Occupational noise and age: A longitudinal study of hearing sensitivity

by

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A dissertation submitted in fulfillment of the requirements for the degree

M. Communication Pathology (Audiology)

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August 2018

ACKNOWLEDGEMENTS

Going so quickly through life,

Running from place to place,

Aware of so little around me,

Taking time to play is foreign,

I find I have succumbed to the pressure,

Thinking of only what is on my list,

Until a moment shakes me,

Delivering a message…

Enjoy and be grateful because you are blessed!

-Author unknown-

Thank you to every person that supported me with love and insight through this journey. I would like to specifically mention:

Prof De Wet Swanepoel,

Dr Susan Strauss,

Prof Piet Becker,

Anton Grobler,

Gert and Marion Jordaan and

Lizelle van Biljon.

Give thanks to the Lord, for He is good: His mercy endures forever

Psalm107:1

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LIST OF ABBREVIATIONS

NIHL	-	Noise-induced hearing loss
ARHL	-	Age-related hearing loss
COIDA	-	Compensation for Occupational Injuries and Diseases Act
dBA	-	A-weighted Decibels
dB HL	-	Decibel hearing level
TWA	-	Time-weighted average
TTS	-	Temporary threshold shift
PLH	-	Percentage loss of hearing

FORMATTING

APA referencing style was utilised in this dissertation.

ABSTRACT

The interaction between age and noise and their individual effects on hearing is complex, making it difficult to distinguish between noise-induced hearing loss and age-related hearing loss at an individual level. This retrospective cohort study aimed to determine the decline in hearing sensitivity in noise-exposed mineworkers as opposed to non-noise-exposed mineworkers over time to evaluate the combined and individual contributions of noise exposure and age.

A mixed effects regression analysis was applied to longitudinal audiological data from a group of mineworkers in South Africa. Four serial (annual) audiograms of 2,583 mineworkers were utilised. Data of a non-noise-exposed group (n=951) and a group exposed to underground noise (≥85 dBA) (n=1632) were included.

Results indicated that base values were significantly higher for the noise-exposed versus non-noise-exposed group, for the low-frequency average (LFA) of 0.5, 1 and 2 KHz (16.1 dB HL versus 11.1 dB HL), and high-frequency average (HFA) of 3, 4 and 6 KHz (25.7 dB HL versus 18.5 dB HL). These results may be indicative of previous noise damage in the noise-exposed group obtained before occupational noise limitations and personal hearing protection use were enforced through legislation in 2001. All year-to-year increases in mean hearing thresholds were statistically significant (p-values of <0.01). When correcting for age, year-to-year increases in mean hearing thresholds were higher for the noise-exposed group than for the non-noise-exposed group when comparing HFA (3.5 dB versus 2.9 dB decline over a four-year period) but similar when comparing LFA (0.6 dB versus 0.7dB decline over a four-year period). Mixed effects regression analyses were repeated without correcting for age to represent year-to-year increases in hearing thresholds including noise and age influences. Year-to-year increases in mean hearing thresholds were significantly higher for the noise-exposed group than for the non-noise-exposed group in comparing HFA (4.0 dB versus 3.5 dB decline over a four-year period), and when comparing LFA (1.5 dB versus 1.1 dB decline over a four-year period). Year-to-year increases in mean hearing thresholds were between 0.4 and 0.9 dB higher in the analysis where age was uncorrected for, for both exposure groups across LFA and HFA, identifying age as a factor in year-to-year decrease in mean hearing thresholds.

It is evident that occupational noise exposure and aging are significant contributors to hearing loss over time for mineworkers, even in a setting where noise exposure is controlled through legislation, and use of personal hearing protection is enforced. Ongoing effort is necessary to increase the effectiveness of noise management programmes in order to counter the prevailing negative effects of noise exposure on hearing thresholds, as well as the possible additive interaction between noise exposure and age-related hearing loss.

Keywords: age-related hearing loss, noise exposure, noise-induced hearing loss

1. INTRODUCTION

Our ears were not designed to withstand long and often repeated exposure to high levels of noise produced by the machinery that surrounds us in modern society (Liberman, 2017). Excessive noise such as this is an occupational hazard with many adverse effects, including elevated blood pressure (Kerns, Masterson, Themann, & Calvert, 2018; Wang et al., 2018), elevated cholesterol (Kerns et al., 2018), increased risk for coronary heart disease (Eriksson et al., 2018), reduced work performance, difficulty sleeping, annoyance, stress, tinnitus, temporary threshold shift (TTS) and noise-induced hearing loss (NIHL) (Nelson, Nelson, Concha-Barrientos, & Fingerhut, 2005).

Although many other adverse effects of high-level noise exposure have been reported, NIHL is recognised as the primary and most direct health effect of noise exposure, which makes it a significant and ongoing health concern with high economic consequences (Agrawal, Niparko, & Dobie, 2010; Hong, Kerr, Poling, & Dhar, 2013; Lie et al., 2016). Worldwide, 16% of disabling hearing loss in adults can be attributed to occupational noise, ranging from 7% to 21% across various regions of the world, with the biggest burden of NIHL presenting in the developing world (Nelson et al., 2005).

NIHL is a permanent shift in hearing thresholds caused by prolonged exposure to high levels of noise, as a direct cause of damage to the sensory hair cells of the inner ear (Sliwinska-Kowalska & Davis, 2012). The first audiometric signs of NIHL can often be observed in the typical 4000 Hz "notch" on the audiogram, indicating a loss of hearing sensitivity in the middle of the frequency range of human voices. This audiometric notch grows deeper and wider with continued noise exposure, causing ever-increasing impacts on speech communication (Nelson et al., 2005).

NIHL is the second largest contributor to hearing loss globally, exceeded only by age-related hearing loss (ARHL). Therefore, most hearing losses not associated with noise can be attributed to age, which, with increasing life expectancy, is on the rise (Lie et al., 2016; Liberman, 2017). ARHL and NIHL in humans are both multifactorial, with contributions from and interactions between numerous intrinsic (e.g. genetic predisposition) as well as extrinsic (e.g. noise exposure) variables that can shape its final outcome (Kujawa & Liberman, 2006; Yamasoba et al., 2013).

The interaction between age and noise and their respective effects on hearing status is still poorly understood, making it difficult to distinguish between NIHL and ARHL at an individual level, often because of the length and magnitude of each exposure are unclear (Gates, Schmid, Kujawa, Nam, & D'Agostino, 2000; Rosenhall, 2003; Xiong, Yang, Lai, & Wang, 2013; Basner et al., 2014; Lie et al., 2016; Aarhus, Tambs, Nafstad, Bjorgan, & Engdahl, 2016). Both age-related and noise-induced hearing loss have similar audiometric features (sensorineural, bilateral, with high frequencies affected more than lower frequencies). Early noise-induced hearing loss may form a notch on the audiogram between 3000 to 6000 Hz, but age-related hearing loss may shift this notch, making the noise-induced hearing loss difficult to diagnose. Noise-induced hearing loss is thought to grow more rapidly in the first years of noise exposure than in the later years of exposure, but serial audiograms that could assist in diagnosis are often unavailable (Dobie, 2008). Numerous studies have examined the interaction between NIHL and ARHL, but because these conditions happen concurrently, it is difficult to determine their individual effects (Gates et al., 2000; Rosenhall, 2003; Xiong et al., 2013; Aarhus et al., 2016).

In recent attempts to explain this complex interaction between NIHL and ARHL, two possible models of interaction have emerged (Aarhus et al., 2016). A possible super-additive interaction follows the notion that an already damaged hair cell is more susceptible to further damage from additional factors. When describing the interaction between NIHL and ARHL as a less than additive effect, the assumption is based on the premise that when a number of hair cells was previously damaged, there is a decreased risk of further damage. Simply stated, hair cells lost from one cause cannot be lost again from a second cause (Gallo & Gloring, 1964; Gates et al., 2000; Dobie, 2008).

