Melbourne Genomics
Health Alliance

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# Baby Beyond Hearing study: Additional screening of the genome in infants

## Background

Melbourne Genomics' Clinical Flagships have been at the forefront of determining when genomic testing makes a demonstrable difference to the safety and quality of patient care.

Congenital deafness is one of 16 areas of health investigated by Melbourne Genomics; the Congenital Deafness Clinical Flagship made genomic testing available to infants diagnosed with hearing impairment (see separate summary). The Flagship's Baby Beyond Hearing (BBH) sub-project investigated the choices parents made when offered genomic screening for unrelated childhood-onset conditions (childhood additional findings, AFs).

## Publication

"A protocol for whole-exome sequencing in newborns with congenital deafness: a prospective population-based cohort", Downie, L., Halliday, J.L., Burt, R.A., Lunke, S., Lynch, E., Martyn, M., Poulakis, Z., Gaff, C., Sung, V., Wake, M., Hunter, M., Saunders, K., Rose, E., Rehm, H.L., Amor, D.J., BMJ Paediatrics Open (2017) doi: 10.1136/bmjpo-2017-000119

"Exome sequencing in newborns with congenital deafness as a model for genomic newborn screening: the Baby Beyond Hearing project", Lilian Downie, Jane Halliday, Sharon Lewis, Sebastian Lunke, Elly Lynch, Melissa Martyn, Clara Gaff, Anna Jarmolowicz and David J Amor, *Genetics in Medicine* (2020) doi.org/10.1038/s41436-019-0745-1

## Project description

The objective: to gain evidence to guide decisions about whether and how childhood AFs can be introduced safely and usefully into practice, through investigating the choices made by a diverse group of parents with newborns.

Infants born in Victoria in 2016 or 2017 with bilateral moderate, severe or profound hearing impairment (identified through population-wide newborn hearing screening) were eligible to participate. Their parents received a decision-support tool and genetic counselling.

If parents agreed to genomic testing for their child's hearing impairment, they could choose three ways to have their child's genome analysed:

- A) only the genes relevant to deafness analysed
- B) choice A genes plus genes for medically actionable childhood-onset conditions (i.e. for which there is a known treatment or intervention)
- C) choice A and choice B genes, plus genes associated with childhood-onset conditions which may not have a clear treatment/intervention for improvement

The study's primary outcome measure was the proportion of participants choosing each of the three analysis options. Secondary measures included predictors of choice and the psychological impact of the process on families.

The Baby Beyond Hearing study was led by Professor David Amor from The University Melbourne, The Royal Children's Hospital and the Murdoch Children's Research Institute. Key coordination and analysis

was provided by Dr Lilian Downie (Murdoch Children's Research Institute); 20 other multidisciplinary health professionals were directly involved.

## Outcomes

A total of 156 patients were contacted and invited to participate (all children born in Victoria in the years 2016 and 2017 with bilateral moderate, severe or profound hearing impairment). Of the 106 families who consented to have genomic sequencing for their child's hearing impairment, 72 (68%) consented to receiving additional findings: 29 families (27%) opted only for medically-actionable conditions (choice B) and 43 families (41%) opted for all additional genes (choice C).

Four infants had reportable additional findings. For one of the patients, positive diagnosis of von Willebrand disease – a blood-clotting disorder – has enabled more precise medical care. Based on this genomic finding, the infant's parents and four siblings were also able to gain testing for von Willebrand disease.

## Lessons learnt

- More than two-thirds (68%) of parents elected to receive additional genomic findings (choice B or choice C), but a significant portion of parents (32%) elected only to analyse genes related to their infant's deafness (choice A, no additional findings).
- Parents whose infant was less than three months of age were least likely to elect to receive additional genomic findings, a result replicated in other similar research internationally.
- Factors such as cultural background and number of children in the family were found to have an impact on desires and expectations around additional findings.
- Families involved in the study generally demonstrated low levels of anxiety and feelings of conflict or regret around the decision to have genomic newborn screening. Parents who sought additional findings had significantly less anxiety at the time of decision-making, less conflict around their decision and were more tolerant of uncertainty.

## Impact

This study provides the first level of evidence to build an ethically sound framework for offering additional findings from genomic testing to parents of newborns. The BBH project was the first to use a population-based cohort (research into newborn genomic screening often reflects a more limited population subset). It is also the first to publish quantitative data on the psychosocial impact of parents' decision-making.

## Clinical Flagship team

| Name | Organisation | Role |
|---|---|---|
| David Amor | MCRI/VCGS | Clinical geneticist |
| Lilian Downie | MCRI/VCGS | Clinical genetics fellow |
| Anna Jarmolowicz | MCRI/VCGS | Genetic counsellor |
| Elly Lynch | Melbourne Genomics | Project manager |
| Jane Halliday | MCRI | Researcher |
| Sebastian Lunke | MCRI/VCGS | Medical scientist |
| Sharon Lewis | MCRI | Researcher |

This Clinical Flagship is collaborating with the Boston-based Genome Sequence-Based Screening for Childhood Risk and Newborn Illness (‘BabySeq’) Project and the North Carolina Newborn Exome Sequencing for Universal Screening team.