14th ICBEN 2023 18 - 22 JUNE BELGRADE

14th ICBEN Congress on Noise as a Public Health Problem

Noise-induced hearing loss: 2020-2022 research highlights

[1] Ravi Reddy1, [2]Sofie Fredriksson

[1]School of Health Sciences, Massey University, New Zealand
[2]Occupational and Environmental Medicine, School of Public Health and Community Medicine, Institute of Medicine, University of Gothenburg, Sweden

Corresponding author's e-mail address: r.reddy@massey.ac.nz

ABSTRACT

Noise-induced hearing loss is the second major cause of hearing loss (after presbycusis; age) and therefore noise exposure is the main modifiable risk factor for hearing loss. We were interested in exploring research in this field from 2020 to 2022. A search with the search term “noise-induced hearing loss” in the ‘all fields’ in Web of Science Core Collection identified over 500 peer reviewed scientific papers. The main areas in which they were published were otorhinolaryngology, public/environmental/occupational health, neurosciences, audiology speech language pathology, and environmental sciences. We will present research highlights from these papers, including publications on noise exposure in association with each of the sub-themes within ICBEN Team 1 “Noise-induced hearing loss”: hearing loss, tinnitus, and balance problems; occupational noise; leisure noise; screening, clinical evaluation, and treatment; and molecular genetics. Based on this overview, knowledge gaps, emerging areas and future research priorities will also be discussed.

Keywords (3-6): Noise-induced hearing loss, tinnitus, vestibular function, hyperacusis, hair cell loss, synaptopathy.

INTRODUCTION:

The World Health Organisation estimates suggest that by 2050, around 2.5 billion people worldwide will have some degree of hearing impairment [1], with noise-induced hearing loss (NIHL) being a major contributor to the global burden. It is well-established in the scientific literature that exposure to loud noise can cause deterioration in threshold sensitivity and damage to sensory hair cells and other structures in the auditory system. Exposure to excessive occupational and recreational can cause a variety of auditory and vestibular problems, including hearing loss, tinnitus, and possibly also balance problems. Increased intensity and duration of exposure lead to more severe damage, resulting in greater hearing loss.

The psychological and emotional effects of hearing loss, such as anxiety, depression, and social isolation, can significantly impact a person's quality of life [2]. Reducing exposure to loud noise can prevent NIHL, and this can be accomplished through the use of hearing protection devices, engineering controls, and education and training on safe listening practices.

In this narrative-style review, we focus on a range of research published between 2020 and 2022. We begin by examining the hearing loss, tinnitus, and balance issues linked to noise exposure. We then highlight some of the latest findings on the effects of noise exposure in both occupational and leisure settings. The review also includes discussions on screening, clinical evaluation, treatment options, and molecular genetics related to NIHL and tinnitus.

HEARING LOSS, TINNITUS AND BALANCE PROBLEMS ASSOCIATED WITH NOISE.

Noise-induced hearing loss (NIHL)

Outer hair cell (OHC) losses and worsening of hearing thresholds near 4 kHz in the basal region of the cochlea has been reported in human to be significantly greater in cases with noise-exposure history than in an age-matched control group [3]. The study found that there was no correlation between noise exposure history and apical OHC loss or pan-cochlear strial degeneration, suggesting that those types of hearing losses are age-related. In addition to OHC loss, there is growing evidence mainly from animal model studies suggesting that noise-induced damage to synaptic connections between the inner hair cell (IHC) and the auditory nerve could lead to cochlear synaptopathy or sometimes called ‘hidden hearing loss’ even when there is no evident damage to the hair cells [4]. Auditory nerve fiber (ANF) loss, exacerbated by noise, has recently been reported also in humans to be significant at all cochlear frequencies, contributing to poor word discrimination [3]. While, noise-induced cochlear synaptopathy can affect the ability to perceive speech in noisy environments, it is difficult to diagnose using conventional hearing tests as thresholds are insensitive to synaptic and neural loss until damage is severe [5].

Tinnitus

Resent research in military personnel have shown that exposure to hazardous levels of noise is significantly associated to tinnitus [6, 7]. Combat noise exposure was found to be a more important risk factor for tinnitus than age and those with tinnitus were be more than 4 times as likely to also have hearing loss, and tinnitus was often a precursor for later hearing loss [7]. Other than occupational noise, exposure to loud music and leisure noise can also be a significant risk factor for developing tinnitus [8].

Vestibular outcomes

A 2020 review suggests that noise exposure may cause damage to the peripheral vestibular system as well [9]. Although, results from Ertugrul et al. suggest that occupational noise exposure may not have an effect on the lateral semicircular canal of the vestibular system, as they did not find any difference in the caloric response as assessed using Videonystagmography (VNG) [10]. Noise-induced peripheral vestibular dysfunction may therefore perhaps not be detected without assessing the vestibular nerve or the saccular function, as suggested by Stewart et al., who showed delayed onset latency and reduced Vestibular short-latency Evoked Potential (VsEP) in rats following noise exposure [9]. Similarly, Viola et al. identified significantly increased cervical Vestibular Evoked Myogenic Potentials (c-VEMP) thresholds and p1-n1 amplitudes in human subjects with documented occupational noise exposure for at least 5 years, while caloric test results were normal [11]. There are however still gaps in our understanding of the relationship and pathways of noise

exposure and vestibular impairment, and few studies were found on this topic for the current review.

