

POSITION STATEMENT: MEDICAL ADVANCEMENTS IN GENETICS AND INTERVENTIONS TO PREVENT OR REDUCE HEARING LOSS



Owner/s:	Director Policy and Campaigns
Author/s:	Head of Policy and Research Development Manager (Audiology & Health)
Issuing Team/Department:	Policy and Campaigns
Version No:	V3
Date Approved:	<ul style="list-style-type: none"> • EDs 13 February 2018 • Committees 1 March 2018 • Trustees 24 March 2018
Review Frequency:	3 years, or earlier if required by developments in medical research
Next Review Date:	2020/21
Circulation (primary location):	Website

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1 Summary

- 1.1. Medical advances in our understanding of genetics and the role different genes play in deafness are happening at a rapid pace. This is likely to increase with the introduction of 'whole genome sequencing' (WGS) into the NHS through the 100,000 Genomes Project.
- 1.2. At the same time, research is giving us a greater understanding of how deafness could be prevented for some children, and/or potentially offering the option of a medical intervention to some deaf children with the aim of reducing their hearing loss.
- 1.3. We recognise the rights of families with deaf children and potential parents from families who have a history of deafness to take advantage of the various medical interventions or genetic technologies and to use the results of any medical/genetic tests in a way that suits the individual family.
- 1.4. It is important that families receive balanced and clear information about deafness, medical interventions and genetic technologies in order to enable them to make an informed choice. This includes all information relating to both benefits and risks. It is also important that professionals act with care and sensitivity in how they engage with families on this issue and in the language they use to refer to deafness and medical interventions.
- 1.5. We will continue to campaign for a world in which families' different choices can be realised in a way that works for them. We will also continue to campaign for a world in which childhood deafness is not stigmatised and deaf children are viewed as individuals who have all the opportunities that are available to hearing people to develop and maximise their skills and abilities.
- 1.6. We support all families irrespective of any choices they make around medical interventions and deafness¹. It is for families and deaf children/young people to own their experiences of deafness and no family or deaf child/young person should be made to feel anything less than positive about the choices they make around deafness.

2 Introduction

National Deaf Children's Society vision and values

This position statement is underpinned by our vision and values.

Our vision is a world without barriers for every deaf child. We believe that:

- a. Deaf children can do anything other children can do, given early diagnosis and the right support from the start.
- b. Deaf children should be involved in decisions which affect them at as an early age as possible.
- c. Families are the most important influence on deaf children and young people, and need clear, balanced information to make informed choices.
- d. Effective language and communication skills lie at the heart of deaf children and young people's social, emotional and intellectual development.

¹ Unless there is clear evidence that this is not in the best interest of the child. The welfare of the child remains paramount but in the vast majority of cases we believe parents are best placed to make that judgement based on all the information available.

- e. Deaf children should be valued by society and have the same opportunities as any other child

- 2.1. We welcome all medical discoveries that give us a better understanding of deafness, empower individuals by giving them choices and enhance the potential of deaf children and young people and their families to lead lives which are as rich and varied as possible.
- 2.2. We also support any research into medical interventions that may prevent hearing loss happening or reduce existing hearing loss that might allow parents the choice of reducing the impact of deafness on their deaf child's social and educational development. We recognise that if any form of intervention does become available in the future the resulting improvement to hearing could possibly be more permanent than that afforded by cochlear implants or hearing aids.
- 2.3. We believe that the prospect of future medical developments in deafness should not detract from the support that deaf children presently need. We will continue to campaign for health, education and social care services to provide the support that deaf children need to achieve their potential.

