

***“According to the World Health Organization 250 million people worldwide have a moderate-to-severe or greater hearing loss.”***

# editorial



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## Hearing loss and tinnitus: 250 million people and a US\$10 billion potential market

► The social and economic demand for therapeutic treatments for hearing loss and tinnitus is enormous. In spite of this, there are currently no FDA-approved drugs or cell-based therapies for these conditions. This special issue of *Drug Discovery Today*, produced in association with the Royal National Institute for Deaf People (RNID; see [Box 1](#)), highlights the remarkable progress that has been made towards understanding the molecular and cellular basis of hearing loss and tinnitus. The key components needed for the development of drug and cell-based therapies now exist, and the rewards that await pharmaceutical and biotechnology companies able to move this research to the clinic, where it can benefit millions of people worldwide, are huge.

### Epidemiology

Millions of people all over the world have hearing loss or associated conditions, such as tinnitus, otitis media and Ménière's disease. According to the World Health Organization 250 million people worldwide have a moderate-to-severe or greater hearing loss ([www.who.int/pbd/deafness/facts/en/index.html](http://www.who.int/pbd/deafness/facts/en/index.html)). This figure more than doubles if people with mild hearing loss are included. The National Institute on Deafness and Other Communication Disorders estimates that 33 children are born every day in the USA with a significant hearing loss, which equates to 12,045 children annually\*. In Europe, one in 51 people carry a specific version of the gene for the most common form of recessive deafness, connexin 26 [1].

Hearing loss becomes increasingly prevalent with age. RNID estimates that there are over 300 million people in the world with age-related hearing loss and this is expected to increase to 900 million by 2050†.

A common cause of hearing loss is repeated exposure to loud noise. 10 million people in the USA and 25–30 million people in Europe work daily in conditions that pose a potential risk to hearing [2]. People working in heavy industry and in the armed forces are at particular risk. Also, in the past 20 years, exposure to 'recreational' noise has increased with the advent of personal stereos and an increased numbers of bars and clubs playing loud music.

### Social and economic burden

Hearing loss is the third most common chronic condition in the older population (after arthritis and

\*NIDCD 2004 Congressional justification ([www.nidcd.nih.gov/about/plans/congressional/FinalStatement.pdf](http://www.nidcd.nih.gov/about/plans/congressional/FinalStatement.pdf))

†Presbycusis (Age-Related Hearing Loss) Market Opportunities for Pharmaceutical and Biotechnology Companies. RNID market report 2004. ([www.rnid.org.uk/VirtualContent/84925/presbycusis.pdf](http://www.rnid.org.uk/VirtualContent/84925/presbycusis.pdf))

**BOX 1****About RNID**

RNID (The Royal National Institute for Deaf People) is the largest not-for-profit organization representing the 9 million deaf and hard of hearing people in the UK. As a membership organization, we aim to achieve a radically better quality of life for deaf and hard of hearing people. We do this by campaigning and lobbying vigorously, by raising awareness of deafness and hearing loss, by providing services and through social, medical and technical research.

**Examples of biomedical research being supported by RNID:**

- RNID-funded research is on the edge of identifying the very first genes that increase an individual's susceptibility to age-related hearing loss. This discovery could lead to diagnostics to identify those at risk and to drug targets for the prevention of age-related hearing loss.
- RNID is supporting unique research exploring the therapeutic potential of human embryonic stem cells to treat hearing loss. This cutting-edge research could produce physiologically relevant cells for high throughput drug screening and cell-based therapies for restoration of hearing.
- RNID-funded research is improving our understanding of the neurobiology of the central auditory system. This vital research will lead to therapeutic strategies for alleviating tinnitus and other central auditory processing disorders.

Visit [www.rnid.org.uk](http://www.rnid.org.uk) for further information about RNID

high blood pressure; [www.pamf.org/health/toyourhealth/hearingloss.html](http://www.pamf.org/health/toyourhealth/hearingloss.html)) [3] and has serious social and economic implications. It can cause considerable difficulties in communication with relatives, friends, colleagues and the outside world in general, and can lead to reduced physical and psychological well-being, social withdrawal, isolation, loneliness and depression [4]. Children who are born profoundly deaf face severe difficulty acquiring spoken language and are often taught in special schools. Deaf children educated in mainstream schools frequently face problems socially interacting with hearing children. Research suggests that such experiences might be detrimental to their mental well-being [5]. Communication disorders are thought to cost the US economy between US\$154–186 billion per year [6] and noise-induced hearing loss causes significant economic losses of between 0.2–2.0% of the gross domestic product [7].

**Current therapeutic interventions**

Hearing loss frequently involves the loss of sensory hair cells and auditory neurons in the cochlea, and today's treatments are limited to the use of prosthetics (e.g. hearing aids and cochlear implants).

*Hearing aids*

Hearing aids amplify the sounds people struggle to hear, improving individuals' ability to communicate. The global hearing aid market is currently worth approximately

US\$8 billion. In recent years, the availability of programmable digital hearing aids, which allow tailored amplification to match users' hearing loss, has increased their possible benefits. Improved directionality, background noise reduction and acoustic feedback suppression have also brought significant quality-of-life improvements to hearing aid users [8].