Other hearing-related outcomes

Given the search term used for this review, the 50 studies related to this sub-theme mainly focused on hearing loss as outcome. Exposure to high levels of noise can however also lead to other hearing-related outcomes, such as a distortion of the temporal cues that are important for speech perception and other sound perception causing listening difficulties, fatigue, and other related problems [12]. It has been reported that subjects with high noise exposure expend significantly more listening effort compared to subject with lower noise exposure, potentially due to hair cell loss as they also have more absence of transient evoked otoacoustic emissions (TEOAEs) and distortion product otoacoustic emissions (DPOAEs) [13]. Another study also found results indicating that auditory pathways and pain pathways interact, and that NIHL may cause increased pain sensitivity which could be relevant for pain hyperacusis [14].

OCCUPATIONAL NOISE EXPOSURE AND HEARING LOSS

An Australian study estimates that occupational noise-induced hearing loss (ONIHL) in workers could potentially cause the loss of approximately 62,000 QALYs and 135,000 PALYs respectively until the age of 65 [15]. The Italian agriculture sector saw a 7% annual increase in NIHL incidence during the 2004-2017 period. [16]. In one of the few studies focusing on migrant workers, a fifth of 3474 examined in Kuwait industrial sector in 2018 were diagnosed with occupational NIHL [17], which demonstrates the vulnerability of migrant workers globally. Furthermore, there is evidence to suggest that there is a socio-economic disparity in the burden of ONIHL, with workers in low- and middle-income countries (LMICs) being more affected than those in high-income countries (HICs) [18]. For example, there is evidence from Myanmar and Vietnam that workers in textile mills and cement plants are at risk of developing hearing loss due to occupational noise exposure [19].

As have been known from previous research, specific occupations tend to have significant risk of NIHL. Recently published studies conducted in South Africa and Australia have shown that mining workers are at a higher risk of developing hearing loss due to their occupational exposure to loud noises [20-22]. Audiograms of noise-exposed mining rock drillers in South Africa revealed higher levels of hearing loss than non-noise-exposed administrative workers, and audiometric records of employees entering coal mining in Australia revealed significant hearing loss in older workers. Moreover, a significant proportion of younger workers showed an audiometric notch at 4 kHz, indicating early risk of hearing damage in their careers. Similarly, military noise exposure research continues to show high noise levels. For example, Luha et al. reported noise levels of 94.2±2.3 - 94.7±1.8 dB(A) in the canvas-covered rear passenger compartment of heavy all-terrain trucks, which pose a risk of hearing damage for those who spend prolonged periods in this environment [23]. Furthermore, Brazilian fishermen are also at risk of developing hearing loss due to exposure to noise from various sources, including boat engines and machinery with sound pressure levels reported to be between 99.5 to 107.9 Leq dBA [24, 25]. This highlights the importance of protecting workers from noise exposure in the workplace, as well as the need for regular hearing tests to monitor and detect hearing loss early on.

We also highlight a study indicating that younger workers may be more likely to be involved in jobs with high levels of noise exposure [26]. The risk in young workers may be supported by evidence that younger early career musicians with highest levels of noise exposure exhibit

greater decline in outer hair cell function compared to individuals with the lowest levels of noise exposure [27].

Interventions

Lack of feasible administrative or engineering controls and inadequate hearing conservation programs have been reported as the most-frequently cited violations of noise standards. [28]. However, strategies such as voluntary daily noise monitoring show promise in preventing ONIHL [29], as part of a broader hearing conservation programme. In addition, educational programmes have been found to be effective in improving hearing conservation outcomes [30, 31], however, research is needed to evaluate the long-term effects of worker training programmes on hearing health. The US National Health and Nutritional Examination Survey (NHANES) found that while occupational noise exposure has significantly increased among the US working-age population from 1999 to 2016, the use of hearing protection remained low at 41.3 and 32.8%, respectively for the study periods [32]. This also brings into question self-efficacy and there is evidence in support of existing literature that fit-testing systems improve the correct use of hearing protection device in workplaces [33]. A full array of prevention strategies including engineering and administrative controls, noise assessments, audiometric testing, education and improved and correct HPD are needed as part of effective hearing conservation programmes. However, current reviews suggest that better quality research is needed effectively evaluate the efficacy of these strategies over time [34, 35].

RECREATIONAL NOISE EXPOSURE AND HEARING LOSS

Noise exposure recorded using the SoundMeter X smartphone application from 10 different urban music venues in Nashville, Tennessee found an average equivalent continuous sound level of 112.0 (±4.9) dBA, and an average maximum sound level of 127.0 (±3.2) dBA [36]. These recordings were obtained for 60 minutes each and included live music performance. In addition, the Apple Hearing Study is the first nationwide study (in the US) to evaluate sound exposure from both headphone audio and environmental sound simultaneously, and the preliminary results published so far indicate that exposure to both types of sound exceeded the WHO recommended sound levels [37]. In a study of 1274 participants from the general population, personal listening devices (PLDs) were reported to be the most frequent source of leisure noise exposure with 58% of respondents reporting self-exposure at least once per month and 23% reporting daily exposure [38]. While many people find them to be enjoyable, there is a risk of NIHL. One factor influencing exposure to hazardous levels of recreational noise is general risk-taking behaviour, where individuals with higher general risk propensity are more likely to engage in risky noise behaviour [38]. Interestingly, another study reported adolescents with a lower socioeconomic status were more likely to engage in unsafe listening but found no significant association between age, gender and educational levels [39]. Health promotion resources such as the Know Your Noise website [40] and smartphone applications [41] could be effective in raising awareness about leisure noise and promoting hearing health across different demographic groups.