Hair cell damage is a key contributor to NIHL and ARHL and therefore most evidence with regard to the interaction between NIHL and ARHL is based on audiometric thresholds as defined by the audiogram, which measures the minimum sound pressure level required for pure tone detection in quiet (Fernandez, Jeffers, Lall, Liberman, & Kujawa, 2015; Libberman, 2017). Recent research, however, demonstrates that in both NIHL and ARHL, synaptic connections between the hair cells and cochlear neurons can be destroyed even before hair cell damage occurs. Even noise exposure causing only reversible hearing threshold shifts (with no hair cell

loss) can cause loss of >50% of the synaptic connections between inner hair cells and the auditory nerve. Similarly, in age-related hearing loss, degeneration of auditory nerve synapses precede both hair cell loss and hearing threshold elevation (Liberman, 2017).

These findings were first observed when mice were exposed as young adults to noise designated to produce a 40 dB permanent threshold shift and then leaving them to age for two years to see if the cochlea deteriorated more rapidly in exposed versus unexposed mice (Kujawa & Liberman, 2006). Two years later, the noise-exposed mice showed >50% loss of spiral ganglion cells in the basal half of the cochlea versus <5% in age-matched controls, despite no significant loss of inner or outer hair cells in either the noise-exposed or non-noise-exposed groups. These progressive age-related changes in the noise-damaged ear involve the inner hair cell and/or the auditory nerve to a greater degree than the outer hair cells (Kujawa & Liberman, 2006). This synaptic loss in the inner hair cells and the auditory nerve has remained hidden for generations because neural cell bodies can survive for years despite loss of synaptic connection. While it damages a large number of cochlear neurons, it is invisible in routine audiological assessments as it does not affect tests of threshold detection, as long as the loss is not complete (Liberman, 2017). Findings like these challenge the traditional view held by researchers (Jonsson & Rosenhall, 1998; Rosenhall, 2003; Dias, Cordeiro, Corrente, & Goncalves, 2006; Teles & Medeiros, 2007; Dobie, 2008) that the influence of noise on hearing is time-limited, meaning the progression of NIHL ceases when noise exposure stops. For years, it has been deducted that noise exposure produces hearing loss and cochlear injury, with its effects being most prevalent at early post-exposure times. This period of fairly rapid recovery was seen to be followed by one of relative stability, giving the impression that noise produces no progressive or delayed consequences as opposed to individual's age (Fernandez et al., 2015). However, it is known that in regard to age-related hearing loss, early events include diffuse loss of synapses between inner hair cells and cochlear nerve fibres. This synaptopathy is progressive in its nature, and evident well before age-related reductions in threshold sensitivity. Similarly, noise exposure causing robust but reversible changes in hearing thresholds can nevertheless destroy neural synapse within the cochlea (Fernandez et al., 2015).

The fact that even apparently reversible noise damage can have a significant long-term effect on exasperating age-related hearing loss is of significance in the consideration of noise-risk assessment of human populations (Fernandez et al., 2015).

One such human population are workers within the mining sector, an industry where noise, its effects and its interaction with age is a current concern. A study based on United States of America (USA) data estimates that the single industry with the highest proportion of workers exposed to hazardous noise is mining, with an estimated 85% of production workers and labourers exposed to noise levels above 85 dB time-weighted average (TWA) (Nelson et al., 2005). These results are also consistent with the results of similar studies (Tak & Calvert, 2008; Engdahl & Tambs, 2010; Masterson, Deddens, Themann, Bertke, & Calvert, 2015). In a study done in South Africa, on average 73.2 per cent of mineworkers were exposed to noise levels above the 85 dBA legislated occupational exposure level. Mean noise exposure levels were measured to range from 63.9 dBA to 113.5 dBA (Edwards, Dekker, & Franz, 2011).

Mining activities, with an employment of 495,568 people in 2014, form the centre of economic activity in modern-day South Africa (Mineral Council of South Africa, 2018). In two studies by Strauss, Swanepoel, Becker, Eloff and Hall (2012; 2014) on the prevalence and degree of NIHL in South African gold miners in the Witwatersrand, it was found that exposure to occupational noise, despite the implementation of hearing conservation programmes, was significantly associated with increased hearing thresholds. In these studies it was also evident that high-frequency hearing loss prevalence was affected by age, and that age is the most important influence on the hearing thresholds of both the noise-exposed and control groups. From the above studies it was recommended that this should be taken into account when determining or predicting the effect of noise on hearing.

This study therefore investigates hearing loss over time, by developing a regression model for the prediction of hearing loss as a function of noise exposure and age in a large longitudinal data set of gold mine employees in South Africa.

2. METHODOLOGY

2.1 Research aims

This study aimed:

1. to determine decline in hearing thresholds in noise-exposed individuals over time, as opposed to decline in hearing thresholds in non-noise-exposed individuals over time;
2. to determine the combined and individual effects of noise exposure and aging on hearing thresholds, over time, as opposed to decline in non-noise-exposed individuals as they age.

2.2 Research design

Observational study designs are often retrospective and are used to assess potential causation in exposure-outcome relationships, and therefore aim to influence preventative measures. In observational research, the investigator is not acting upon study participants, but instead observe natural relationships between different factors and outcomes (Thiese, 2014). The research conducted in this study was observational in nature, utilising a regression model to retrospectively investigate two significant contributors (noise exposure and age) to hearing loss over time.

Observational research studies include three elements, as listed in Table 1 (Thiese, 2014).

Table 1: The three elements of observational research

Element	Implementation in study
Definition and measure of exposure in two or more groups	Two groups: data from a noise-exposed and non-noise-exposed group were analysed and compared
Measure of health outcomes in these same groups	Measurement of hearing thresholds of both noise-exposed and non-noise-exposed groups over time
Statistical comparison made between groups to assess potential relationships between the exposure and outcome	A mixed effects regression analysis was applied to assess the individual effects of noise and age on the hearing thresholds of both the noise-exposed and non-noise exposed groups over time

A retrospective cohort study involves identifying study participants based on their exposure status and either following them through time to identify which participants develop the outcome(s) of interest or, as in this case, to reflect on data that were created in the past (Thiese, 2014). In this study, longitudinal audiological data that were gathered between 2001 and 2008 were utilised. The data were gathered over an 8-year period by the Occupational Health Department of the AngloGold Ashanti Gold Mine in Witwatersrand, Johannesburg. In an ideal retrospective cohort study, case status is tracked by utilising historical data that were created at that point in time. Occupational groups (in this case mineworkers), particularly those that have regular surveillance (in this case legislated annual audiological screening), are particularly well positioned for retrospective cohort studies. This is because records of both exposure and outcome are created as part of regulatory processes (Checkoway, Pearse, & Kriebel, 2004).

2.3 Ethical considerations

Ethical clearance was obtained from the Research and Ethics Committee of the Faculty of Humanities of the University of Pretoria (Appendix A) before the commencement of the study. This study was conducted within the framework of the ethical guidelines as set out in the South African National Health Act (2007) as well as the Guidelines of Practice in the Conduct of Clinical Trials in Human Subjects in South Africa (South African Department of Health, 2000). Principles presented in these documents are discussed next.

Principle 1 states that the safety and wellbeing of the participants are the most important considerations and should prevail over interest of science and society. Foreseeable risks and inconveniences should be weighed against the anticipated benefit for participants and society. A study should be initiated and continued only if the anticipated benefits justify the risks.

All data used in this study were obtained during routine audiological screening, as well as diagnostic follow-up testing. No audiological tests were performed merely for the purpose of the study. Testing was conducted in a controlled and safe environment by audiologists, medical practitioners, audiometrists and occupational medical personnel registered with the Health Professions Council of South Africa.

According to principle 2, research or experimentation on an individual may be conducted only after the participant has been informed of the objectives of the research or experimentation and any possible positive or negative consequences on their health. This study was a retrospective analysis of audiological records; all audiometric records were obtained prior to the commencement of this study.

In respect to principle 3**,** the healthcare provider must, where possible, inform the individual in a language that the individual understands and in a manner that takes into account the individual's level of literacy. Audiologists, medical practitioners, audiometrists and occupational medical personnel stationed at mines ensured that all instructions for audiometric testing were well understood before the testing.

