HEAR's Why We Need the Hearing Health Genetic Cohorts Study

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Introduction

The lack of bespoke therapies for those with hearing loss (HL) is a limitation. The combination of new genetic tests to identify individuals with heritable causes of HL and new technologies to target and correct specific genetic variants could prove to be a powerful tool in future therapies and management of genetic forms of HL and deafness.

To do this, there has to a better understanding of the different genetic aetiologies of HL. The Hearing Health Genetic Cohorts Study (HHGCS) would facilitate this. By monitoring those with genetic variants associated with HL, the HHGCS will observe the natural history of genetic variants underlying HL; understand the individual differences in treatment and outcomes; facilitate research and raise awareness.

Background

- Abnormalities within the auditory system can lead to the disruption of sound transmission from the outer ear to the brain.
- Hearing Loss (HL) is heterogenous in both aetiology and phenotype and may be classified as environmental (infections, trauma) and/or genetic (>120 genes, syndromic/non-syndromic, autosomal dominant/recessive, sex-linked or mitochondrial); conductive, sensorineural, or mixed; progressive or non-progressive; congenital or age-related[1].
- Figure 1 shows the anatomy of the ear with key structures which can be affected and cause HL

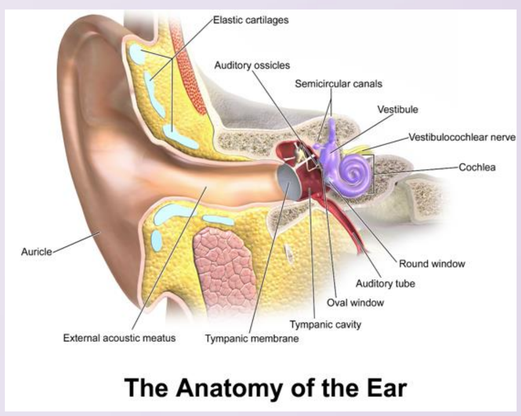


Figure 1: The anatomy of the ear.
Comprised of the outer, middle and inner ear. The primary function of the auditory system is to transmit and transduce sound waves to the brain. Abnormalities in any of the ear's structures or sound transmission pathways can lead to HL.
(Image:https://commons.wikimedia.org/wiki/File:Blausen_0328_EarAnatomy.png)

We need a better understanding of genes in HL

HL can lead to reduced cognitive development[5] in children and has been associated with abnormalities in different organ systems of the body, leading to a range of pathologies including vision impairments, diabetes, anaemia and chronic kidney disease[7,8].

With approximately 50-60% of individuals with HL having a genetic aetiology[3], improved understanding of the different genetic variants associated with HL is therefore necessary.

Genes associated with hearing loss on the NHS HL panel

- 115 genes (Figure 2) will be included in the National Health Service (NHS) newborn hearing screening programme (NHSP) through the NHS Genomic Laboratories in Manchester/Liverpool and London.
- These genes have been reported in the literature, and validated, as being associated with HL.
- Individuals with genetic variants of certain syndromes, such as Usher and Waardenburg, will be identified through the NHSP.
- New genes are still being identified.

ABHD12	*DNMT1*	*KCNQ1*	*OTOGL*	
ACTG1	*DSPP*	*KCNQ4*	*P2RX2*	
ADGRV1	*EDN3*	*KIT*	*PAX2*	
ALMS1	*EDNRB*	*LARS2*	*PAX3*	*SNAI2*
ATP6V1	*EPS8*	*LHFPL2*	*PCDH15*	*SPATA5*
BCS1L	*ESPN*	*LOXHDL1*	*PDZD7*	*SOX2*
BSND	*ESRRB*	*LRT0MT*	*PNPT1*	*SOX10*
CABP2	*EYA1*	*MARVELD*	*POU3F4*	*STRC*
CCDC50	*EYA4*	*MASP1*	*POU4F3*	*SYNE4*
CDH23	*FGF3*	*MITF*	*PRPS1*	*TBC1D24*
CEACAM1	*GATA3*	*MSRB3*	*PTPRQ*	*TECTA*
CEP78	*GIPC3*	*MT-RNR1*	*RDX*	*TIMM8A*
CHD7	*GJB2*	*MT-TS1*	*S1PR2*	*TMC1*
CIB2	*GHB3*	*MYH9*	*SALL1*	*TMIE*
CLDN14	*GPSM2*	*MYH14*	*SALL4*	*TMPRSS3*
CLPP	*GRHL2*	*MYO15A*	*SERAC1*	*TPRN*
CLRN1	*GRXCR1*	*MYO3A*	*SERPINB6*	*TRIOBP*
COCH	*HAAD*	*MYO6*	*SGPL1*	*USH1C*
COL11A2	*HOXA2*	*MYO7A*	*SIX1*	*USH1G*
COL4A5	*HSD17B4*	*OPA1*	*SLC17A8*	*USH2A*
COL4A6	*ILDR1*	*OSBPL2*	*SLC26A4*	*WFS1*
DFNA5	*KARS*	*OTOA*	*SLC26A5*	*WHRN*
DFNB59	*KCNE1*	*OTOF*	*SLC4A11*	
DIAPH1	*KCNJ10*	*OTOG*	*SMPX*	

Figure 2. The National Health Service (NHS) newborn hearing screening programme (NHSP) gene panel.
The 115 gene HL panel will be offered to the parents of each baby that is identified as having a HL in the NHSP

Hearing Health Genetic Cohorts Study

The HHGCS will consist of three cohorts (Figure 3): babies that are born with HL (Cohort 1), children that develop HL by 9 years of age (Cohort 2), anyone else that develops HL as they age (Cohort 3).

The HHGCS will collate healthcare data, including genetic data where available, from individuals over their lifetimes to enable the investigation of healthcare disparities and other outcome measures as shown in Figure 4.