SCREENING, CLINICAL EVALUATION AND TREATMENT OF NOISE-INDUCED HEARING LOSS

Screening and clinical evaluation

Pure-tone audiometry, speech audiometry, otoacoustic emissions (OAEs), and auditory brainstem response (ABR) are common methods used for screening NIHL. A recent study suggest that DPOAE amplitude maps (the amplitude of the DPOAE signal at different frequency pairs plotted on a two-dimensional grid) are more reliable and provide a more comprehensive picture of outer hair cell responses than audiometry and standard DPOAEs

[42]. Research using functional Magnetic Resonance Imaging (fMRI) responses have also found that individuals with higher lifetime noise exposure have greater responses throughout the auditory system than controls with low lifetime noise exposure [43]. While the effect size was small but statistically significant, this study provides the first evaluation of noise exposure and fMRI response in humans. Although diagnosis of synaptopathy in humans is still not considered fully developed, continued interest in and results from electrophysiological tests such as the ABR and the envelope-following response (EFR) may prove to be useful in identifying cochlear synaptopathy in individuals who have been exposed to high-intensity noise [44]. Interestingly, a study on noise exposed rats found, in addition to reduced DPOAEs and corresponding loss of OHCs, frequency-dependent results from cochlear compound action potential (CAP) latency and forward masking, and the researchers hypothesised that their results may reflect different types of synaptic sub-injuries, with different underlying mechanisms, reflecting different functional outcomes such as reduced sound localisation (represented by delayed CAPs) or poor speech perception in noise (represented by enhanced forward masking) [45].

Pure tone audiometry is though still considered a gold standard test of peripheral hearing function. Therefore, the study of [46] shows that the calibration error for supra-aural transducers mimics a notch-like pattern in the absence of noise-induced cochlear damage is important. The error should be taken into consideration as to not overestimate the prevalence of NIHL based on audiometric notches. Moreover, recommendations from a medicolegal perspective on the diagnosing of NIHL based on the audiogram in military personnel has been published by Moore et al. [47]. In a separate paper they also describe how audiograms from subjects with different types of noise exposures, such as continuous, tonal, impulse noise exposure, should be assessed, as differences in the audiogram may be found depending on type of exposure [48].

Treatment

Almost 70 papers on different treatments were screened. A few are highlighted here, many of which are based on the mechanism relating to oxidative stress and generation of reactive oxygen species (ROS) within the inner ear. Hence, several antioxidant treatments were assessed, including several studies on Dexamethasone alone, or as adjuvant treatment, or methods to improve the uptake (e.g.,[49-54]). These studies generally suggested a positive effect of the treatment. For example, while not significantly influencing loss of inner hair cells (IHCs), forskolin treatment may be beneficial in reducing the oxidative damage in outer hair cells (OHCs) and attenuating NIHL [55]. In addition, anti-HMGB1 antibody treatment has been shown to reduce cochlear ROS or reactive nitrogen species (RNS) production and preservation of OHCs, thus limiting the decline in auditory threshold shifts that occur following noise exposure [56]. A few other studies assessed antioxidative effects from diverse sources, such as Curcumin [57], Sesamin [58], Ecklonia cava [59], antioxidant vitamins A, C, E, and Magnesium [60], Myricetin [61] and Ginseng [62]. Although these smaller animal studies reported positive treatment effects, publication bias should be taken into consideration and more investigation is necessary to comprehensively ascertain both safety and effectiveness of such treatments in humans.

Another study reported the novel treatment using mesenchymal stem/stromal cells (MSCs) derived from human umbilical cord Wharton's jelly, and was injected after severe sound trauma into the perilymph of four week old female C57BL/6 mice [63]. The authors concluded that the treatment induced a moderate protective effect by up-regulation of genes related to immune modulation, hypoxia response, mitochondrial function and regulation of apoptosis, and a down-regulation of genes related to synaptic remodelling, calcium homeostasis and

the extracellular matrix. Kim et al. also found a benefit, with lower ABR thresholds and more preserved spiral ganglial cells and outer hair cells, in noise exposed rats who received systematic administration of human embryonic stem cell-derived MSCs compared to controls who were only noise exposed [64]. In support of these two studies on NIHL, a recent review from 2020 including twelve studies on sensorineural hearing loss (i.e., not only NIHL), also suggest there might be a beneficial effect of mesenchymal stem/stromal cell (MSC) administration [65]. However, the authors advise caution regarding the transferability of results given the limited data, potential bias, and fundamental differences in audible frequency range in animals and humans.

MOLECULAR GENETICS OF NOISE-INDUCED HEARING LOSS AND TINNITUS

Several genes have been identified as regulators of oxidative stress and inflammation within the inner ear. For example published in the latest years, Maeda et al. (2021) identified 273 differentially expressed genes (DEGs) by RNA-sequencing and microarray analyses, which included 25 transcription factor genes and 28 neurotransmitter receptor genes, that were either up or down regulated shortly after noise exposure in mice [66]. Recent research has also revealed new insights that highlight connections between oxidative stress pathways within the cochlear mitochondria that are crucial for preserving oxidative homeostasis [67, 68].

