POCT Pharmacogenomics, the PALOH-UK Study

2025 Weqas Annual POCT Conference

Sian Hilton

PALOH-UK

Pharmacogenetics to Avoid Loss of Hearing – UK (PALOH-UK)

Background

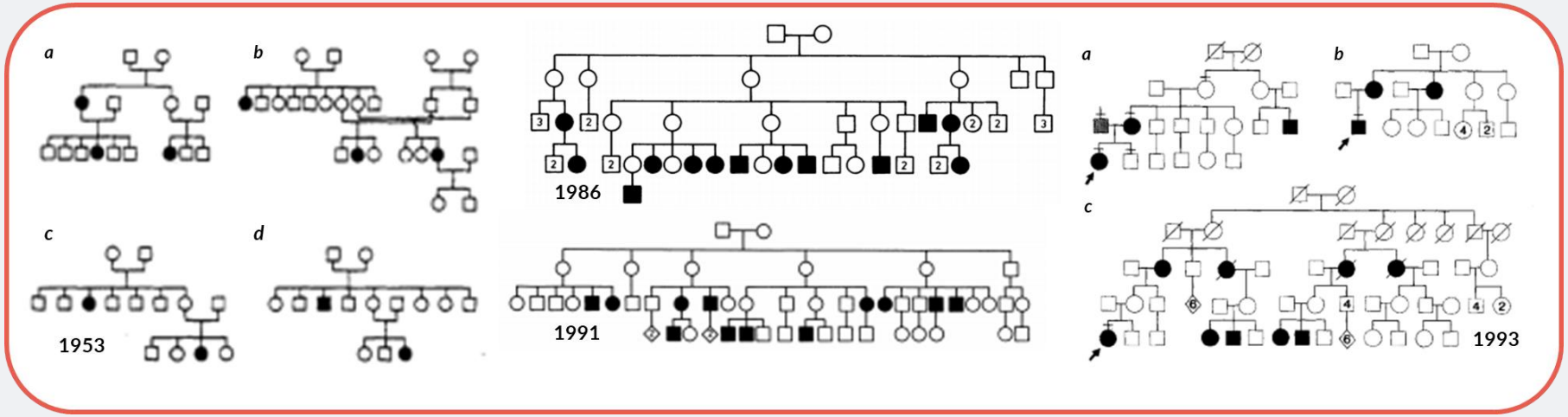
Aminoglycoside Antibiotics

- Widely used antibiotics worldwide since 1940s, with many drugs in class.
- Effective against gram-negative and some gram-positive bacteria in many clinical settings.
- Gentamicin is the aminoglycoside of choice in the UK and is used widely for the treatment of serious infections.
- Side effects – nephrotoxicity and ototoxicity.

