumonia and children re-hospitalised with pneumonia at the point of hospitalisation.
4. Diversity of ARGs in the NPR of children hospitalised with pneumonia and children re-hospitalised with pneumonia at the point of hospitalisation.

Key secondary outcome(s))
1. Diversity of antibiotic resistance genes (ARGs) in the nasopharyngeal resistome (NPR) of children hospitalised with pneumonia when measured at admission, discharge and 3-month follow up using metagenomic sequencing of nasopharyngeal swabs (NPS), to assess whether there is a significant difference between these time-points.
2. Relative abundance of ARGs in the NPR of children hospitalised with pneumonia when measured at admission, discharge and 3-month follow (as above).
3. Diversity of ARGs in the NPR of children with pneumonia in the community at presentation to a healthcare centre and 3-month follow up.
4. Relative abundance of ARGs in the NPR of children with pneumonia in the community at presentation to a healthcare centre and 3-month follow up.
5. Diversity of ARGs in the NPR of healthy children in Blantyre and children with pneumonia in the community at presentation to a healthcare centre.
6. Relative abundance of ARGs in the NPR of healthy children in Blantyre and children with pneumonia in the community at presentation to a healthcare centre.

7. Repeat antibiotic exposure is measured using caregiver report and health passport records at 3-month follow-up in children discharged from hospital
8. Re-hospitalisation for pneumonia is measured using caregiver report and health passport records at 3-month follow-up in children discharged from hospital

Completion date
12/02/2027

Eligibility

Key inclusion criteria
Inclusion criteria for healthy children in the community:
1. Child aged between 12-24 months living in Ndirande community, in Blantyre, Malawi.

Inclusion criteria for children with pneumonia in the community:
1. Child aged between 12-24 months presenting to Ndirande community healthcare centre, Blantyre, Malawi.
2. Presence of ALL of the following symptoms: fever, cough, difficulty in breathing and fast breathing.
3. Participant has been prescribed antibiotics for treatment of a lower respiratory tract infection on this presentation.

Inclusion criteria for children hospitalised with pneumonia:
1. Child aged between 12-24 months admitted to Queen Elizabeth Central Hospital, Blantyre, Malawi.
2. Presence of ALL of the following symptoms: fever, cough, difficulty in breathing and fast breathing.
3. Participant has been prescribed antibiotics for treatment of a lower respiratory tract infection on this presentation.

Inclusion criteria for children re-hospitalised with pneumonia:
1. Child aged between 12-24 months admitted to Queen Elizabeth Central Hospital, Blantyre, Malawi.
2. Presence of all of the following symptoms: fever, cough, difficulty in breathing and fast breathing.
3. Participant has been prescribed antibiotics for treatment of a lower respiratory tract infection on this admission.
4. Hospital admission to ANY hospital with a lower respiratory tract infection within the past 3 months.

Participant type(s)
Healthy volunteer, Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
12 months

Upper age limit
24 months

Sex
All

Key exclusion criteria
Exclusion criteria for healthy children in the community:
1. Presence of any of the following symptoms: fever, cough, difficulty in breathing or fast breathing.
2. Currently taking long-term antibiotic prophylaxis, TB treatment or immunosuppressive medications.
3. Diagnosis of an immunosuppressive illness, including HIV infection.
4. Hospital admission within the past six months.

Exclusion criteria for children with pneumonia in the community and children hospitalised with pneumonia:
1. Severe anaemia, with a recorded haemoglobin level < 70 grams per Litre.
2. Currently taking long-term antibiotic prophylaxis, TB treatment or immunosuppressive medications.
3. Diagnosis of an immunosuppressive illness, including HIV infection.
4. Hospital admission within the past six months.

Exclusion criteria for children re-hospitalised with pneumonia:
1. Severe anaemia, with a recorded haemoglobin level < 70 grams per Litre.
2. Currently taking long-term antibiotic prophylaxis, TB treatment or immunosuppressive medications.
3. Diagnosis of an immunosuppressive illness, including HIV infection.

Date of first enrolment
13/08/2025

Date of final enrolment
13/02/2027

Locations

Countries of recruitment
Malawi

Study participating centre
Ndirande Health Centre
Ndirande Ring Road
Blantyre
Malawi
-

Study participating centre
Queen Elizabeth Central Hospital
Chipatala Avenue
Blantyre
Malawi
-

Sponsor information

Organisation
Liverpool School of Tropical Medicine

ROR
https://ror.org/03svjbs84

Funder(s)

Funder type
Charity

Funder Name
Wellcome

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a publicly available repository on GitHub: https://github.com/locucl/NP_Resistome_Study

After completion of the study, the following types of data will be shared:
• Anonymised, curated microbiome and resistome data will be shared with researchers on the

GitHub repository.
• R code for statistical analysis of the metagenomic sequence data and clinical metadata will be shared with researchers on the GitHub repository.
• Anonymised clinical metadata will only be shared with scientific collaborators.

All human genome sequence data will be removed in the bioinformatic pipeline; no human genome sequence data will be shared with researchers.

The following types of anonymised metadata will be stored, but not shared publicly:
• Human subject demographic data, including age in months and gender.
• Clinical metadata, including mid-upper arm circumference in centimetres, co-morbidities, HIV status, haemoglobin level, malaria test result, antibiotic use (type and number of days).

Non-collaborating scientific researchers must submit a formal project proposal for review by investigators to access the metadata, which if approved, will be released following receipt of a signed data user's agreement setting out roles and responsibilities of data originators and recipients.

Consent has been obtained from participants for sharing of anonymised data.

IPD sharing plan summary
Stored in publicly available repository

Study outputs

Output type	Details	Date created
Participant information sheet	Community_Pneumonia_Participant_Information_Sheet_and_Consent_Form_Chichewa version 5.0	21/05/2025
Participant information sheet	Community_Pneumonia_Participant_Information_Sheet_and_Consent_Form_English version 5.0	21/05/2025
Participant information sheet	Healthy_Community_Participant_Information_Sheet_and_Consent_Form_Chichewa version 5.0	21/05/2025
Participant information sheet	Healthy_Community_Participant_Information_Sheet_and_Consent_Form_English version 5.0	21/05/2025
Participant information sheet	Hospital_Pneumonia_First_Admission_Participant_Information_Sheet_and_Consent_Form_Chichewa version 5.0	21/05/2025
Participant information sheet	Hospital_Pneumonia_First_Admission_Participant_Information_Sheet_and_Consent_Form_English version 5.0	21/05/2025
Participant information sheet	Hospital_Pneumonia_Readmission_Participant_Information_Sheet_and_Consent_Form_Chichewa version 5.0	21/05/2025
Participant information sheet	Hospital_Pneumonia_Readmission_Participant_Information_Sheet_and_Consent_Form_English version 5.0	21/05/2025
Protocol file	version 5.0	21/05/2025