Furthermore, GC-A/cGMP-dependent signalling pathways play a crucial role in protecting the ears from damage, and by enhancing natriuretic peptide GC-A signaling, it may be possible to counteract hidden hearing loss and NIHL [69]. In addition, the guanine nucleotide binding protein (GNAS) alpha stimulating gene, acting as a crucial transcription factor with the adrenergic signalling pathway, plays a significant role in regulating the severity of temporary threshold shift (TTS) [70]. Another study presented evidence from peripherin gene (Prph) knockout mouse models showing decreased medial olivocochlear (MOC) efferent-mediated contralateral suppression and a reduced protection against NIHL, indicating that Prph-expressing auditory neurons play a role in the sensory component of the MOC feedback circuit [71].

Most of the studies within this sub-theme (in total almost 70) were animal studies. However, Chen et al. for example studied 1269 workers in China who were exposed to noise [72]. The researchers explored the link between susceptibility to noise-induced hearing loss and single nucleotide polymorphisms (SNPs) of cochlear clock genes (CRY1, CRY2, PER1, and PER2), the DNF gene (brain-derived neurotrophic factor), and the NTF3 (neurotrophin3) gene. The findings revealed that individuals with the GC/CC genotype at PER1 gene rs2585405 may have a higher risk of developing NIHL. The study highlights the future possibility of genetic testing to detect individuals who may have a greater susceptibility. Other studies analysed telomere length (TL) as a biomarker for NIHL in humans. [73] did not find any clear causal relationship between shorter TLs and increased risk of HL in a very large study including almost 80,000 participants, while [74] found that the longer the relative TL, the lower the risk of NIHL.

A rather novel contribution was the studies by Zhang et al.[75] and Boullaud et al. [76] who focused on metabolomic analyses, which is an emerging area where biomarkers for health outcomes can be identified. There are limited studies in the field of NIHL. Boullaud et al. performed their analysis on perilymph fluid from six sheep to assess immediate and early changes after noise exposure. The analysis found over 200 metabolites, where four were significantly changed after noise exposure compared to before exposure (urocanate, S-(5'-Adenosyl)-L-Homocysteine, trigonelline and N-Acetyl-L-Leucine). The interpretation of main metabolic pathways associated with NIHL were hypothesised to relate to mechanical destruction of hair cells, damages of the synapses and nerve, and oxidative stress due to

inflammatory reactions. In the other study reviewed here, Zhang et al. assessed metabolites from plasma samples 60 Chinese factory workers, with approximately half diagnosed with NIHL, and another 30 control workers without noise exposure. The study identified several metabolites that differed between NIHL and non-NIHL cases, of which seven showed significant differences and good diagnostic power between the NIHL and non-NIHL cases. They also found several signaling pathways related to noise exposure, of which six were common for noise exposure and NIHL (including retrograde endocannabinoid signaling, sphingolipid signaling pathway, vitamin digestion and absorption, Fc gamma R-mediated phagocytosis, phospholipase D signaling pathway, and central carbon metabolism in cancer). Although these results are from rather limited samples, they provide interesting preliminary data for future metabolomic studies, which might prove important for early identification of NIHL using biomarkers, understanding of the mechanisms and development of effective treatments.

To gain a complete comprehension of the underlying mechanisms and to devise efficacious treatments of NIHL, additional research is required. The availability of large human genetic datasets, including a variety of ethnic populations and data on noise exposure, could if feasible prove an interesting and novel addition to this area.

CONCLUSION

The study of NIHL has been continued on understanding the mechanisms that result in hearing impairment. Both occupational and recreational noise exposure have been a cause of concern for workers and young individuals. To prevent further damage and improve outcomes for individuals suffering from noise-induced hearing loss, tinnitus, balance problems or other outcomes such as hyperacusis, early detection and intervention are important. This requires further knowledge and development of the diagnostics of noise-induced auditory damage beyond pure tone audiometry.

While the factors causing noise-induced auditory disorders are intricate and not entirely understood, recent research has yielded valuable insights into the mechanisms leading to hearing disorders and the techniques that can be employed to prevent them. For example, the function of genetics in determining an individual's vulnerability to NIHL is being further explored, and novel research in metabolomics, as well as stem cell therapy. However, there is still a lack of comprehensive knowledge in the variability of specific mechanisms related to genes, proteins, pathways, etc and their effect on cells and hearing in general.

Further research in the field of noise-induced auditory effects is necessary for improving the health and safety of workers and the general public who are exposed to loud noise, especially considering that noise exposure is a preventable cause of (often and so far, permanent and irreversible) hearing damage.

REFERENCES

1. Chadha S, Kamenov K and Cieza A. The world report on hearing, 2021. *Bulletin of the World Health Organization* 2021; 99: 242-+. DOI: 10.2471/blt.21.285643.
2. Nordvik Ø, Laugen Heggdal PO, Brännström J, Vassbotn F, Aarstad AK and Aarstad HJ. Generic quality of life in persons with hearing loss: a systematic literature review. *BMC Ear Nose Throat Disord* 2018; 18: 1. 2018/02/02. DOI: 10.1186/s12901-018-0051-6.
3. Wu PZ, O'Malley JT, de Gruttola V and Liberman MC. Primary Neural Degeneration in Noise-Exposed Human Cochleas: Correlations with Outer Hair Cell Loss and Word-Discrimination Scores. *J Neurosci* 2021; 41: 4439-4447. DOI: 10.1523/jneurosci.3238-20.2021.