Principle 4 states that freely given informed consent should be obtained from every participant prior to clinical trial participation. In the study, informed consent was obtained from the specific gold mine to use the data for research purposes. An agreement exists between the authorities of the gold mine and participants that data from audiological testing may be used in research projects (Appendix B).

Principle 5 states that the participant should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. Participants did not need to participate in any way for the study, as the study was a retrospective analysis of data previously collected. An agreement consists between the mine authorities and participants that data may be used. If a mineworker objects to data being kept, it was noted.

Principle 6 outlines the importance of confidentiality of records that could identify participants. Such records should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s). In this study, data were anonymised by omitting the participants' names and ID numbers on all data processing documentation. The researcher implemented a coding system by which each participant was allocated a specific number for data processing purposes. Data were stored securely on an electronic database and will be kept for a minimum of 15 years at the University of Pretoria.

2.4 Research setting

Data were made available by the occupational health departments of seven mines in the AngloGold Ashanti group of gold mines in South Africa, the world's third largest gold mining company when measured by production (AngloGold Ashanti, 2018). Data included demographic and audiological information of participants between 2001 and 2008.

2.5 Participants

The participants in this study were employees at two gold mine groups, consisting of seven gold mines within the AngloGold Ashanti group. The data set included audiological, biographical and environmental information. Records included data for 57,714 employees, comprising a total of 232,458 audiograms. Every employee had at least a baseline audiogram and an annual audiogram. All participants above 18 years across all genders and cultural groups were included. All data were collected between 2001 and 2008 from routine audiological screening, as well as diagnostic follow-up measures, made available by the mine's occupational health department. Available audiological thresholds were comprised of the following frequencies: 0.5, 1, 2, 3, 4, 6 and 8 kHz. Employees were further defined in terms of specific noise exposure levels, based on noise measurements made available from the mine's noise hygienist. Within these noise categories, specific occupations were used to further classify employees (e.g. rock driller or administration worker).

2.6 Materials and apparatus

Audiological testing was conducted between 2001 and 2008, in sound-treated rooms that complied with the requirements as stipulated in the South African National Standards (SANS) document (SANS 10154-1:2001). A Tremetrics RA600 Type 4 audiometer was used for testing, coupled with TDH39 headphones. Ten workers can be tested simultaneously, using the automatic testing setting of the Tremetrics audiometer. From here, audiological information is automatically updated to a database on software specifically for this purpose (Everest). Follow-up diagnostic audiometry was performed on employees whose percentage loss of hearing (PLH) had dropped by more than 10% from their baseline test, using a GSI 61 diagnostic audiometer. All diagnostic test results were also captured with the Everest software.

Screening and diagnostic audiometers had valid calibration certificates at the time of testing. The Everest database was made available for research purposes in 2012, and utilized by Strauss (2012). The current study is a follow up study from the original study.

2.7 Procedures for data collection

The Mine Health and Safety Act, Instruction 171 (COIDA, 2001), and the South African National Standard (SANS 10083:2004) require that all employees with noise exposure of 85 dBA normalised in an eight-hour working day or forty-hour working week be monitored audiologically. Legislation as set out in Instruction 171 (COIDA, 2001) makes it compulsory for all employees to have a baseline audiogram within two years of the legislation being passed (2001), or within 30 days of employment for new employees. AngloGold Ashanti complied with these regulations, and therefore audiograms from 2001 onwards were available within this data set. All data collected complied with this guideline; audiograms consisted of baseline, annual screening and exit audiograms, performed by Occupational Health Personnel, as well as results of diagnostic testing performed by audiologists registered with the Health Professional Counsel of South Africa. Diagnostic audiograms were performed on all employees where their PLH values exceed their baseline audiogram by 10%, as regulated by Instruction 171 (COIDA, 2001). Where PLH was under 10%, only baseline, screening and exit results were used. Audiological data were comprised of thresholds in dB HL for the following frequencies: 0.5, 1, 2, 3, 4, 6 and 8 kHz, for both the left and right ear. The left and right ears were averaged and then, using these values, an average was worked out for the low frequencies (0.5, 1 and 2 kHz) referred to as LFA, and high frequencies (3,4 and 6 kHz), referred to as HFA. High frequencies and low frequencies were separated, as both noise and age have a greater influence on higher frequencies (Dias et al., 2006; Teles et al., 2007).

Apart from the above, age of employee, occupation (classified according to noise exposure level), years of service, race and gender were also gathered from the database. Data were exported from the mine's electronic database (Everest) into Microsoft Excel for data processing.

2.8 Data processing

Data processing involves the preparation of data for analysis by categorising it in an orderly manner (Robson, 2011).

Data were extracted from Everest and imported in Microsoft Excel (2013). Data cleaning was applied to the original data set, as set out in Table 1 (Strauss, 2012).

Table 2. Summary of data cleaning done, reasoning and amount of audiogram data disregarded

Disregarded audiogram records	Reason for deletion	Records deleted
All duplicates were removed (same worker, same day, same time, same audiogram).	Redundant	3,855
All rows where an audiogram error code was recorded in threshold value cells between 500-4000 Hz were deleted.	Values in these frequencies are important for calculations of hearing impairment.	640
All rows where No Response (NR) values were recorded in more than four frequencies in one ear. Where a diagnostic test for these workers was available, the results of the diagnostic tests were kept in file.	Values in these frequencies are important for calculations of hearing impairment. No hearing impairment calculations are possible without values at these frequencies. According to the Occupational Medical Doctor, mostly NR values are given when the mine worker did not give reliable responses	150
Where NR values were recorded for one or two frequencies (mostly high frequencies), and where results correlated with previous audiogram results (within 10 dB's) maximum values (100 dB) were given.	The mine audiometer has a maximum value of 99 dB. If no value is given to these NRs, the calculation would be invalid. A 100 dB value makes the researcher's change apparent and reflects the hearing loss without affecting the calculation significantly.	976
No date of birth, thus no age group.		331
All rows where one ear had normal threshold values and the other NR values.	These results indicate a unilateral functional hearing loss (malingering). Interaural attenuation makes this scenario impossible.	33
All audiograms marked as type 2 (monitor) were changed to screen.	This code was used very infrequently and no differences in patterns of use could be distinguished between the use of the screening code (1) and code (2).	

Table 2. Summary of data cleaning done, reasoning and amount of audiogram data disregarded

All rows where two or more tests were done on the same day were reduced in the following manner: ▪ If a baseline (3) and a baseline check (7) were similar, the check (7) was deleted; ▪ If two audiograms done on the same day were similar, but a third not, the third was deleted; ▪ If a screen (1) was followed by a diagnostic test (5) on the same day, the screen was deleted; ▪ A test done for compensation (4) was kept if more than one test for the day was available; ▪ If a diagnostic (5) or baseline audiogram (3) or screen (1) was repeated, the second test was kept (If it was similar to the first) (+/- 5 dB); ▪ Tests done more frequently than once a year were not kept; ▪ Exit tests (6) were done very often on the same day as a screening test (1). Only one test was kept and a code 6 was regarded as the same as a screening test.	Most baseline tests (3) followed a baseline check (7). Baseline tests were done after the check and are more reliable. If more than one test of the same worker done on the same day were used, more weighting would be given to the audiogram. Diagnostic tests are more reliable than screening tests. Tests done for compensation are regarded as the final diagnosis.	46,447

From the above, employees were divided into four noise exposure groups, namely above surface noise exposure (≥ 85 dBA), below surface noise exposure (≥ 85 dBA), no noise exposure and uncertain noise exposure (Strauss,2012).

From the data cleaned by Strauss (2012), two sub-groups from the below surface noise exposure group, and the non-noise exposure group were selected for comparison in this study: namely, the rock drillers (noise-exposed group) and administration personnel (non-noise-exposed group).