Selman A. Waksman

Background

Aminoglycosides Antibiotics



RNR1 m.1555A>G

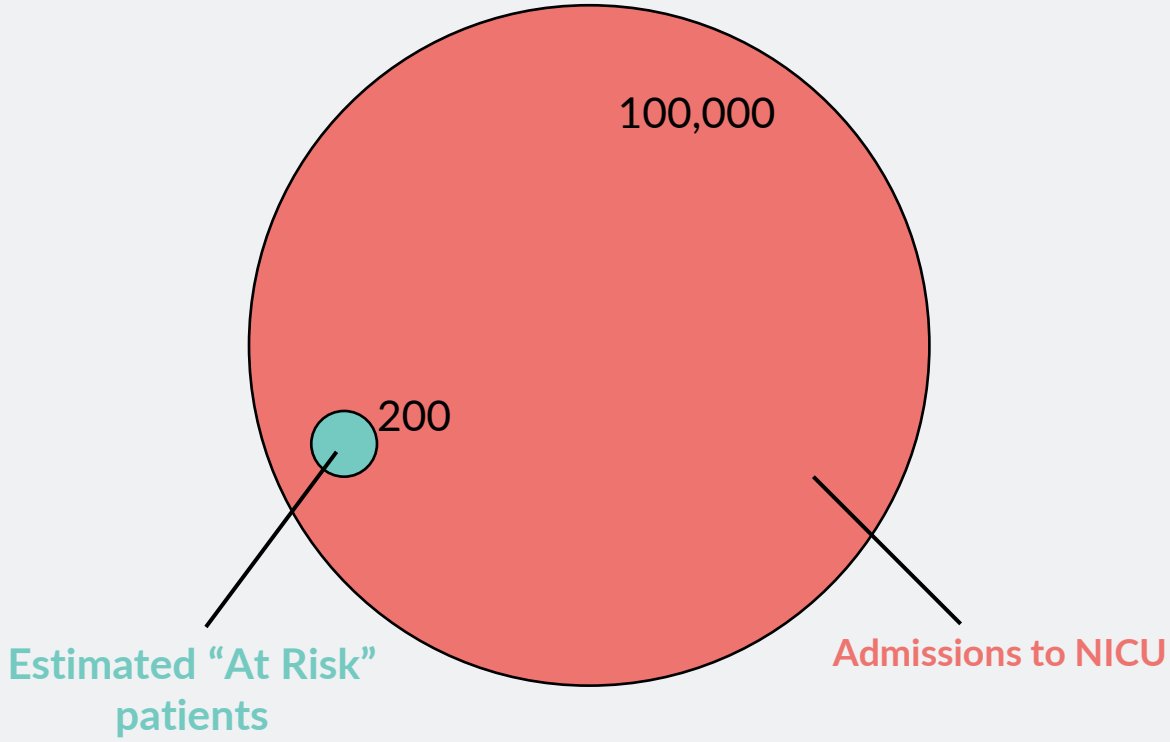
Frequency ~1 in 500 individuals – worldwide

Background

Pharmacogenetic Testing of m.1555 A>G

Child Diagnosed with Cystic Fibrosis → Genetic Testing → Antibiotics Required Months to Years Later

Septic Neonate → Genetic Testing possible?? → Abx Required Minutes Later



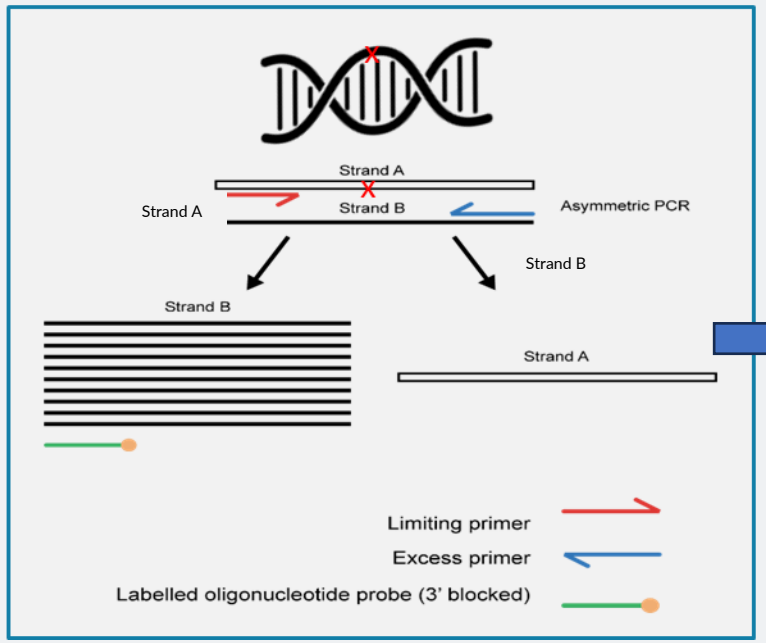
https://www.england.nhs.uk/publication/national-genomic-test-directories/

