

# Pharmacogenetics to avoid loss of hearing

<b>Submission date</b> 18/04/2019	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 25/04/2019	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 06/05/2025	<b>Condition category</b> Neonatal Diseases	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Gentamicin is an antibiotic that is routinely used to treat or protect against infection in over 95% of babies admitted to Neonatal Intensive Care Units (NICUs). Some children have a genetic change (variant) that predisposes to severe hearing loss or total deafness after a single dose of gentamicin. About 1 in 500 people have this variant. Groups with a higher risk of repeated chest infections throughout their lives (i.e. people with cystic fibrosis) are routinely tested for this variant using a technique known as pyrosequencing. This current test takes at least three days to return a clinically relevant result. Newborn babies with suspected sepsis should be treated within the first hour of suspicion. The current genetic test is therefore unsuitable in this situation. The researchers have developed a point-of-care test (PoCT) to detect this genetic variant via a buccal (mouth) swab, delivering a reliable result in less than 40 minutes. This study aims to trial this new genetic testing approach in two large newborn intensive care units (NICUs). The aim is to assess the performance of this device in providing an accurate result, in a time that will indicate if the child can or cannot be treated with gentamicin (a safe alternative can be used), and therefore avoid the risk of deafness.

### Who can participate?

Babies admitted to the NICU or requiring a screen for infection within 72 hours of birth

### What does the study involve?

All participating babies are tested for the genetic variant before antibiotic treatment. There is no follow up as part of the study.

### What are the possible benefits and risks of participating?

Babies included in this study will benefit from a rapid, non-invasive genetic test which will allow personalised antibiotic prescribing to avoid hearing loss in at-risk individuals. If successful, the use of this technology across the UK could avoid permanent, severe hearing loss in about 180 babies every year.

### Where is the study run from?

1. Manchester University NHS Foundation Trust (UK)
2. Liverpool Women's NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?  
June 2018 to November 2020

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

Who is the main contact?  
Dr Rachel Mahood  
rachel.mahood@mft.nhs.uk

## Contact information

**Type(s)**  
Public

**Contact name**  
Dr Rachel Mahood

**Contact details**  
Manchester Centre for Genomic Medicine  
6th Floor, St Mary's Hospital  
Oxford Road  
Manchester  
United Kingdom  
M13 9WL  
+44 (0)1617019139  
rachel.mahood@mft.nhs.uk

**Type(s)**  
Scientific

**Contact name**  
Prof William Newman

**Contact details**  
Manchester Centre for Genomic Medicine  
6th Floor, St Mary's Hospital  
Oxford Road  
Manchester  
United Kingdom  
M13 9WL  
+44 (0)1617019139  
william.newman@manchester.ac.uk

## Additional identifiers

**EudraCT/CTIS number**  
Nil known

**IRAS number**

253102

**ClinicalTrials.gov number**

Nil known

**Secondary identifying numbers**

B00321, IRAS 253102

## **Study information**

**Scientific Title**

Pharmacogenetics to avoid loss of hearing (clinical implementation study)

**Acronym**

PALOH

**Study objectives**

A clinical implementation study to critically assess the use of a novel point-of-care pharmacogenetic testing device to detect neonates at risk of aminoglycoside-induced hearing loss secondary to the genetic variant m.1555A>G. The primary objective is to assess the performance of the device and any barriers to implementation.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Current ethics approval as of 04/11/2019:

Approved 22/08/2019, North West - Liverpool East Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ; nrescommittee.northwest-liverpooleast@nhs.net), ref: 19/NW/0400

Previous ethics approval:

NHS Health Research Authority Research Ethics Service - approval pending

**Study design**

Multi-centre clinical feasibility study

**Primary study design**

Observational

**Secondary study design**

Feasibility study

**Study setting(s)**

Hospital

**Study type(s)**

Screening

**Participant information sheet**

Not available in a web format, please use contact details to request a participant information sheet.

## **Health condition(s) or problem(s) studied**

Neonatal intensive care

## **Interventions**

This study involves the use of a novel genetic test to detect the m.1555A>G variant which is associated with aminoglycoside-induced hearing loss. All neonates admitted to the participating neonatal intensive care units during the study period will be tested for this variant prior to antibiotic treatment, to allow personalised prescribing and avoiding permanent, irreversible hearing loss in at-risk individuals.