The rock drillers were chosen because noise exposure in mining is mainly due to the use of heavy equipment, drilling and rock breaking, transferring, sorting and milling of rock, and the confined working environment (Hermanus, 2007). In a study conducted in South-Africa in 2007, the mean noise levels of four commonly used drills (self-propelled drill, pneumatic drill, hydraulic drill and electrical drill), were measured between 84.9 and 107.9 dBA (Phillips, Heyns and Nelson, 2007)These levels falls close to, or above the maximum defined occupational noise exposure of ≥ 85 dBA, as classified according to the South African regulations on the daily permissible level of noise exposure (COIDA, 2001).

Data received included records for 4,399 rock drillers and 2211 administration personnel. For this study, only data where employees had four longitudinal (annual) audiograms, falling in sequence from 2001 to 2008 (for example 2001, 2002, 2003 and 2004, or 2003, 2004, 2005 and 2006) were used in order to be able to perform a mixed effects regression analysis. For this, raw data were exported to a Sequential Query Language (SQL) database where the data were segregated into islands of serial data, and thereafter exported back into Microsoft Excel for statistical analysis. This reduced the total participant number to 2,583 employees. This included 1,632 in the noise-exposed (rock driller) group, and 951 in the non-noise-exposed (administration worker) group. A visual representation of the data processing is presented in Figure 1. Participants' ages, race and gender are set out in Table 3. The majority of participants in this study were black males, with a mean age of 36.2 years for the non-noise exposed group, and 43.3 years for the noise exposed group.

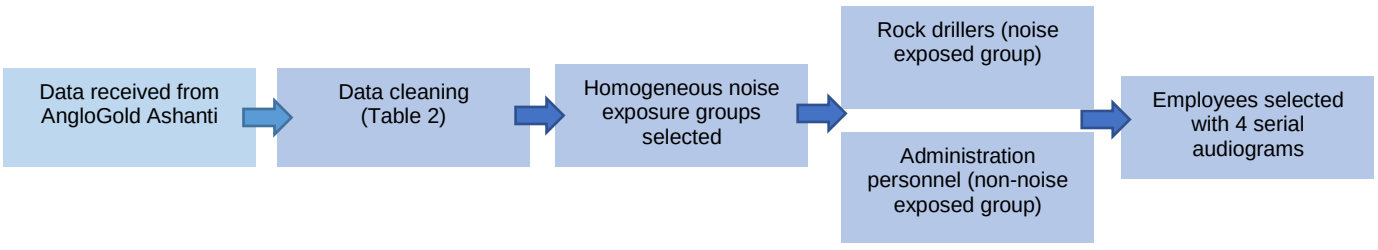

Figure 1. Overview of data processing procedure

Table 3. Age, race and gender distribution of the 2,583 gold mine workers

	Age (at first test)			Gender		Race	
	Mean	**Min age**	**Max age**	**Female**	**Male**	**White**	**Black**
Non-noise	36.2	20	61	9	942	38	913
				52.9%	36.7%	80.9%	36%
Noise	43.3	19	60	8	1624	9	1623
				47.1%	63,3%	19.1%	64%
Total				17	2566	47	2536
				100%	100%	100%	100%

2.9 Data analysis

After data processing, data were analysed in collaboration with Professor Piet Becker, biostatistician of the Faculty of Health Sciences, University of Pretoria.

A mixed effects regression analysis was employed to the data where four longitudinal (annual) audiograms were available for an individual in the cohort. A mixed effects regression analysis can allow for the prediction of an outcome variable (for example hearing loss) from a predictor variable (for example noise exposure) over time, by using repeated measures (Field, 2009). These panel data (repeated observations within an individual) were analysed using a mixed effects REML (restricted maximum likelihood) regression for both noise-exposed and non-noise-exposed groups. Because of the many similarities and interactions between NIHL and ARHL, it is imperative to take into consideration the total relevant contribution of age-related hearing loss when determining the effect of noise exposure on hearing (Strauss et al., 2012). The model was therefore adjusted for age, as well as baseline hearing threshold. The model was also repeated without adjusting for age in order to determine the separate contributions of age and noise on the total hearing loss of the participant over a four-year period. High-frequency averages of 3, 4 and 6 kHz (HFA) and low-frequency averages of 0.5, 1 and 2 kHz (LFA) were analysed separately. Statistical significance was set to the $p<0.01$ level.

2.10 Reliability and validity

Reliability and validity are both central issues in research. Both are concerned with how we connect concrete measures to abstract concepts. Researchers strive to have reliable and valid measures, as it helps to establish the truthfulness, credibility and acceptability of the research (Neuman, 2012).

Reliability refers to dependability or consistency. It suggests that repeatable outcomes will be the same under identical or similar conditions, while validity is the extent to which the instrument measures what it is supposed to measure (Neuman, 2012; Leedy & Omrod, 2013).

When looking at validity, both the internal and external validity of a research project have to be investigated.

Internal validity refers to the extent to which a research design and the data it yields allow the researcher to draw accurate conclusions regarding relationships within the data (Leedy & Omrod, 2013). Internal validity therefore has to do with what occurred during the implementation of the study that could influence the relationship between the variables (DeForge, 2010). The audiometric data that were used for this study were collected using standards that are accepted as a valid and reliable measure of hearing thresholds as set out in the South African National Standard (10083:2004). Extensive data cleaning was employed (Table 1) to eliminate any inconsistencies within the data, for the purpose of increasing internal validity. The researchers were also limited by monitoring (screening) audiograms, as diagnostic audiograms were available only when PLH values deteriorated by more than 10%. Diagnostic tests were favoured where possible during the data cleaning process. To aid comparative analysis and again increase internal validity, only two homogeneous exposure groups (rock drillers and administration personnel) were selected in order to exclude occupational variables from the sample, as original data were comprised of records including 234 unique occupations.

Threats to the internal validity of the study are unknown exposure to non-occupational noise outside the workplace, such as attending leisure activities where loud music is present, listening to personal music systems or attending sporting events. One such instance can be the attending of football games as a popular sporting activity in South

Africa. Football games have shown to yield a risk of noise-induced hearing loss, partly because of high levels of noise emitted by the vuvuzela – a long horn blown at football matches in South Africa (Swanepoel & Hall, 2010). Another factor that may have influenced the internal validity of the research is the fact that no previous employment history or medical history was available.

When looking at external validity, the researcher has to determine whether the results obtained can be used to make generalisations about the world beyond that specific research context (Leedy & Omrod, 2013). For this study, 2,583 employee records (10,332 audiograms) were selected from the total data set of 57,714 employee records (232,458 audiograms). Records decreased from the original number due to extensive data cleaning, limiting the research to two homogeneous exposure groups, and because four serial (annual) audiograms per participant were needed for the purpose of employing a mixed effects regression analysis. The sample represented 22% of all original data received. The external validity will be limited to the gold mining sector within South Africa, as other factors such as migrant living conditions, prevalent health co-morbidities and social lifestyle will be unique to the population sampled. However, as the entire population of the seven gold mines that partook in this study is represented in the sample, conclusions reached can reliably represent these specific mines.

3. OCCUPATIONAL NOISE AND AGE: A LONGITUDINAL STUDY OF HEARING SENSITIVITY

Authors: L.M. Grobler, D.W. Swanepoel, S. Strauss, P. Becker & Z. Eloff.

Journal: Noise & Health[1]

Submitted: 19 August 2018

3.1 Abstract

Objective: This retrospective cohort study aimed to investigate hearing loss as a function of occupational noise exposure and age over time.

Methods and Material: Audiological data from 2,536 mine workers in South Africa were utilised. Longitudinal data of a non-noise-exposed group (n=961) and a noise-exposed group (≥85 dBA) (n=1632) were compared in a mixed effects regression analysis.

Results: Base threshold values were significantly higher for the noise-exposed than for the non-noise-exposed group when averaging 0.5, 1 and 2 kHz (LFA), and when averaging 3, 4 and 6 kHz (HFA). All year-to-year increases in mean hearing thresholds were statistically significant (p-values of <0.01) for both exposure groups. When correcting for age, increases in mean hearing thresholds were higher for the noise-exposed than for the non-noise-exposed group when comparing HFA (3.5 dB versus 2.9 dB decline over four-year period) but similar when comparing LFA (0.6 dB versus 0.7 dB decline). When uncorrected for age, increases in mean hearing thresholds were higher than in the analysis corrected for age, identifying age as a significant factor in a year-to-year increase in mean hearing thresholds for both exposure groups across all frequencies.