4. Henry KS. Animal models of hidden hearing loss: Does auditory-nerve-fiber loss cause real-world listening difficulties? *Mol Cell Neurosci* 2022; 118: 103692. 2021/12/10. DOI: 10.1016/j.mcn.2021.103692.
5. Fernandez KA, Guo D, Micucci S, De Gruttola V, Liberman MC and Kujawa SG. Noise-induced Cochlear Synaptopathy with and Without Sensory Cell Loss. *Neuroscience* 2020; 427: 43-57. DOI: 10.1016/j.neuroscience.2019.11.051.
6. Henry JA, Griest S, Reavis KM, et al. Noise Outcomes in Servicemembers Epidemiology (NOISE) Study: Design, Methods, and Baseline Results. *Ear and Hearing* 2021; 42: 870-885. DOI: 10.1097/aud.0000000000000974.
7. Clifford RE, Ryan AF and Program VAMV. The Interrelationship of Tinnitus and Hearing Loss Secondary to Age, Noise Exposure, and Traumatic Brain Injury. *Ear and Hearing* 2022; 43: 1114-1124. DOI: 10.1097/aud.0000000000001222.
8. Pienkowski M. Loud Music and Leisure Noise Is a Common Cause of Chronic Hearing Loss, Tinnitus and Hyperacusis. *International Journal of Environmental Research and Public Health* 2021; 18. DOI: 10.3390/ijerph18084236.
9. Stewart CE, Holt AG, Altschuler RA, et al. Effects of Noise Exposure on the Vestibular System: A Systematic Review. *Frontiers in Neurology* 2020; 11. DOI: 10.3389/fneur.2020.593919.
10. Ertugrul S, Soylemez E and Gurel T. Effectiveness of hearing protection apparatus in preventing noise induced vestibular loss. *International Journal of Environmental Health Research* 2022; 32: 2708-2717. DOI: 10.1080/09603123.2021.1987395.
11. Viola P, Scarpa A, Pisani D, et al. SUB-CLINICAL EFFECTS OF CHRONIC NOISE EXPOSURE ON VESTIBULAR SYSTEM. *Translational Medicine at Unisa* 2020; 22: 19-23.
12. Shetty HN, Raju S, Kumar Y and Singh SS. Listening effort in individuals with noise-induced hearing loss. *Hearing Balance and Communication* 2022; 20: 263-271. DOI: 10.1080/21695717.2022.2102733.
13. Degeest S, Kestens K and Keppler H. Listening Effort Measured Using a Dual-task Paradigm in Adults With Different Amounts of Noise Exposure. *Ear and Hearing* 2022; 43: 899-912. DOI: 10.1097/aud.0000000000001138.
14. Manohar S, Adler HJ, Radziwon K and Salvi R. Interaction of auditory and pain pathways: Effects of stimulus intensity, hearing loss and opioid signaling. *Hearing Research* 2020; 393. DOI: 10.1016/j.heares.2020.108012.
15. Si S, Lewkowski K, Fritschi L, Heyworth J, Liew D and Li IA. Productivity Burden of Occupational Noise-Induced Hearing Loss in Australia: A Life Table Modelling Study. *International Journal of Environmental Research and Public Health* 2020; 17. DOI: 10.3390/ijerph17134667.
16. van der Molen HF, Marsili C, Vitali A and Colosio C. Trends in occupational diseases in the Italian agricultural sector, 2004-2017. *Occupational and Environmental Medicine* 2020; 77: 340-343. DOI: 10.1136/oemed-2019-106168.
17. Buqammaz M, Gasana J, Alahmad B, Shebl M and Albloushi D. Occupational Noise-Induced Hearing Loss among Migrant Workers in Kuwait. *International Journal of Environmental Research and Public Health* 2021; 18. DOI: 10.3390/ijerph18105295.
18. Zhou HJ, Zhou Y, Zhang HN, Yu AQ, Zhu B and Zhang L. Socio-economic disparity in the global burden of occupational noise-induced hearing loss: an analysis for 2017 and the trend since 1990. *Occupational and Environmental Medicine* 2021; 78: 125-128. DOI: 10.1136/oemed-2020-106556.
19. Thai T, Kucera P and Bernatik A. Noise Pollution and Its Correlations with Occupational Noise-Induced Hearing Loss in Cement Plants in Vietnam. *International Journal of Environmental Research and Public Health* 2021; 18. DOI: 10.3390/ijerph18084229.
20. Grobler LM, Swanepoel D, Strauss S, Becker P and Eloff Z. Occupational noise and age: A longitudinal study of hearing sensitivity as a function of noise exposure and age in South African gold mine workers. *South African Journal of Communication Disorders* 2020; 67. DOI: 10.4102/sajcd.v67i2.687.