Genetic counselling and testing

- 2.4. There are many factors that may result in deafness and only about half of the causes of deafness can be attributed to genetic factors. Until recently only a few genes known to cause deafness were routinely tested for, meaning that even if genetic testing was carried out the responsible gene may not have been identified. With the introduction of a new genomic service by the NHS, families who have a child with severe to profound bilateral deafness will be offered 'whole genome sequencing' (WGS). This is much more likely to be able to locate a responsible gene meaning that more families will get information about the cause of their child's deafness. We welcome the rapid advances in our understanding of the genetics of deafness, but stress that the wider implications of all genetic testing are extremely complex, families must be given clear information about the potential implications of such testing, and the data collected must be treated with the utmost sensitivity and care (see section 3 for further information).
- 2.5. Genetic testing and counselling services should be offered to deaf children and young people and their parents where it is wanted and considered to be appropriate in providing beneficial knowledge to either the child or the family.
- 2.6. It is important that services for families are fully accessible to deaf parents and young people who have sign language as their first language. Families should also be signposted to resources such as the National Deaf Children's Society resource *Genetic counselling: Information for families* available from our website.
- 2.7. We support the development of research and services that:
- enables the early identification of disabilities or health conditions that may, at some point in childhood, co-exist with deafness so that appropriate monitoring, intervention plans and services can be put in place
 - identifies the vulnerability of a child to medication that, if administered, will create hearing loss or exacerbate the degree of hearing loss

Genetic screening

- 2.8. We do not support whole-population screening for genetic conditions, with the consequent risk of moving towards a society in which difference is no longer accepted or tolerated.

Prenatal genetic testing

- 2.9. We acknowledge that some parents, whether deaf or hearing, choose to undergo prenatal genetic testing in order to prepare for the child's future, while others may consider a termination of the pregnancy. It is important that parents are aware of any risks involved in such testing. It is not our role to express an opinion about the way in which an individual chooses to use the information, but fundamental messages that we will continue to promote include:
- a. Deaf children and people can make a positive contribution to society and can have happy and rewarding lives
 - b. If appropriate support is provided to the family and child and positive attitudes are fostered, there is no reason why deaf children should not achieve at the same level as hearing children

In vitro fertilisation and pre-implantation genetic diagnosis

- 2.10. It is not our role to express an opinion on the way society decides to make use of pre-implantation genetic diagnosis. (See supporting section paragraphs 3.17 and 3.18)

Stem cell and gene therapies

- 2.11. There are significant research developments into how stem cell and gene therapies can be used to prevent or reduce hearing loss. We support any medical research that might allow parents the choice of reducing the impact of deafness on their deaf child's social and educational development. Where clinically appropriate, we will campaign for families to have access to any such interventions if they make an informed choice to do so.
- 2.12. We understand that a number of obstacles need to be overcome before gene and stem cell therapies can be used safely and it will take a number of years to overcome these obstacles. It is also unlikely that those therapies will have the same impact in all deaf people. It is not our role to express an opinion about the way in which stem cells are used or in how these therapies are developed.
- 2.13. It is important that families and deaf children/young people are given clear and balanced information about any benefits and risks involved in any intervention, particularly if they are undergoing any clinical trials. Information should be tailored to the needs of the child, recognising that medical interventions available may depend on the type of deafness that children have and/or on any interventions they have already received (such as cochlear implantation). If families or deaf young people seek a medical intervention abroad, they should ensure they have comprehensive information on standards for clinical trials and interventions in that country.
- 2.14. It is important that services anticipate the needs of deaf children and young people following any interventions. Deaf children and young people may still experience delays in their language and communication. In addition, some deaf young people and their families

may need counselling and emotional support to help them come to terms with the impact of the medical intervention.

3 Supporting information for the position statement

Note: Factual changes to this section will be made from time to time to keep up with recent developments in genetics without requiring Trustee Board approval unless they necessitate changes to policy.

- 3.1. We are committed to empowering parents of deaf children, and deaf children and young people themselves, to make informed choices by providing impartial advice and information on all aspects of childhood deafness.
- 3.2. Our attitude to medical interventions and genetic developments is based on:
 - a. A belief that families are best-placed to make decisions about their child. Similarly, deaf children and young people should be involved and supported in any decisions in this area. Families and deaf children/young people should be provided with clear and balanced information to enable them to make informed choices. We support all families and deaf children/young people regardless of any choices they make around medical interventions and deafness. It is for families to own their experiences of deafness and no family or deaf child should be made to feel anything less than positive about the choices they make around deafness.
 - b. A belief that deafness should not be regarded as an illness or a life-threatening or life limiting condition. The social model of disability asserts that deafness in itself is not a disability, but the way society responds to it does disable people. For this reason, we believe that it is important that professionals act with care and sensitivity in how they engage with families and in the language that they use.
 - c. Our policy on inclusion states that we believe that inclusive practice arises from a philosophy which views diversity of strengths, abilities and needs as natural and desirable, bringing to any community the opportunity to respond in ways which lead to learning and growth for the whole community, and giving each and every member a valued role.