Conclusions: Age and occupational noise exposure influence hearing thresholds over time, even in a setting where occupational exposure limits and use of personal hearing protection are enforced. The longitudinal increase in hearing thresholds of the noise-exposed group could be attributed to ineffective noise management implementation

[1]This article was edited in accordance with the editorial specifications required by the journal and may differ from the editorial style of the rest of this document.

and/or support the fact that early noise exposure leads to a higher burden of hearing loss in later life – even after noise exposure has stopped.

Keywords: age-related hearing loss, noise exposure, noise-induced hearing loss

Key Messages:
Longitudinal increases in hearing thresholds in occupationally noise-exposed individuals, corrected for age, could be attributed to ineffective noise management programmes and/or support the notion that early noise exposure leads to a higher burden of hearing loss in later life, even after noise exposure has stopped.

3.2 Introduction

Excessive noise is an occupational hazard with many adverse effects, including elevated blood pressure,[1,2] elevated cholesterol,[1] increased risk for coronary heart disease,[3] reduced work performance, difficulty in sleeping, annoyance, stress, tinnitus, temporary threshold shift (TTS) and noise-induced hearing loss[4] (NIHL). Although many other adverse effects of high-level noise exposure have been reported, NIHL is recognised as the primary and most direct health effect of noise exposure, which makes it a significant and ongoing health concern with economic consequences.[5,6,7]

NIHL is a permanent shift in hearing thresholds caused by prolonged exposure to high levels of noise, as a direct cause of damage to the sensory hair cells of the inner ear.[8] Worldwide, 16% of disabling hearing loss in adults can be attributed to occupational noise, ranging from 7% to 21% across various regions of the world, with the biggest burden of NIHL in the developing world.[4] NIHL is the second largest contributor to hearing loss globally, exceeded only by age-related hearing loss (ARHL). Therefore, most hearing losses not associated with noise can be attributed to age.[7]

ARHL and NIHL in humans are both multifactorial, with contributions from and interactions between numerous intrinsic (e.g. genetic predisposition) as well as extrinsic (e.g. noise exposure) variables that can shape its final outcome.[9,10] The interaction between age and noise and their respective effects on hearing status are still poorly understood, making it difficult to distinguish between NIHL and ARHL at an individual level, often because the time and magnitude of each exposure are unclear.[11,12,13,14] Numerous studies have examined the interaction between NIHL and ARHL but, because these conditions happen concurrently, it is difficult to determine their individual effects on hearing.[11,12,13,15]

In recent attempts to explain this complex interaction between NIHL and ARHL, two possible models of interaction have emerged.[15] A possible super-additive interaction follows the notion that an already damaged hair cell is more susceptible to further damage from additional factors. When describing the interaction between NIHL and ARHL as a less than additive effect, the assumption is based on the premise that when a number of hair cells had been previously damaged, there is a decreased risk of further damage. Simply stated, hair cells lost from one cause cannot be lost again from a second cause.[11,16,17]

We know that hair cell damage is a key contributor to NIHL and ARHL as defined by the audiogram. Traditionally, most evidence gathered pertaining to the interaction between NIHL and ARHL is based on audiometric thresholds, which measure the minimum sound pressure level required for pure tone detection in quiet.[18,19]

For years it has been assumed that cochlear neural loss manifested only after hair cell loss and was rarely seen as significant in NIHL and ARHL. Recent research, however, demonstrates that in both NIHL and ARHL, synaptic connections between the hair cells and cochlear neurons can be destroyed even before hair cell damage occurs.[19] This synaptic loss then forms a basis of damage that negatively impacts the progression of their hearing loss over time. This challenges the traditional view by various authors[12,17,20,21,22] that the influence of noise on hearing is time-limited, meaning the progression of NIHL ceases when noise exposure stops.

A study based on data from the United States of America, estimated that the single industry with the highest proportion of workers exposed to hazardous noise is mining, with an estimated 85% of production workers and labourers exposed to noise levels above 85 dB (TWA).[4] These results are consistent with the results from similar studies in the United States and Scandanavia.[23,24,25] Results also correspond to those reported from South Africa, where on average 73.2 percent of mine workers were exposed to noise levels above the 85 dBA legislated occupational exposure level.[26]

3.3 Subjects and methods

The aim of this study was to further investigate hearing loss as a function of occupational noise exposure and age over time. This was done by developing a regression model for the prediction of hearing loss as a function of noise exposure and age, over time, in a large longitudinal data set of gold mine employees in South Africa.

A retrospective cohort design was followed.[27] The study was conducted with audiological data received from the AngloGold Ashanti group of mines in the Witwatersrand area in South Africa. This data set therefore offered access to a large population within an industry known for high levels of occupational noise exposure.

Audiological records were analysed that were obtained from the mine's electronic database, Everest. Approval was obtained from the relevant mines, as well as the

Research Ethics Committee of the University of Pretoria prior to the commencement of the study.

Participant selection

A data set including audiological, biographical and environmental information was received for all employees at two gold mine groups, consisting of seven gold mines. Records included data for 57,714 employees, comprising a total of 232,458 audiograms. All data were collected between 2001 and 2008 from routine audiological screening, as well as diagnostic follow-up measures, made available by the mine's occupational health department. Available audiological thresholds were comprised of the following frequencies: 0.5, 1, 2, 3, 4, 6 and 8 kHz. Results for the right and left ears were combined. Testing was conducted in sound-treated rooms that complied with the requirements as stipulated in the South African National Standards (SANS) document (SANS 10154-1:2001). A Tremetrics RA600 Type 4 audiometer was used for testing, coupled with TDH39 headphones. Follow-up diagnostic audiometry was performed on employees whose percentage loss of hearing (PLH) dropped by more than 10%[29] from their baseline test, using a GSI 61 diagnostic audiometer. All test results were captured within an electronic database (Everest).

Participants were divided into four noise exposure groups, namely above surface noise exposure (≥ 85 dBA), below surface noise exposure (≥ 85 dBA), no noise exposure, and uncertain noise exposure. To have homogeneous exposure groups for comparison in this study, two sub-groups from the below surface noise exposure group, and the non-noise exposure group were selected, namely the rock drillers (noise-exposed group) and administration personnel (non-noise-exposed group). The rock drillers were chosen because noise exposure in mining is mainly due to the use of heavy equipment, drilling and rock breaking, transferring, sorting and milling of rock, and the confined working environment.[28] Drillers in underground gold mines in South-Africa are exposed to an average of 105 dBA[26], which therefore falls above the maximum defined occupational noise exposure of ≥ 85 dBA, as classified according to the South African regulations on the daily permissible level of noise exposure.[29] Data received included records for 4,399 rock drillers and 2,211 administration personnel. For this study, only data where participants had four longitudinal (annual) audiograms, falling in sequence within 2001 to 2008, for example, 2001, 2002, 2003

and 2004, or 2003, 2004, 2005 and 2006 were used. This reduced the total participant number to 2,583 employees, which included 1,632 in the noise-exposed (rock driller) group, and 951 in the non-noise-exposed (administration worker) group. Participant demographics are depicted in Table 2.

Table 3. Age, race and gender distribution of the 2,583 gold mine workers

	Age (at first test)			**Gender**		**Race**	
	Mean	**Min age**	**Max age**	**Female**	**Male**	**White**	**Black**
Non- noise	36.2	20	61	9	942	38	913
				52.9%	36.7%	80.9%	36%
Noise	43.3	19	60	8	1624	9	1623
				47.1%	63,3%	19.1%	64%
Total				17	2566	47	2536
				100%	100%	100%	100%

Procedures

The Mine Health and Safety Act, Instruction 171[29] and South African National Standard[30] require that all employees with noise exposure of 85 dBA normalised in an eight-hour working day or forty-hour working week be monitored audiologically. Legislation as set out in Instruction 171[29] makes it compulsory for all employees to have a baseline audiogram within two years of the legislation being passed (2001), or within 30 days of employment for new employees. All data collected complied with this guideline; audiograms consisted of baseline , annual screening and exit audiograms performed by Occupational Health Personnel as well as results of diagnostic testing performed by audiologists registered with the Health Professional Council of South Africa.