Genetic point-of-care test

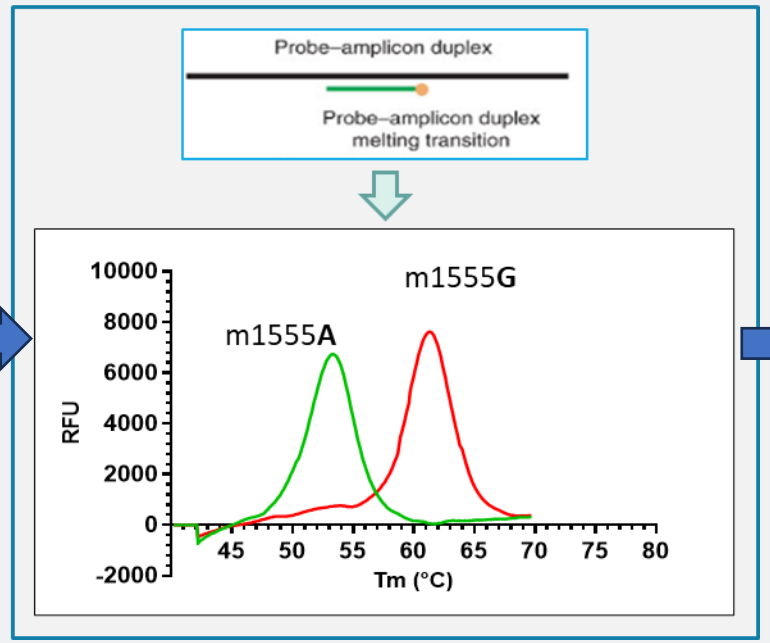
Development of the POCT

- ❖ Clinically Relevant Result
- ❖ Clinically Relevant Timeframe
- ❖ POCT
- ❖ Cost Effective
- ❖ Acceptable to stakeholders

LAMP PCR



Melt curve analysis



Result comparable to gold standard in **26 Minutes** from cheek swab

Pharmacogenetics to Avoid Loss of Hearing (PALOH)

A Prospective Observational Trial to Assess the Implementation of Rapid Genotyping to Avoid Aminoglycoside Induced Ototoxicity in Newborns

Research

JAMA Pediatrics | Original Investigation

Rapid Point-of-Care Genotyping to Avoid Aminoglycoside-Induced Ototoxicity in Neonatal Intensive Care

John H. McDermott, MD, MRes; Ajit Mahaveer, MD; Rachel A. James, PhD; Nicola Booth, RN, PhD; Mark Turner, MD, PhD; Karen E. Harvey, RN; Gino Miele, PhD; Glenda M. Beaman, PhD; Duncan C. Stoddard, MSc; Karen Tricker, PhD; Rachel J. Corry, MSc; Julia Garlick, MSc; Shaun Ainsworth, PhD; Thomas Beevers, BSc; Iain A. Bruce, MD, PhD; Richard Body, MD, PhD; Fiona Ulph, PhD; Rhona MacLeod, PhD; Peter L. Roberts, BA; Paul M. Wilson, BA; William G. Newman, MD, PhD; for the PALOH Study Team

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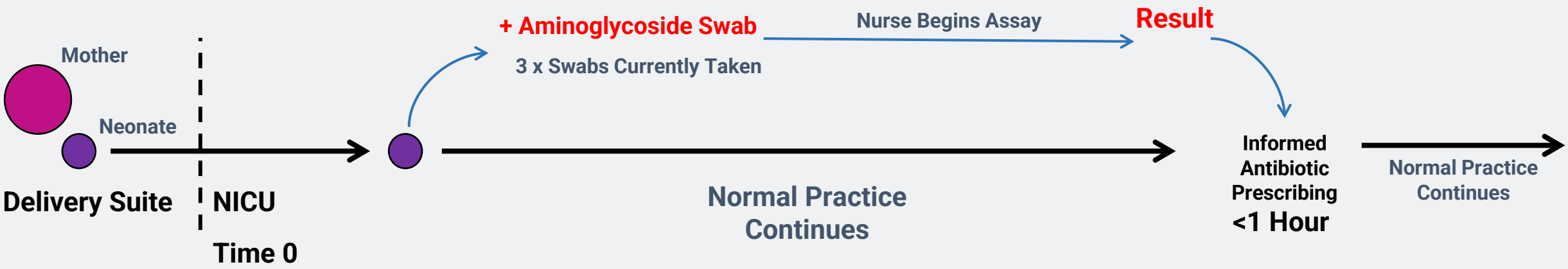