The intervention is a one-off genetic test at the point of admission to neonatal intensive care. The objective is to look at feasibility of incorporating the test into the current clinical pathway rather than the efficacy of the intervention, which is already known. There is no follow up period as part of the study.

## **Intervention Type**

Genetic

## **Primary outcome measure**

The total number of neonates who are successfully tested for the m. 1555A>G genetic variant out of all babies given antibiotics on admission or assessment in the two participating sites, measured using patient medical notes and real-time data collection at the end of the study period

## **Secondary outcome measures**

1. The total number of neonates identified with the m. 1555A>G genetic variant, measured using retrospective data collection from device at the end of the study period
2. Average time from admission to antibiotic administration for all participants tested throughout the 6-month study period, measured using patient medical notes and real-time data collection
3. Total number of incidences where time to antibiotic administration exceeds the 60-minute target and the reasons for these, measured using patient medical notes and real-time data collection
4. Total number of assay failures within the 6-month testing period and the reasons for these, measured using retrospective data collection from device
5. Resource impact: additional staff time required to secure samples and undertake testing, measured using staff observations
6. Total number of babies where testing was not undertaken during the 6-month testing period and the reasons for these, measured using patient medical notes and real-time data collection
7. The overall correlation of the point-of-care testing result with the current in-house reference assay (pyrosequencing)

## **Overall study start date**

01/06/2018

## **Completion date**

30/11/2020

# Eligibility

## Key inclusion criteria

1. All babies admitted to NICU at Manchester University NHS Foundation Trust (MFT, Oxford Road Campus) and Liverpool Women's NHS Foundation Trust (LWH), for 6 months commencing from the trial start date
2. Babies requiring a screen for infection within 72 hours of birth (an infection screen for suspected early onset neonatal infection) at LWH who are not formally admitted to the neonatal unit, for 6 months commencing from the trial start date

## Participant type(s)

Patient

## Age group

Neonate

## Sex

Both

## Target number of participants

900

## Total final enrolment

751

## Key exclusion criteria

Neonates requiring antibiotics immediately with already established IV access

## Date of first enrolment

01/01/2020

## Date of final enrolment

30/11/2020

# Locations

## Countries of recruitment

England

United Kingdom

## Study participating centre

**Manchester University NHS Foundation Trust**

Oxford Road

Manchester

United Kingdom

M13 9WL

**Study participating centre**  
**Liverpool Women's NHS Foundation Trust**  
Liverpool Women's Hospital  
Crown Street  
Liverpool  
United Kingdom  
L8 7SS

## **Sponsor information**

**Organisation**  
Manchester University NHS Foundation Trust

**Sponsor details**  
Oxford Road  
Manchester  
England  
United Kingdom  
M13 9WL  
+44 (0)161 276 4125  
lynne.webster@mft.nhs.uk

**Sponsor type**  
Hospital/treatment centre

**Website**  
<https://mft.nhs.uk/>

**ROR**  
<https://ror.org/00he80998>

## **Funder(s)**

**Funder type**  
Government

**Funder Name**  
National Institute for Health 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

### Publication and dissemination plan

The researchers intend to publish the protocol. Outcomes relating to the project will be published in peer-reviewed medical journals and presented at regional, national and international meetings for paediatrics, neonates, genetics and audiology. The researchers will work with Bliss (Charity for the care of neonates) and the National Deaf Children's Society to disseminate the project outcomes through their websites and other media. Plans for an implementation strategy, if outcomes are positive, will be developed in consultation with NIHR.

**Intention to publish date**  
31/12/2021

### Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. William Newman (William.newman@manchester.ac.uk). Data pertaining to clinical timings associated with testing (e.g. time of NICU admission, time of swab, time of antibiotic administration etc) can be provided to researchers upon request to CI Prof Newman. Data will be anonymised. Consent for this data collection was presumed under an "opt-out" consent model.

The datasets generated and/or analysed during the current study will be included in the subsequent results publication.

### IPD sharing plan summary

Available on request, Published as a supplement to the results publication

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol article</a>	Qualitative study	16/06/2021	18/06/2021	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Results article</a>		07/01/2024	08/01/2024	Yes	No
<a href="#">Other publications</a>		23/07/2020	06/05/2025	Yes	No
<a href="#">Other publications</a>		22/01/2021	06/05/2025	Yes	No
<a href="#">Results article</a>		21/03/2022	06/05/2025	Yes	No