From this core data set researchers would be able to use the HHGCS to:
- Support the development of new treatments and therapies for HL
- Investigate the implications and outcomes of these therapies
- Identify predictors and markers of HL
- Evaluate therapeutic options
- Investigate the impact of therapies on the progression of HL
- Identify disparities in care for those with HL

Figure 3. The cohort structure of the HHGCS and UK prevalence of HL in each of the proposed cohorts
(Images CC Baby, Child with bubbles, adult thumbnails)

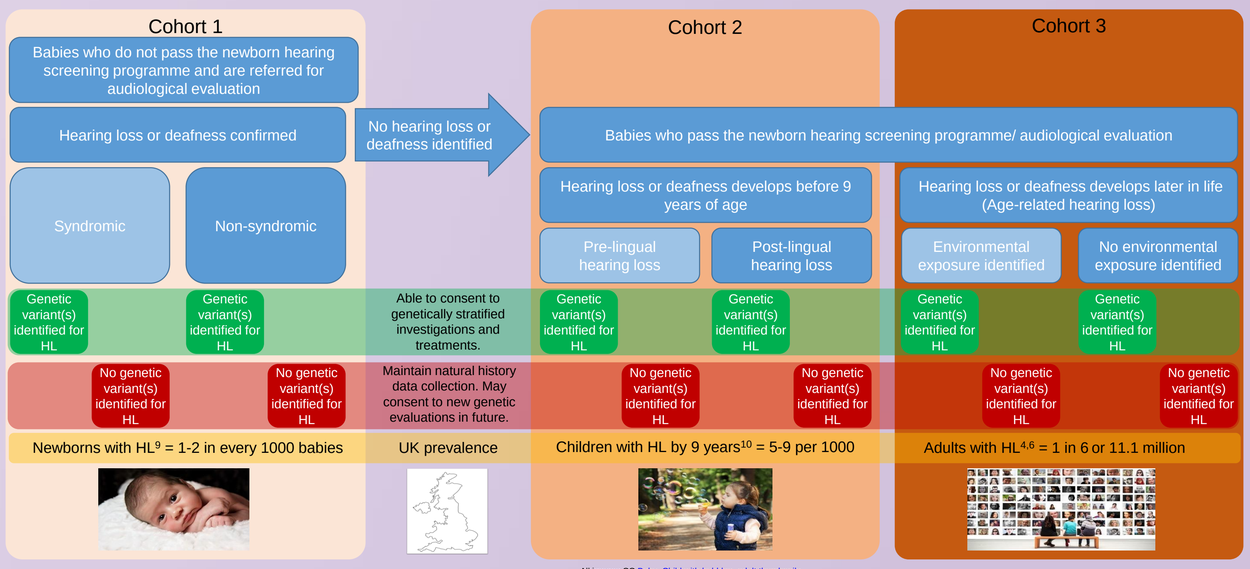
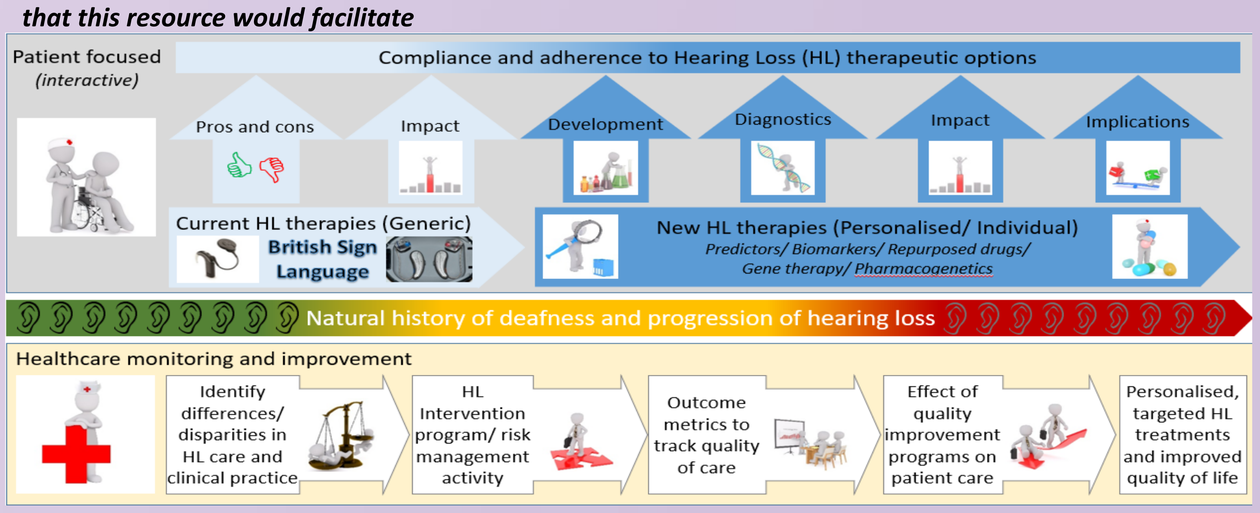


Figure 4. Core data set collected by the HHGCS and potential outcome measures and developments that this resource would facilitate



Conclusions

- **The genetics of hearing loss is complex and involves more than 100 genes.**
- **The HHGCS, alongside the NHSP HL genetic panel, will make it possible to stratify individuals based on genotype.**
- **Serving as a hub to collect genetic data and clinical findings around different genetic variants, the HHGCS will be a powerful tool for combatting genetic forms of HL and deafness, thereby delivering a personalised therapeutic approach.**

Have your say on the HHGCS.....

- **Please either scan the QR code or click on the link below to fill in our HHGCS survey**

https://redcap.link/HHGCS_Professional_Opinion_Survey

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