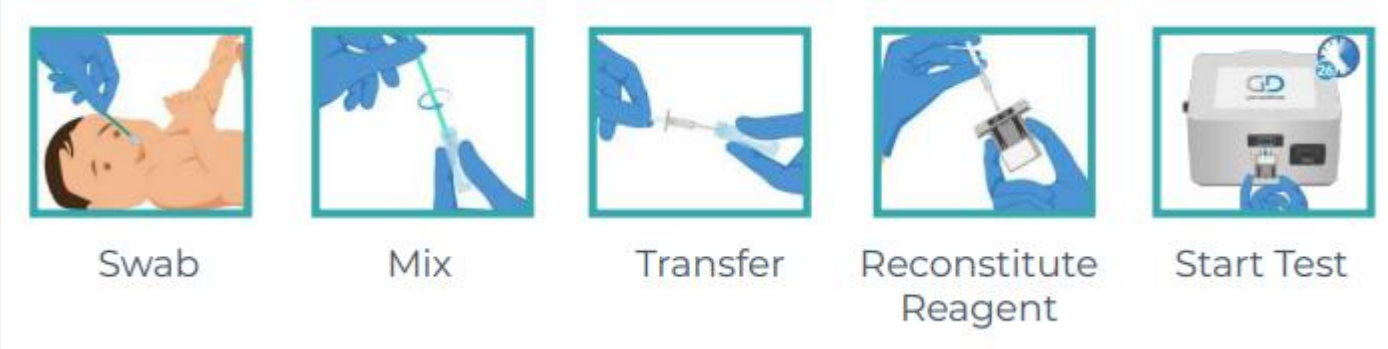

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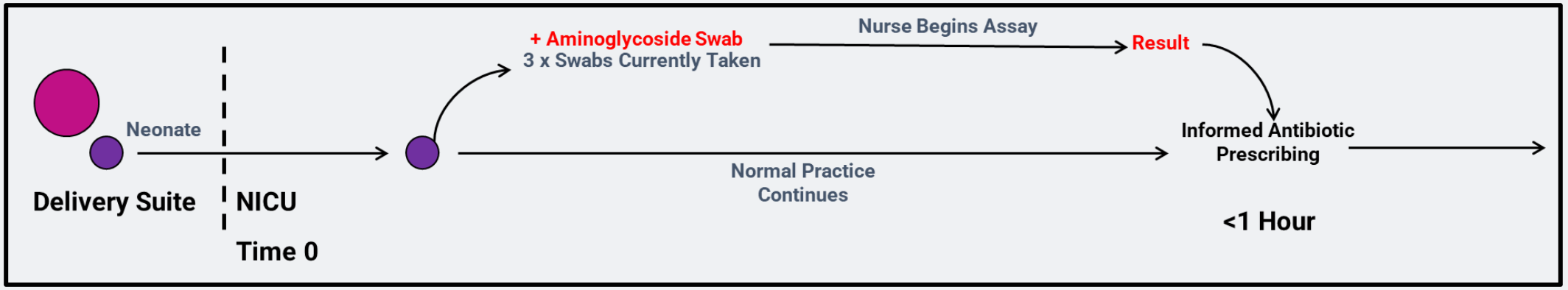
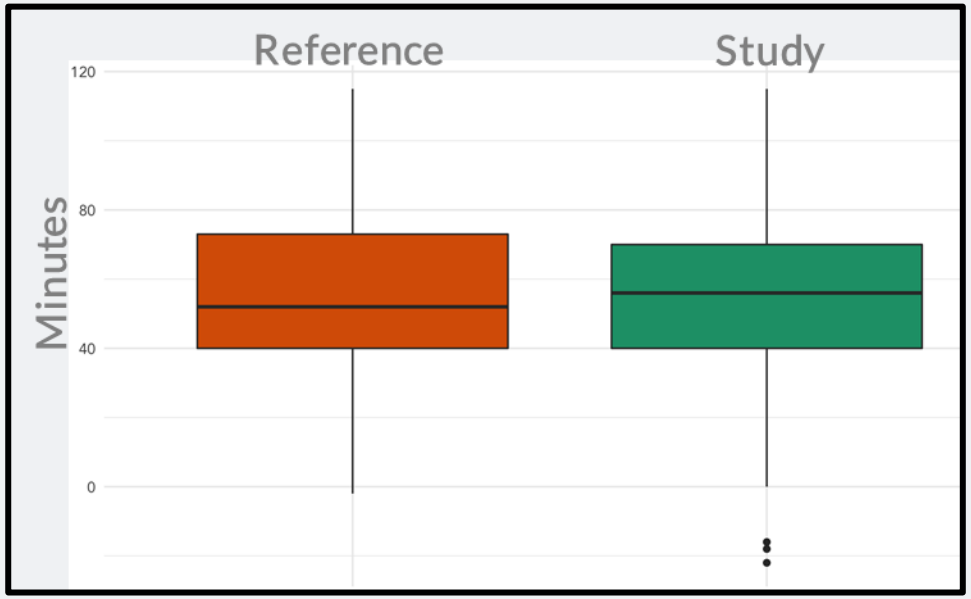