21. Liebenberg A, Brichta AM, Nie VLM, Ahmadi S and James CL. Hearing threshold levels of Australian coal mine workers: a retrospective cross-sectional study of 64196 audiograms. *International Journal of Audiology* 2021; 60: 808-819. DOI: 10.1080/14992027.2021.1884908.
22. Liebenberg A, Nie VM, Brichta AM, Ahmadi S and James CL. Pre-employment hearing threshold levels of 59,601 Australian male coal miners compared to an otologically normal international male population (ISO7029:2019). *International Journal of Audiology* 2022. DOI: 10.1080/14992027.2022.2088625.
23. Luha A, Merisalu E, Reinvee M, Kinnas S, Jogeva R and Orru H. In-vehicle noise exposure among military personnel depending on type of vehicle, riding compartment and road surface. *Bmj Military Health* 2020; 166: 214-220. DOI: 10.1136/jramc-2018-001091.
24. Albizu EJ, Goncalves CGD, de Lacerda ABM, Zeigelboim BS and Marques JM. Noise exposure and effects on hearing in Brazilian fishermen. *Work-a Journal of Prevention Assessment & Rehabilitation* 2020; 65: 881-889. DOI: 10.3233/wor-203139.
25. Burella G, Moro L and Neis B. Is on-board noise putting fish harvesters' hearing at risk? A study of noise exposures in small-scale fisheries in Newfoundland and Labrador. *Safety Science* 2021; 140. DOI: 10.1016/j.ssci.2021.105325.
26. Stokholm ZA, Erlandsen M, Schlunssen V, et al. A Quantitative General Population Job Exposure Matrix for Occupational Noise Exposure. *Annals of Work Exposures and Health* 2020; 64: 604-613. DOI: 10.1093/annweh/wxaa034.
27. Couth S, Prendergast G, Guest H, et al. Investigating the effects of noise exposure on self-report, behavioral and electrophysiological indices of hearing damage in musicians with normal audiometric thresholds. *Hearing Research* 2020; 395. DOI: 10.1016/j.heares.2020.108021.
28. Park S, Johnson MD and Hong O. Analysis of Occupational Safety and Health Administration (OSHA) noise standard violations over 50 years: 1972 to 2019. *American Journal of Industrial Medicine* 2020; 63: 616-623. DOI: 10.1002/ajim.23116.
29. Rabinowitz P, Galusha D, Cantley LF, Dixon-Ernst C and Neitzel R. Feasibility of a daily noise monitoring intervention for prevention of noise-induced hearing loss. *Occupational and Environmental Medicine* 2021; 78: 835-840. DOI: 10.1136/oemed-2020-107351.
30. Bramati L, Marques JM, Goncalves CGO, Welch D, Reddy R and Lacerda ABD. Evaluation of the Dangerous Decibels Brazil Program in Workers Exposed to Noise. *Frontiers in Integrative Neuroscience* 2022; 16. DOI: 10.3389/fnint.2022.909972.
31. Takada MM, Rocha CH, Neves-Lobo IF, Moreira RR and Samelli AG. Training in the proper use of earplugs: An objective evaluation. *Work-a Journal of Prevention Assessment & Rehabilitation* 2020; 65: 401-407. DOI: 10.3233/wor-203092.
32. Pan DW, Choi JS, Hokan A and Doherty JK. Trends in Hearing Protection Use With Occupational Noise Exposure in the United States 1999 to 2016. *Otology & Neurotology* 2022; 43: E14-E22. DOI: 10.1097/mao.0000000000003343.
33. Hayes ME, Hammond S, Montgomery AP and Stephenson L. Improving Hearing Protection Device Noise Attenuation Through Fit-Testing in an Occupational Health Clinic. *Workplace Health & Safety* 2022; 70: 196-204. DOI: 10.1177/21650799211067927.
34. Tikka C, Verbeek J, Kateman E, Morata TC, Dreschler W and Ferrite S. Cochrane method for systematic review and meta-analysis of interventions to prevent occupational noise-induced hearing loss - abridged. *Codas* 2020; 32. DOI: 10.1590/2317-1782/20192019127.
35. Samelli AG, Matas CG, Gomes RF and Morata TC. Systematic review of interventions to prevent occupational noise-induced hearing loss - a follow-up. *Codas* 2020; 33. DOI: 10.1590/2317-1782/20202019189.
36. Tittman SM, Yawn RJ, Manzoor N, Dedmon MM, Haynes DS and Rivas A. No Shortage of Decibels in Music City: Evaluation of Noise Exposure in Urban Music Venues. *Laryngoscope* 2021; 131: 25-27. DOI: 10.1002/lary.28556.
37. Neitzel RL, Smith L, Wang LY, et al. Toward a better understanding of nonoccupational sound exposures and associated health impacts: Methods of the Apple