Data analysis

A mixed effects regression analysis was employed on the data where four longitudinal (annual) audiograms were available for an individual in the cohort. A mixed effects regression analysis can allow for the prediction of an outcome variable (for example hearing loss or age) from a predictor variable (for example noise exposure) over time, by using repeated measures.[31] These panel data (repeated observations within an

individual) were analysed using a mixed effects REML (restricted maximum likelihood) regression, for both noise-exposed and non-noise-exposed groups, where mine workers were specified as the random effects. Because of the many similarities and interactions between NIHL and ARHL, it is imperative to take into consideration the total relevant contribution of age-related hearing loss when determining the effect of noise exposure on hearing.[32] The model was therefore adjusted for age as well as baseline hearing threshold. The model was also repeated without adjusting for age in order to determine the separate contributions of age and noise on the total hearing loss of the participant over a four-year period. High-frequency averages of 3, 4 and 6 kHz (HFA) and low-frequency averages of 0.5, 1 and 2 kHz (LFA) were analysed separately. Testing was done at the $p<0.01$ level of significance.

3.4 Results

Year-to-year increases in mean hearing thresholds were all statistically significant (p-values of <0.01; Table 4). Mean values for year 1 (baseline year per participant from 2001–2008) were significantly higher for the noise-exposed group than for the non-noise-exposed group. This was seen in both LFA analysis as well as HFA, although it was more prominent for HFA. Year-to-year increases in mean hearing thresholds were higher for the noise-exposed group than for the non-noise-exposed group when comparing HFA but similar when comparing LFA.

Table 4. Mixed effects regression analysis of hearing over the four annual audiograms for the non-noise-exposed and noise-exposed groups, corrected for age, for the high-frequency average (HFA; 0.5,1 and 2 kHz) and low-frequency average (LFA; 2,4 and 6 kHz)

Frequency	Exposure group	Year	Mean (95% confidence interval) in dB HL	Change from baseline (dB HL)	p-Value
HFA	**Noise**	1	25.7 (25.3:26.1)		
		2	28.5 (28.2:28.9)	2.8	<0,001
		3	29.0 (28.6:29.4)	3.3	<0,001
		4	29.2 (28.8:29.6)	3.5	<0,001
HFA	**Non-noise**	1	18.5 (18.1:19.0)		
		2	20.9 (20.4:21.3)	2.3	<0,001
		3	21.0 (20.5:21.4)	2.4	<0,001
		4	21.4 (21.0:21.8)	2.9	<0,001
LFA	**Noise**	1	16.1 (15.7:16.6)		
		2	17.5 (17.0:17.9)	1.3	<0,001
		3	17,0 (16.6:17.6)	1.0	<0,001
		4	16.8 (16.3:17.2)	0.6	<0,001
LFA	**Non-noise**	1	11.1 (10.6:11.5)		
		2	12.1 (11.6:12.6)	1.1	<0,001
		3	11.8 (11.3:12.3)	0.8	<0,001
		4	11.1 (11.3:12.3)	0.7	<0,001

Additionally, mixed effects regression results were repeated without correcting for age to represent year-to-year increases in hearing thresholds including noise and age influences. Year-to-year increases in mean hearing thresholds were all statistically significant, with p-values of <0.01 (Table 3). Mean values for year 1 (baseline) were higher for the noise-exposed group than for the non-noise-exposed group. This was

seen in both LFA analysis as well as HFA, although more prominent for HFA. Year-to-year increases in mean hearing thresholds were higher for the noise-exposed group than for the non-noise-exposed group in comparing HFA but similar when comparing LFA. Year-to-year increases in mean hearing thresholds were higher in the analysis where age was uncorrected, identifying age as a significant (p-values of <0.01) factor in year-to-year increases in mean hearing thresholds for both exposure groups across LFA and HFA.

Table 5. Mixed effects regression analysis of hearing over the four annual audiograms for the non-noise-exposed and noise-exposed groups, uncorrected for age, for the high-frequency average (HFA; 0.5,1 and 2 kHz), and the low-frequency average (LFA; 2,4 and 6 kHz)

Frequency	Exposure group	Year	Mean (95% confidence interval) (dB HL)	Change from baseline (dB HL)	p-Value
HFA	Noise	1	25.4 (25.06:25.82)		
		2	28.4 (23,08:28.83)	3.0	<0,001
		3	29.1 (28.69:29.44)	3.6	<0,001
		4	29.4 (29.06:29.81)	4.0	<0,001
HFA	Non-noise	1	18.2 (17.8:18.7)		
		2	20.8 (20.3:21.2)	2.6	<0,001
		3	21.1 (20.6:21.6)	2.9	<0,001
		4	21.1 (21.3:22.2)	3.5	<0,001
LFA	Noise	1	15.9 (15.4:16.3)		
		2	17.4 (16.9:17.83)	1.5	<0,001
		3	17.2 (16.7:17.6)	1.3	<0,001
		4	17.0 (16.5:17.5)	1.1	<0,001
LFA	Non-noise	1	10.9 (10.4:11.3)		
		2	12.1 (11.6:12.5)	1.2	<0,001
		3	11.9 (11.4:12.3)	1.0	<0,001
		4	12.0 (11.5:12.5)	1.1	<0,001

3.5 Discussion

The noise-exposed group was on average 6.7 years older than the non-noise-exposed group at the time of their first audiogram. Therefore, age was corrected for in the original analysis with the specific aim to separate the effects of noise exposure from the joint effect of noise exposure and aging. Baseline values from year 1 were higher in the noise-exposed group compared to the non-noise-exposed group, for LFA and HFA, when corrected for age. The noise-exposed group therefore had damage to their hearing prior to their first audiogram within this set of audiograms. The earliest audiograms within this sample were conducted in 2001, in accordance with legislation that makes it compulsory in South Africa for baseline audiograms and annual testing in occupational settings with high levels of noise.[29] Previous unprotected noise exposure is therefore a probable contributor to the higher baseline values seen in the noise-exposed group. This previous noise exposure may be the result of mining authorities not implementing hearing conservation programs, ineffective hearing conservation programs or non-compliance to hearing conservation programs on the side of the mine workers.

There was a statistically significant increase (p-values of <0.01) in mean hearing thresholds, from year to year, as well as over the four-year period in both exposure groups for LFA and HFA. The increase in mean hearing thresholds was, however, higher in the noise-exposed group in both LFA and HFA. Noise is therefore an ongoing factor in employees' total hearing loss even with legislated control of noise exposure. The classic view of NIHL has been that the primary damage areas are the hair cells, and that auditory nerve loss is mostly secondary to hair cell loss. Evidence by Fernandez et al.[18] and Liberman[19] suggests that in both NIHL and ARHL, synaptic connections between the hair cells and cochlear neurons can be destroyed even before hair cell damage occurs. These progressive age-related changes in the noise-damaged ear involve the inner hair cell and/or the auditory nerve to a greater degree than the outer hair cells.[18] Noise-exposed individuals can therefore have a basis of damage to their inner hair cells and/or the auditory nerve that can negatively impact the progression of their hearing loss over time.

This challenges the traditional view that the influence of noise on hearing is time-limited, meaning the progression of NIHL ceases when noise exposure stops.[18] In our

sample, it is therefore possible that even after the introduction of annual testing and noise hygiene programmes in 2001,[29] the hearing thresholds of the noise-exposed group kept increasing at a faster pace than their non-noise counterparts, which will support a super-additive interaction between aging and noise exposure, following the notion that an already damaged hair cell, as well as hair cells with synaptic loss, is more susceptible to further damage from additional factors, such as aging and noise exposure.