Average Time to Swab

6 Minutes



3 babies detected with mt-RNR1 variant – given alternative antibiotics

Reference time to antibiotics was **55.87 minutes**

Study time to antibiotics was **56.43 minutes**

Pharmacogenetics to Avoid Loss of Hearing (PALOH)

A Prospective Observational Trial to Assess the Implementation of Rapid Genotyping to Avoid Aminoglycoside Induced Ototoxicity in Newborns

Genedrive MT-RNR1 ID Kit for detecting a genetic variant to guide antibiotic use and prevent hearing loss in babies: early value assessment

Health technology evaluation | HTE6 | Published: 30 March 2023 | Last updated: 10 August 2023

Essential

EG1 – How the test impacts time to antibiotic therapy
EG2 – How the test result affected prescribing practice
EG3 – Failure Rate
EG4 – Diagnostic Accuracy
EG5 – Use in smaller non-specialist centers

Desirable

EG6 – Use in centers with babies from diverse ethnic background
EG7 – Use in a wide range of geographical regions

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Aiming to Address Evidence Gaps

Two-year programme – ending October 2026

Fourteen neonatal units across the UK

- Nine Group 1 sites
- Five Group 2 sites
- A range of LNUs, SCBUs, NICUs of varying sizes
- N based on power calculation (n= 4,887) and need for geographical spread

Primary Objective: To assess whether the Genedrive MT-RNR1 system can be integrated into routine neonatal care pathways to guide antibiotic therapy without disrupting normal clinical practice

FUNDED BY
NIHR | National Institute for Health and Care Research

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Aiming to Address Evidence Gaps

- **Inclusion:** All babies admitted will be eligible for recruitment to the study.
- **Exclusion:** Babies requiring antibiotics immediately on admission with already established IV access, where the clinical risk of waiting for the m.1555A>G result is considered, by the attending clinician, to be too great.
- Where there is a “test fail” – a repeat test should be performed (with a new swab/kit) and if antibiotics are required urgently, the local prescribing pathway should be followed.
- The result of the test should be recorded in the patient’s healthcare record (e.g. under the allergy section).

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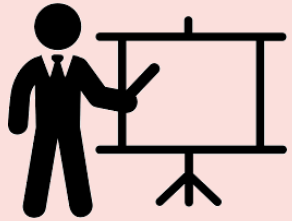
Implementation challenges

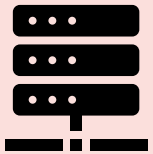
Funding & Commissioning

Training & Education



Verification & Integration

Digital connectivity – results reporting



Quality Assurance

Public and patient views

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Best Practice Packages

1. **Education & Training**: Strategies and associated material to train a workforce in how to use the MT-RNR1 platform.
2. **Installation & Verification**: Standardised, United Kingdom Accreditation Service (UKAS) compliant, protocols and timelines detailing how the MT-RNR1 system can be installed and verified by point of care testing (POCT) teams will be developed.
3. **Ethical & Legal**: A clear and concise overview of how rapid genetic testing is permissible under the Human Tissue Act (HTA), with provision of relevant patient facing material.
4. **Local Business Cases**: Template local business cases will be developed which can be used by NHS Hospital Trusts