However, market penetration of hearing aids remains low, at around 20% of possible end users, even in the developed world. In many countries, a shortage of suitable audiological facilities with qualified audiologists has meant that potential users have not been able to gain access to hearing aids. Reimbursement issues and lack of awareness of the benefits of well-fitted hearing aids conspire to suppress market growth. Additionally, hearing aids can only offer benefit to people with residual hearing.

*Cochlear implants*

A cochlear implant bypasses the hair cells and directly stimulates the auditory nerve. They are only routinely provided to prelingual profoundly deaf children or postlingual deafened children and adults who do not benefit from hearing aids. Consequently, they are only suitable for a minority of people with hearing loss. Although the cochlear implant market is estimated to be worth approximately US\$410 million, it is relatively small compared with the hearing aid market. The cost of assessment, implantation, intensive support and maintenance for the first three years alone is typically around US\$100,000\*. Whether or not the patient will receive a cochlear implant is dependent on the cause of the hearing loss, the reimbursement policy of the local healthcare provider or his/her ability to pay.

Although these prosthetics bring real benefit to those who use them, a considerable gap exists that could be addressed by pharmaceuticals focusing on the underlying biological causes of hearing loss.

**Tinnitus**

Tinnitus (commonly referred to as ringing in the ears or head) is often one of the first signs of potential damage to hearing, especially after exposure to loud noise. Fortunately, for many, tinnitus is a temporary phenomenon lasting for only a short period but 1 in 10 adults have clinically significant tinnitus (regular prolonged spontaneous tinnitus lasting 5 minutes or more), and for 1 in 100 adults tinnitus severely affects their ability to lead a normal life. RNID estimates that 13 million people in western Europe and the USA currently seek medical advice for their tinnitus. Over 4 million prescriptions are written each year for tinnitus relief but these are all for off-label drugs from a wide variety of therapeutic classes and most are associated with considerable side effects.

\*Nottingham Cochlear Implant Programme Price list for 2003/2004, Queen's Medical Centre Nottingham University Hospital NHS Trust.

Despite the significant unmet clinical need for a safe and effective drug targeting tinnitus relief, there is currently not a single FDA-approved drug on the market. RNID estimates that a novel tinnitus drug could have a product value of US\$689 million in its first year of launch<sup>§</sup>.

### The time is right

So why, despite the existence of the vast potential markets described above and the significant unmet clinical need that could be addressed through novel drug intervention or cell-based therapies, have the pharmaceutical and biotechnology industries been slow to get involved? In the past, a lack of fundamental knowledge of the biological basis of hearing and hearing loss, and the absence of assays for drug screening were probably the main reasons. But, as Matthew Holley's keynote review and the related reviews in this issue of *Drug Discovery Today* demonstrate, this no longer holds true: there has never been a better time for investment in translational hearing research.

There are already cases of compounds moving from pre-clinical to clinical development (see Lynch and Kil, this issue). A good example is ebselen, a compound that is thought to reduce damage caused by reactive oxygen species, which has been shown in animal models to reduce permanent hearing loss following noise exposure. Sound Pharmaceuticals have now secured FDA approval to conduct a Phase II clinical trial to test the ability of this compound to protect hearing in army recruits.

There are also opportunities for companies with expertise in developing gene- and cell-based therapies. Ground-breaking research has shown that *Math1*-expressing viruses produced some structural and functional recovery of the sensory structures in the cochlea of deafened guinea pigs. Other researchers have shown that mouse embryonic stem cells can give rise to sensory hair cells when transplanted into the developing chick ear. The possibility that such technology could be used to restore hearing is very exciting (see Matsui *et al.* in this issue).

In the field of tinnitus research, there are exciting opportunities for companies with an interest in neuroscience, particularly for those working on chronic pain. The neurobiology underling these two conditions is remarkably similar and combining expertise in these areas could be very productive.

Government (e.g. the US National Institutes of Health, the UK Medical Research Council and the European Commission) and non-government agencies, including RNID, recognize the importance of hearing research and have been investing in this area for many years. Our own research grants programme ([www.rnid.org.uk/research-grants](http://www.rnid.org.uk/research-grants)) invests around US\$1 million annually in research worldwide and we expect to see this level of support grow over the coming years. There is now a real opportunity to move this promising research from the laboratory to the clinic: the pharmaceutical and biotechnology industries are vital to this process. RNID is already working closely with industry to highlight the vast markets available for novel treatments, the current unmet clinical needs and the potential avenues of research that are open to them. We believe our considerable expertise in this field, our novel market reports ([www.rnid.org.uk/marketreports](http://www.rnid.org.uk/marketreports)) and links with both academia and industry have enabled a variety of key collaborations to date.

This special issue brings together an impressive body of evidence to demonstrate that the science now exists to deliver radical improvements in therapeutic interventions for hearing loss and tinnitus. By getting involved, industry will not only address the significant unmet clinical needs of millions of people but also be rewarded with at least US\$10 billion worth of added revenue.

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<sup>§</sup>Tinnitus Market Situation Analysis. RNID market report 2004. ([http://www.rnid.org.uk/VirtualContent/84925/tinnitus\\_market.pdf](http://www.rnid.org.uk/VirtualContent/84925/tinnitus_market.pdf))