Genetics

- 3.3. Just as children inherit features, such as hair or eye colour, from their parents, sometimes deafness is inherited. This can happen where there is an alteration or change in a particular gene that results in a different characteristic, for example deafness. The change in a gene can be called a 'fault' or 'mutation'.
- 3.4. Genes can work in different ways. Sometimes a child only needs to inherit one faulty gene from either their mother or their father to have that particular characteristic (*dominant inheritance*). Sometimes the child will need to have the same faulty gene passed on from both parents in order to have the condition (*recessive inheritance*). There are other different patterns of genetic inheritance that are less common.
- 3.5. Some people are known as *carriers*. This is where they have the altered gene but do not have the characteristic. So a person who is a carrier for deafness would carry the altered gene, but would not have deafness themselves.

- 3.6. Sometimes a gene mutation is a one-off that simply occurred by chance. This means that, although the deafness has a genetic cause, it has happened for the first time in that person and has not been inherited. However, it could be passed on to future generations.

Genetic counselling

- 3.7. Genetic counselling provides information and support for individuals and families who are or have a chance of being affected by a range of inherited conditions, including deafness. It provides families with information about the cause of the condition, how it might affect the child and family in the future and, if the family wish to know, how likely they are to have another child with the same condition. It also enables families to make informed decisions about their child, their child's future and may help them when planning for their family.
- 3.8. Some families find it helpful to know whether deafness and any other associated medical condition were inherited. Other families prefer to wait until their children are grown up and able to decide for themselves.
- 3.9. We believe that families should be offered the chance to receive genetics counselling by a trained professional locally or be referred to their local clinical genetics (genetic counselling) team by the doctor in charge of their child's audiological care. We also encourage services to signpost families to resources such as the National Deaf Children's Society resource *Genetic counselling: Information for families*².

Genetics testing

- 3.10. Families with a deaf child may be offered a genetic test or 'whole genome sequencing' (WGS). This may happen shortly after a baby has been identified as being deaf following newborn hearing screening. Alternatively, families with older children and young people themselves may be offered a test.
- 3.11. Genetic testing involves the child and possibly other family members having a blood test. The blood sample is used to look for a gene or genes known to be involved with deafness. Families will also be asked about any family history of deafness and this information can be a very important part of identifying a genetic cause. It has been established that permanent deafness in about 50 per cent of children is due to a genetic cause. At the time of writing, not all the genes related to deafness have yet been identified and only one (called *GJB2* or *Connexin 26*) is routinely tested for in the genetics clinic. Some others may be tested for depending on the circumstances, or others can be requested specially (for susceptibility to ototoxic medications, auditory neuropathy spectrum disorder, some syndromes and so on, for example).
- 3.12. Whole genome sequencing (WGS) involves the child and possible other family members having a blood test. This time the blood sample is used to analyse the individual's genetic material. This means that more genes can be identified as causing deafness that would be missed by traditional testing that looks for a specific gene only. However it also means that other genes not related to deafness are also analysed (see 3.16).
- 3.13. In about 30 per cent of children with genetic deafness, the deafness is part of a more complicated picture, known as a *syndrome*. A syndrome is simply a medical term meaning a collection of signs or symptoms that doctors recognise as being linked or having the same

² Available from the National Deaf Children's Society website.

cause. For example, in Ushers syndrome progressive blindness is part of the syndrome in addition to the deafness. Again, some of these syndromes have been confirmed with a genetic test, but not always. WGS may help identify the gene or genes responsible for many unknown or un-named syndromes.