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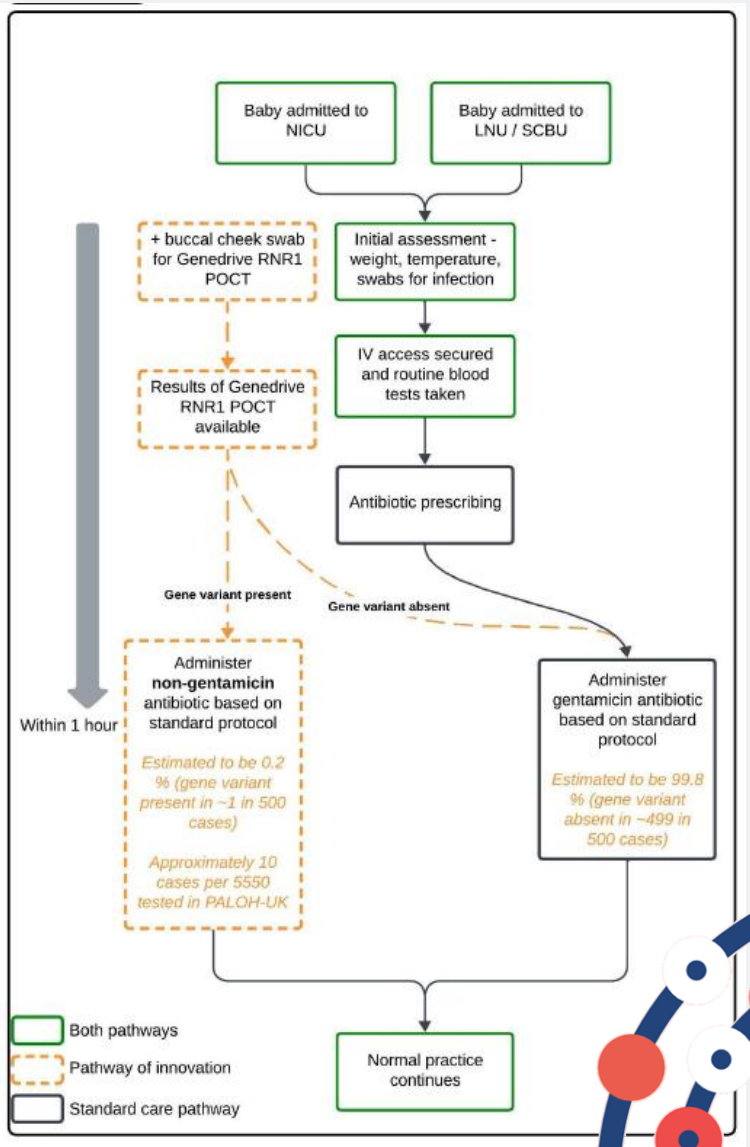
The Potential Impact & Future Directions

- The end of the research study is defined once the final patient has been recruited, defined by the power calculation, and their sample has undergone gold standard genotyping.
- PALOH-UK will comprehensively address the evidence gaps outlined in the **NICE EVA, with formal submission expected in Autumn 2026**
- During PALOH-UK, **10-15 babies** could avoid aminoglycoside induced hearing loss.
- If MT-RNR1 testing can successfully be adopted into routine practice, the hearing of hundreds of newborns could be preserved each year, whilst saving money in the NHS.



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PALOH / PALOH-UK study

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- Rachel James
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- Dr Ajit Mahaveer
- Prof Paul Wilson / Amy Mathieson
- Prof Katherine Payne
- Dr Videha Sharma
- Sinduja Manohar / VOCAL team

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2. North Manchester General Hospital
3. Wythenshawe Hospital
4. The Royal Oldham Hospital
5. Stepping Hill Hospital
6. Royal Bolton Hospital
7. Royal Albert Edward Infirmary - Wigan
8. Tameside General Hospital
9. Royal Sussex County Hospital
10. Royal Jubilee Maternity Hospital - Belfast
11. Royal Hospital for Children - Glasgow
12. University Hospital of Wales - Cardiff
13. Norfolk and Norwich University Hospital
14. Betsi Cadwaladr University Health Board

21 November 2024

Genetic test for deafness in newborns to be trialled across the UK

FUNDED BY NIHR | National Institute for Health and Care Research