Hearing Study. *Journal of the Acoustical Society of America* 2022; 151: 1476-1489. DOI: 10.1121/10.0009620.
38. Snapp HA, Coto J, Solle NS, Khan U, Millet B and Rajguru SM. Risk-taking propensity as a risk factor for noise-induced hearing loss in the general population. *International Journal of Audiology* 2022. DOI: 10.1080/14992027.2022.2114023.
39. Paping DE, Vroegop JL, El Marroun H, De Jong RJB and Van der Schroeff MP. The association of sociodemographic factors and risk behavior with unsafe use of personal listening devices in adolescents. *International Journal of Environmental Health Research* 2022. DOI: 10.1080/09603123.2022.2047901.
40. Gilliver M and Beach EF. "Know Your Noise" Helps Young People Understand Risks Associated with Recreational Noise Exposure and Take Action to Prevent Hearing Damage. *Journal of Consumer Health on the Internet* 2021; 25: 350-365. DOI: 10.1080/15398285.2021.1980693.
41. Chang JL, Huwyler C, Yoshida N, Sabes JH and Cheung SW. A Smartphone Application and Education Program for Hearing Health Promotion in High School Teenagers. *Laryngoscope* 2022. DOI: 10.1002/lary.30411.
42. Brooks CA, Clavier OH, Fellows AM, et al. Distortion product otoacoustic mapping measured pre- and post-loud sound exposures. *International Journal of Audiology* 2022; 61: 187-196. DOI: 10.1080/14992027.2021.1928303.
43. Dewey RS, Francis ST, Guest H, et al. The association between subcortical and cortical fMRI and lifetime noise exposure in listeners with normal hearing thresholds. *Neuroimage* 2020; 204. DOI: 10.1016/j.neuroimage.2019.116239.
44. Bramhall NF, McMillan GP and Kampel SD. Envelope following response measurements in young veterans are consistent with noise-induced cochlear synaptopathy. *Hearing Research* 2021; 408. DOI: 10.1016/j.heares.2021.108310.
45. Li L, Liu XP, Chen GD and Salvi R. Temporal characteristics of the cochlear response after noise exposure. *Hearing Research* 2021; 404. DOI: 10.1016/j.heares.2021.108208.
46. Bhatt IS. Determinants of the Audiometric Notch at 4000 and 6000 Hz in Young Adults. *Journal of the American Academy of Audiology* 2020; 31: 371-383. DOI: 10.3766/jaaa.19030.
47. Moore BCJ, Humes LE, Cox G, Lowe D and Gockel HE. Modification of a Method for Diagnosing Noise-Induced Hearing Loss Sustained During Military Service. *Trends in Hearing* 2022; 26. DOI: 10.1177/23312165221145005.
48. Moore BCJ, Lowe DA and Cox G. Guidelines for Diagnosing and Quantifying Noise-Induced Hearing Loss. *Trends in Hearing* 2022; 26. DOI: 10.1177/23312165221093156.
49. Kim YC, Kim H, Kim YS, et al. Objective Verification of Acute Tinnitus and Validation of Efficacy of Systemic Steroids in Rats. *Journal of Korean Medical Science* 2020; 35. DOI: 10.3346/jkms.2020.35.e81.
50. Chen HC, Wang CH, Chien WC, et al. Dextromethorphan Attenuates Sensorineural Hearing Loss in an Animal Model and Population-Based Cohort Study. *International Journal of Environmental Research and Public Health* 2020; 17. DOI: 10.3390/ijerph17176336.
51. Han JS, Kim YL, Yu HJ, et al. Safety and Efficacy of Intratympanic Alpha-Lipoic Acid Injection in a Mouse Model of Noise-Induced Hearing Loss. *Antioxidants* 2022; 11. DOI: 10.3390/antiox11081423.
52. Li Y, Zhang R, Li XY, Li W, Lu Y and Dai CF. The preparation of dexamethasone sodium phosphate multivesicular liposomes thermosensative hydrogel and its impact on noise-induced hearing loss in the Guinea pigs. *Experimental Cell Research* 2020; 387. DOI: 10.1016/j.yexcr.2019.111755.
53. Wang JL, Wang C, Wang Q, et al. Microfluidic Preparation of Gelatin Methacryloyl Microgels as Local Drug Delivery Vehicles for Hearing Loss Therapy. *Acs Applied Materials & Interfaces* 2022. DOI: 10.1021/acsami.2c11647.
54. Jeong SH, Kim Y, Lyu AR, et al. Junctional Modulation of Round Window Membrane Enhances Dexamethasone Uptake into the Inner Ear and Recovery after NIHL. *International Journal of Molecular Sciences* 2021; 22. DOI: 10.3390/ijms221810061.