A second probability of the increase of the noise-exposed groups' hearing thresholds over time can possibly be attributed to findings by Basner et al.,[14] indicating that despite the introduction of standards for hearing protection, hearing loss due to occupational noise remains a problem. Many countries enforce health and safety legislation pertaining to noise exposure; however, for legislation to work effectively, strict adherence should be enforced. In a study investigating hearing protection device usage at a South African mine, observed use of hearing protection devices (50%) was much lower than reported use (93%).[33] These reports are concerning as evidence exists that even a single synoptopathic exposure can accelerate cochlear aging.[18] It is therefore possible that this study population is still exposed to occupational noise, even with legislated hearing conservation programmes. This highlights the necessity of not only implementing a hearing conservation program, but also measuring its effectiveness and outcomes continuously.

Although noise exposure tends to be classified as a predominantly high-frequency hearing loss,[21,22] the difference between mean hearing thresholds in the noise-exposed and the non-noise-exposed groups in this sample were noticed in both the low frequencies (LFA) and high frequencies (HFA), although more prominently in the high frequencies. A possible explanation for the increase in low-frequency thresholds in the noise-exposed group can be found in a study conducted by Fernandez et al.[18] In this study, permanent versus non-permanent synaptic loss between hair cells and auditory nerve fibres in mice was compared as they aged. As exposed adult mice aged, synaptopathy was exacerbated compared to controls and, over time, damage spread from the high frequencies to the lower frequencies, which correlates with the findings in the current study.

When the analysis was repeated without correcting for age (to get a view of the combined effect of noise and age), there was a marked difference in mean hearing thresholds in both exposure groups when compared with the analysis where age was corrected for. This was observed for both LFA and HFA. The relative contribution of age to the total hearing loss was similar when comparing LFA between exposure groups, but more dominant in the noise-exposed group when comparing HFA. Age is therefore a contributor, although more prominent in the high frequencies, and the noise-exposed group.

The reassessment of the assumptions that have been made on the relative contributions of ARHL and NIHL in cross-sectional analysis may be necessary. Cross-sectional data can overestimate the relevant contribution of age because the accelerated time-related degeneration would be attributed only to age, rather than to previous noise damage.[11] In a cross-sectional study of 40,123 gold miners in South Africa, employing the same data as the current study, it was found that age was the most important influence on hearing thresholds, for both noise-exposed and non-noise-exposed mine workers.[32] In the above study, it is therefore possible that the conclusion could over-state the relative contribution of age because in its cross-sectional nature the accelerated time-related degeneration as an interaction between noise and age was not taken into consideration. It should, however, also be noted that the mentioned study made use of a much larger cohort of the total data set (40,123 mine employees) compared to the current study (2,536 mine employees of the same sample). Caution should therefore be taken when making direct comparisons between the two studies.

The mean age for the first test was higher in the noise-exposed group (43.3 years) as opposed to the non-noise-exposed group (36.6 years), which may act as a moderating factor in the sense that the older the subject, due to the effect of aging on the ear, the higher their initial hearing thresholds will be. This finding can also be compared to findings that suggest pathological changes from early noise exposure to substantially increase the risk of inner-ear aging and related hearing loss in later years.[9,11,34,35] Although the specific mechanism for the accelerated increase in hearing thresholds seen in this analysis cannot be identified accurately, it seems possible that the noise-damaged ear does not age at the same rate as an ear without known noise damage. This again points to a possible super-additive interaction between NIHL and ARHL.

As previously discussed, this is supported by evidence by Fernandez et al. and Liberman[18,19] that both noise exposure (even noise exposure causing only TTS) and aging cause early synaptic damage, which will not be detected by a standard audiogram, but which may influence the progression of hearing loss in later years.

The existence of cochlear synaptopathy in humans will have major implications for audiological practice, specifically in health surveillance and noise exposure regulations. An obstacle to the quantification of cochlear synaptopathy, and to the eventual incorporation thereof into audiological practice, is the absence of a reliable and validated diagnostic test for the disorder.[36] Wave I of the transient-evoked auditory brainstem response is a non-invasive electrophysiological measure of auditory nerve function that have been validated in animal studies, however in humans, wave I amplitude shows high inter in inner-subject variability. Another test, called the frequency-following response is a sustained evoked potential reflecting synchronous neural activity in the rostral brainstem, and can potentially be a more robust test that the auditory brainstem response wave I. The frequency-following test however is a measure of central activity, and may be dependent on individual differences in central processing. Despite the obstacles, a diagnostic test for cochlear synaptopathy is a worthwhile goal, with important implications for both for clinical practice and health surveillance.[36]

While noise exposure and aging can be seen as the main contributors in the total increase in average hearing thresholds over time for both exposure groups in this sample, caution should be taken to disregard other possible contributions to the increase in hearing thresholds in these groups. Hearing loss in the sample should be regarded as multifactorial, with contributions from numerous intrinsic (e.g. genetic predisposition) as well as extrinsic (e.g. noise exposure) variables.[9,10] Certain factors that may affect the audiological outcome of the study participants such as genetic predisposition to hearing loss, health co-morbidities and environmental influences on hearing were not considered. These factors were not considered since sample sizes for Caucasian and female participants were too small for statistical analysis and no data were available for health conditions known to influence hearing, such as tuberculosis and diabetes. Further, no data were available for non-occupational noise exposure of participants. The participants in this study do, however, all come from the same occupational background, with similar socio-economic status, living conditions,

health exposures and leisure activities. Therefore, comparisons between noise exposure groups in this study could be made without fear of one group having substantial other hearing risks above a second group.

3.6 Conclusion

Both age and occupational noise exposure influence hearing thresholds over time, even in a setting where noise exposure is controlled through legislation, and the use of personal hearing protection is enforced. The continued increase in hearing thresholds of the noise-exposed group can either be related to ineffective noise management programme implementation and/or support the fact that early noise exposure leads to a higher burden of hearing loss in later life, even after noise exposure has stopped.

3.7 Compliance with ethical standards

Conflict of interest: The authors declare that they have no conflict of interest.

3.8 References:

1. Kerns E, Masterson EA, Themann CL, Calvert GM. Cardivascular conditions, hearing difficulty, and occupational noise exposure within US industries and occupation. Am J Ind Med 2018;6:1-15.

2. Wang D, Zhou M, Li W, Kng W, Wang Z, Guo Y, et al. Occupational noise exposure and hypertension: The Dongfeng-Tongji Cohort Study. Journal of the American Society of Hypertension 2018;12:71-9.

3. Eriksson HP, Andersson E, Schiőler L, Sőderberg MS, Rosengren A, Torén K. Longitudinal study of occupational noise exposure and joint effects with job strain and risk for coronary heart disease and stroke in Swedish men. BMJ Open 2018;8:e019160.

4. Nelson DI, Nelson RY, Concha-Barrientos M, Fingerhut M. The global burden of occupational noise-induced hearing loss. Am J Ind Med 2005;48:446-58.

5. Agrawal Y, Niparko JK, Dobie RA. Estimating the effect of occupational noise exposure on hearing thresholds: The importance of adjusting for confounding variables. Ear Hear 2010;31:234-7.

6. Hong O, Kerr MJ, Poling GL, Dhar S. Understanding and preventing noise-induced hearing loss. Dis Mon 2013;59:110-8.

7. Lie A, Skogstad M, Johannessen HA, Tynes T, Mehlum IS, Nordby K, et al. Occupational noise exposure and hearing: A systematic review. Int Arch Occup Environ Health 2016;89:351-72.

8. Sliwinska-Kowalska M, Davis A. Noise-induced hearing loss. Noise Health 2012;14:274-80.

9. Kujawa SG, Liberman MC. Acceleration of age-related hearing loss by early noise exposure: Evidence of a misspent youth. Journal of Neuroscience 2006;26:2115-23.

10. Yamasoba T, Lin FR, Someya S, Kashio A, Sakamoto T, Kondo K. Current concepts in age-related hearing loss: Epidemiology and mechanistic pathways. Hear Res 2013;303:30-8.