- 3.14. Improved knowledge of genetics and improvements in genetic diagnosis could enable earlier identification of other disabilities or health conditions that coexist with deafness and develop later in life (for example: visual disorders such as Usher syndrome, keratitis-ichthyosis-deafness (KID) syndrome, Alstrom syndrome; kidney dysfunctions such as in Alport syndrome; heart conditions as part of Jervell and Lange-Nielsen-syndrome). This will help families and professionals plan for educational and health care needs, including audiology care. Having a certain syndrome, for example, may mean that a hearing loss will worsen over time and therefore more frequent hearing checks may be needed. It might also mean that hearing aids will not provide a child with access to sound and that families should consider cochlear implants for their child, particularly for children with some types of auditory neuropathy.
- 3.15. WGS can also give families information on 'additional findings' in their genome. These are not related to the deafness that led them to have the testing. 'Additional findings' are genomic changes that are known to cause serious, life threatening conditions. The changes are in certain genes that may cause an increased risk of certain genetic diseases. These diseases can often be prevented or reduced by NHS interventions. These conditions are quite rare and only childhood-onset diseases will be reported for child participants. It is therefore vital that families receive clear information on the risks and benefits of different types of genetic testing before consenting so that they can choose to opt out of looking for additional findings if they wish.
- 3.16. We support the development of genetic diagnosis and services. The NHS should ensure that these developments are widely available and accessible to deaf children, young people and their families.

Genetic vulnerability to medicines

- 3.17. Some children have a rare genetic increased susceptibility to deafness caused by the administration of certain antibiotics, most frequently given in response to life-threatening conditions. It is possible to have a genetic test to identify whether they have the A1555G mutation. If they do, the information can help inform the family and their doctor prior to the intervention so that alternative medication can be given. These antibiotics are widely used for extremely premature babies and older children with life-long conditions such as cystic fibrosis. At the moment the genetic test takes too long to return from the lab for the results to be useful prior to urgent need to administer the drugs. However research is ongoing looking at non-invasive bedside screening for the gene, speeding up the process and allowing the families to know the risks and give informed consent before antibiotic use.

Genetic screening

- 3.18. Genetic screening of individuals is used to determine whether they carry a gene for a particular disease or condition that may affect them in the future or may be passed on to their children. The term 'genetic screening' is used to mean a test which is offered to a whole population or group within the population rather than specifically offered to an individual because of their personal or family history of a condition ('genetic testing').

Gene therapy

- 3.19. Gene therapy is the introduction of a gene into the human body in order to treat a disease or condition. Gene therapy can be used to replace a faulty gene with a normal copy or activate a gene that has been switched-off. One way of introducing a gene is by incorporating it to a harmless virus which “infects” the appropriate cells and delivers copies of the therapeutic gene. Once inside the cell, the gene is switched on and is able to have its biological effect.
- 3.20. A gene known as Atoh1 was discovered more than 10 years ago that acts as a “switch”. A gene therapy to deliver this “switch” is currently being trialled in 45 profoundly deaf people in the USA. Results expected 2017.

Prenatal genetic diagnosis

- 3.21. If a family has a history of deafness and a known genetic cause has been identified, i.e. the particular gene has been confirmed through testing, an individual or couple may choose to have prenatal genetic testing in a future pregnancy. This type of testing may identify whether the foetus has inherited the familial deafness gene but is usually unable to predict exactly the level of deafness the child will have. It is important that parents are given clear information on any risks involved. These risks may include miscarriage, depending on the test used.

In vitro fertilisation (IVF) and pre-implantation genetic diagnosis (PGD)

- 3.22. Pre-implantation genetic diagnosis involves IVF techniques to produce embryos, but with the additional step a few cells are removed from each embryo and tested to see whether or not that embryo has inherited a particular gene or not. This allows selection of which embryos will be placed in the uterus. It is available for couples who have a chance of passing on a specific genetic condition. As with prenatal genetic diagnosis, a genetic cause (i.e. a particular gene) must already be identified in the family for PGD to be an option. PGD is possible and licensed by the Human Fertilisation and Embryology Authority (HFEA) for a range of genetic conditions. This does include several genetic causes of deafness. Most of these, though not all, are syndromes where deafness is one part of the condition and there are implications for health.
- 3.23. We acknowledge that some families with a history of deafness may wish to use this type of technology in planning their family. Section 14 of the *Human Fertilisation and Embryology Act 2008* states that, where families are undergoing pre-implantation genetic diagnosis, an embryo with an ‘abnormality’ that will develop into a ‘serious physical or mental disability’ must not be deliberately selected. The Act does not require families to undergo screening for such abnormalities (i.e. if a family are undergoing PGD for one condition at their request, there is no requirement for their embryos to be tested for other conditions within the family), but where a screening has taken place, such embryos cannot then be ‘preferred’ if other healthy embryos are available.