55. Wu F, Xiong H and Sha SH. Noise-induced loss of sensory hair cells is mediated by ROS/AMPK alpha pathway. *Redox Biology* 2020; 29. DOI: 10.1016/j.redox.2019.101406.
56. Shih CP, Kuo CY, Lin YY, et al. Inhibition of Cochlear HMGB1 Expression Attenuates Oxidative Stress and Inflammation in an Experimental Murine Model of Noise-Induced Hearing Loss. *Cells* 2021; 10. DOI: 10.3390/cells10040810.
57. Haryuna TSH, Amellya D, Munir D and Zubaidah TSH. The Benefits of Curcuminoid to Expression Nuclear Factor Erythroid 2 Related Factor 2 (NRF2) and Signal to Noise Ratio (SNR) Value in the Noise Exposed Organ of Corti of Rattus Norvegicus. *Reports of Biochemistry and Molecular Biology* 2021; 10: 373-379.
58. Kim YH, Kim EY, Rodriguez I, et al. Sesamum indicum L. Oil and Sesamin Induce Auditory-Protective Effects Through Changes in Hearing Loss-Related Gene Expression. *J Med Food* 2020; 23: 491-498. DOI: 10.1089/jmf.2019.4542.
59. Woo H, Kim MK, Park S, et al. Effect of Phlorofucofuroeckol A and Dieckol Extracted from Ecklonia cava on Noise-induced Hearing Loss in a Mouse Model. *Marine Drugs* 2021; 19. DOI: 10.3390/md19080443.
60. Alvarado JC, Fuentes-Santamaria V, Melgar-Rojas P, Gabaldon-Ull MC, Cabanes-Sanchis JJ and Juiz JM. Oral Antioxidant Vitamins and Magnesium Limit Noise-Induced Hearing Loss by Promoting Sensory Hair Cell Survival: Role of Antioxidant Enzymes and Apoptosis Genes. *Antioxidants* 2020; 9. DOI: 10.3390/antiox9121177.
61. Bahaloo M, Rezvani ME, Yazd EF, et al. Effect of myricetin on the gene expressions of NOX3, TGF-beta 1, prestin, and HSP-70 and anti-oxidant activity in the cochlea of noise-exposed rats. *Iran J Basic Med Sci* 2020; 23: 594-599. DOI: 10.22038/ijbms.2020.41007.9693.
62. Chen XM, Ji SF, Liu YH, et al. Ginsenoside Rd Ameliorates Auditory Cortex Injury Associated With Military Aviation Noise-Induced Hearing Loss by Activating SIRT1/PGC-1 alpha Signaling Pathway. *Frontiers in Physiology* 2020; 11. DOI: 10.3389/fphys.2020.00788.
63. Warnecke A, Harre J, Shew M, et al. Successful Treatment of Noise-Induced Hearing Loss by Mesenchymal Stromal Cells: An RNAseq Analysis of Protective/Repair Pathways. *Frontiers in Cellular Neuroscience* 2021; 15. DOI: 10.3389/fncel.2021.656930.
64. Kim SY, Lee JE, Kang SH, Lee SM, Jeon J and Lee DR. The Protective Effects of Human Embryonic Stem Cell-Derived Mesenchymal Stem Cells in Noise-Induced Hearing Loss of Rats. *Cells* 2022; 11. DOI: 10.3390/cells11213524.
65. Chorath K, Willis M, Morton-Gonzaba N and Moreira A. Mesenchymal stem cells for sensorineural hearing loss: a systematic review of preclinical studies. *Mol Biol Rep* 2020; 47: 4723-4736. 2020/04/24. DOI: 10.1007/s11033-020-05460-0.
66. Maeda Y, Kariya S, Uraguchi K, et al. Immediate changes in transcription factors and synaptic transmission in the cochlea following acoustic trauma: A gene transcriptome study. *Neuroscience Research* 2021; 165: 6-13. DOI: 10.1016/j.neures.2020.05.001.
67. Patel S, Shah L, Dang NA, Tan XD, Almudevar A and White PM. SIRT3 promotes auditory function in young adult FVB/nJ mice but is dispensable for hearing recovery after noise exposure. *Plos One* 2020; 15. DOI: 10.1371/journal.pone.0235491.
68. Affortit C, Casas F, Ladrech S, et al. Exacerbated age-related hearing loss in mice lacking the p43 mitochondrial T3 receptor. *Bmc Biology* 2021; 19. DOI: 10.1186/s12915-021-00953-1.
69. Marchetta P, Mohrle D, Eckert P, et al. Guanylyl Cyclase A/cGMP Signaling Slows Hidden, Age- and Acoustic Trauma-Induced Hearing Loss. *Frontiers in Aging Neuroscience* 2020; 12. DOI: 10.3389/fnagi.2020.00083.
70. Wei W, Shi X, Xiong W, et al. RNA-seq Profiling and Co-expression Network Analysis of Long Noncoding RNAs and mRNAs Reveal Novel Pathogenesis of Noise-induced Hidden Hearing Loss. *Neuroscience* 2020; 434: 120-135. DOI: 10.1016/j.neuroscience.2020.03.023.
71. Cederholm JME, Parley KE, Perera CJ, et al. Noise-induced hearing loss vulnerability in type III intermediate filament peripherin gene knockout mice. *Front Neurol* 2022; 13. DOI: 10.3389/fneur.2022.962227.

72. Chen H, Ding XX, Ding EM, et al. A missense variant rs2585405 in clock gene PER1 is associated with the increased risk of noise-induced hearing loss in a Chinese occupational population. *Bmc Medical Genomics* 2021; 14. DOI: 10.1186/s12920-021-01075-x.
73. Liu Y, Liu SY, Xin JR, et al. Telomere Length and Hearing Loss: A Two-Sample Mendelian Randomization. *International Journal of Environmental Research and Public Health* 2022; 19. DOI: 10.3390/ijerph19158937.
74. Lu Y, Liu XX, Zhao ZQ, et al. Telomere length in peripheral leukocytes is a sensitive marker for assessing genetic damage among workers exposed to isopropanol, lead and noise: the case of an electronics manufacturer. *Genes and Environment* 2021; 43. DOI: 10.1186/s41021-021-00226-x.
75. Zhang XZ, Li NN, Cui YA, et al. Plasma metabolomics analyses highlight the multifaceted effects of noise exposure and the diagnostic power of dysregulated metabolites for noise-induced hearing loss in steel workers. *Frontiers in Molecular Biosciences* 2022; 9. DOI: 10.3389/fmolb.2022.907832.
76. Boullaud L, Blasco H, Caillaud E, Emond P and Bakhos D. Immediate-Early Modifications to the Metabolomic Profile of the Perilymph Following an Acoustic Trauma in a Sheep Model. *Journal of Clinical Medicine* 2022; 11. DOI: 10.3390/jcm11164668.