Chemotherapy induced deafness

- 3.24. Research in this area is looking at development of a drug to use alongside chemotherapy to prevent deafness happening (research in progress). Currently cisplatin-based chemotherapy agents used in childhood cancer treatment are known to cause hearing loss.

Hair cell regeneration

- 3.25. Research in this area broadly falls into three areas – growing hair cells in the lab, investigating the genes that may be responsible for switching on the regeneration of hair cells, and developing drugs to encourage regeneration. Hair cells within the inner ear are easily damaged by noise, ototoxic drugs (such as the antibiotics and chemotherapy mentioned above), and aging. It affects a large proportion of people (including almost all age-related deafness). In humans (and other mammals) hair cells are never repaired or replaced. However, this is not the case in some other animals so efforts to understand the basis of regeneration in other species means there is a lot of interest in this area.
- 3.26. There are lots of challenges in this area, including that the inner ear is made up of a lot of other supporting cells and structures as well as hair cells. Even if hair cells can be grown successfully in a lab lots of other questions remain; how would we get them into the inner ear, how would they would function in the human ear, would other develop in response, would cell growth stop at the usual number or continue proliferating, how well would they survive? etc.
- 3.27. One recent study looked at using a gene to convert stem cells into hair cells and found that when they were converted to auditory cells too quickly abnormal cellular growth occurred (risk factor for cancer).
- 3.28. Separately, there has been early work on using drugs to encourage growth of hair cells within the cochlea. Issues still relate to getting the drug into the cochlea but one method that has been tried is by using a cochlear implant electrode as the conduit. This may have some success in improving outcomes for the implant user by encouraging nerve growth closer to the electrode.

Stem cell therapy (umbilical cord blood)

- 3.29. Florida Hospital in the USA began a study in 2014 of 10 deaf children aged between 6 weeks and 6 years to be given their own cord blood stem cells in an attempt to trigger the body's own repair mechanisms with the hope of attaining normal hearing.

4 Definition of syndromes mentioned in this statement

- 4.1. **Alport syndrome:** The second most common inherited cause of kidney failure. Hearing loss and, occasionally, visual problems are associated with Alport syndrome.
- 4.2. **Alstrom syndrome:** A rare progressive genetic disorder characterised by obesity, deafness and visual problems in childhood and diabetes and kidney failure in adults.
- 4.3. **Keratitis-ichthyosis-deafness syndrome:** An inherited disorder in which affected persons have:
- Keratitis – gradual destruction of the cornea of the eye sometimes leading to blindness.
 - Ichthyosis – localised areas of disfiguring reddish thickened skin.
 - Deafness at birth.

- 4.4. **Jervell and Lange-Nielsen-syndrome:** A rare syndrome that causes deafness and a disruption of the heart's normal rhythm. Beginning in childhood, the irregular heartbeats increase the risk of fainting and sudden death.
- 4.5. **Usher syndrome (sometimes referred to as "Usher's syndrome"):** A relatively rare genetic disorder that is associated with a mutation in any one of 10 genes resulting in a combination of hearing loss and visual impairment and is a leading cause of deafblindness.

5 References

- 5.1 *Guidelines for Aetiological Investigations*, British Association of Audiological Physicians (BAAP), available from <http://baap.org.uk/Resources/Documents/GuidelinesClinicalStandards.aspx>
- 5.2 Making Babies: reproductive decisions and genetic technologies, Human Genetics Commission, January 2006.
- 5.3 100,000 Genomes Project <https://www.genomicsengland.co.uk>