11. Gates GA, Schmid P, Kujaw, SG, Nam B, D'Agostino R. (2000). Longitudinal threshold changes in older men with audiometric notches. Hear Res 2000;14;220-8.

12. Rosenhall U. The influence of ageing on noise-induced hearing loss. Noise Health 2003;5:47-53.

13. Xiong M, Yang C, Lai H, Wang J. Impulse noise exposure in early adulthood accelerates age-related hearing loss. Eur Arch Otorhinolaryngology 2013;271:1351-4.

14. Basner M, Babisch W, Davis A, Brink M. Clark C, Janssen S, Stansfeld S. Auditory and non-auditory effects of noise on health. Lance 2014;383:1325-32.

15. Aarhus L, Tambs K, Nafstad P, Bjorgan E, Engdahl B. Childhood sensorineural hearing loss: Effects of combined exposure with aging or noise exposure in later life. Eur Arch Otorhinolaryngol 2016;273:1099-105.

16. Gallo R, Gloring A. Permanent threshold shift changes produced by noise exposure and aging. Am. Ind. Hyg. 1964;25:237-45.

17. Dobie RA. The burdens of age-related and occupational noise-induced hearing loss in the United States. Ear Hear 2008;29:565-77.

18. Fernandez A, Jeffers WC, Lall K, Libberman MC, Kujawa SG. Aging after noise exposure: Acceleration of cochlear synaptopathy in "recovered" ears. Journal of Neuroscience 2015;35:7509-20.

19. Liberman MC. Noise-induced and age-related hearing loss: New perspectives and potential therapies [version 1]. F1000Research 2017;6(F1000 Faculty Rev):927

20. Jonsson R, Rosenhall U. (1998). Hearing in advance age. A study of presbycusis in 85-, 88- and 90-yaer-old people. Audiology 1998;37:207-18.

21. Dias RC, Cordeiro R, Corente JE, Concalves CGO. Association between noise induced hearing loss and tinnitus. Cadernos de Saúde Pública 2006;22:63-8.

22. Teles RM, Medeiros MPH. Audiometric profile of Maracanau's industrial district workers. Rev. Soc. Bras. Fonoaudiol 2007;12:233-9.

23. Tak S, Calvert GM. (2008). Hearing difficulty attributable to employment by industry and occupation: An analysis of the National Health Interview Survey - United States, 1997-2003 J Occup Environ Med 2008;50:46-56.

24. Engdahl B, Tambs K. Occupation and the risk of hearing impairment- results from the Nord-Trondelag study on hearing loss. Scand J Work Environ Health 2010;36:250-7.

25. Masterson E, Deddens J, Themann CL, Bertke S, Calvert, GM. Trends in worker hearing loss by industry sector, 1981-2010. Am J Ind Med 2015;58:392-401.

26. Edwards A, Dekker J, Franz AM. Profiles of noise exposure levels in South African mining. Journal of the Southern African Institute of Mining and Metallurgy 2011;11:315-22.

27. Thiese MS. Observational and interventional study design types; an overview. Biochemia Medica 2014;24(2):199-210.

28. Hermanus MA. Occupational health and safety in mining-status, new developments, and concern. Journal of the Southern African Institute of Mining and Metallurgy 2007;107:531-8.

29. COIDA. Compensation for Occupational Injuries and diseases Act, No. 130 of 1993. Circular Instruction No. 171, South Africa Government Gazette 2001;no. 22296,A61311, A10/4/3/4.

30. SANS10083:2004.The measurement and assessment of occupational noise for hearing conservation purposes. Pretoria: South African National Standards; 2013.

31. Field A. Discovering statistics using SPSS, 3rd ed. London: Sage Publications;2009.

32. Strauss S, Swanepoel DW, Becker P, Eloff Z, Hall III JW. Noise and age-related hearing loss: A study of 40 123 gold miners in South Africa. International Journal of Audiology 2014;53:S66-75.

33. Hansia MR, Dickinson D. Hearing protection device usage at a South African gold mine. Occup Med 2010;60:72-4.

34. Campo P, Venet T, Rumeau C, Thomas A, Rieger B, Cour C, et al. Impact of noise on styrene exposure on the kinetics of presbycusis. Hear Res 2011;280:122-32.

35. Meneses-Barriviera CL, Melo JJ, De Moraes Marchiori LL. Hearing loss in the elderly: History of occupational noise exposure. Int Arch Otorhinolaryngol 2013;17:179-183.

36. Plack CJ, Léger A, Prendergast G, Kluk K, Guest H, Munro KJ. Toward a Diagnostic Test for Hidden Hearing Loss. Trends in Hearing 2016;20:1-9.

4. DISCUSSION AND CONCLUSION

4.1 Summary and discussion of findings

Baseline values from year 1 were higher in the noise-exposed group compared to the non-noise-exposed group, for LFA and HFA, in both the analyses corrected for age and uncorrected for age. Although the difference was seen in both LFA and HFA, the difference was more pronounced for HFA.

When corrected for age and baseline, there was a statistically significant (p-values <0.01) increase in mean hearing thresholds, from year to year, as well as over the four-year period in both exposure groups for LFA and HFA. The increase in mean hearing thresholds was, however, higher in the noise-exposed group in both LFA and HFA. As this analysis was corrected for both age and baseline, it provided an exclusive look at the effect of noise exposure on the hearing thresholds of the sample population. As the increase in mean hearing thresholds was higher in the noise-exposed group as opposed to the non-noise-exposed group, it suggests that noise continues to be a contributor to hearing loss over time, even in a setting where noise exposure is controlled through legislated monitoring of hearing thresholds and large-scale controlling of noise exposure.

When the analysis was repeated without correcting for age (to get a view of the combined effect of noise and age), there was a marked difference in mean hearing thresholds in both exposure groups when compared with the analysis where age was corrected for. This was observed for both LFA and HFA. The relative contribution of age to the total hearing loss between the exposure groups was similar when comparing LFA, but more dominant in the noise-exposed group when comparing HFA.

The earliest audiograms within this sample were conducted in 2001, in accordance with legislation that makes it compulsory in South Africa for baseline audiograms and annual testing in occupational settings with high levels of noise (COIDA,2001). Previous unprotected noise exposure is therefore a probable contributor to the higher baseline values seen in the noise-exposed group. This previous noise exposure may be the result of mining authorities not implementing hearing conservation programs, ineffective hearing conservation programs or non-compliance to hearing conservation programs on the side of the mine workers.

This is a limitation of the study, as no work history data or noise exposure data were available prior to 2001.

Although noise exposure tends to be classified as a predominantly high-frequency hearing loss (Dias et al., 2006; Teles et al., 2007), the difference between mean hearing thresholds in the noise-exposed and non-noise-exposed groups in this sample were noticed in both LFA and HFA, although more prominent in the high frequencies. A possible contribution to the decrease in low-frequency thresholds in the noise-exposed group may relate to findings by Fernandez et al. (2015). In this study, permanent versus non-permanent synaptic loss between hair cells and auditory nerve fibres in mice were compared as they aged. As exposed adult mice aged, synoptopathy was exacerbated compared with controls and, over time, damage spread from the high frequencies to the lower frequencies, which corresponds with the findings in this study. Therefore, noise exposure seems to not only have an exclusive effect on the high frequencies, but can, over time, also affect the low frequencies.

The two scenarios discussed next could be possible contributors to the higher increase in hearing thresholds seen in the noise-exposed group as opposed to the non-noise-exposed group. It should, however, be remembered that hearing loss in the sample should be seen as complex and multifactorial, with contributions from as well as potential interactions between numerous intrinsic (e.g. genetic predisposition) and extrinsic (e.g. noise exposure) variables that could not be accounted for in this study (Kujawa et al., 2006; Yamasoba et al., 2013).

First, as AngloGold Ashanti adopted major noise management, audiological monitoring and use of personal hearing protection devices from 2001 when legislation was passed (COIDA, 2001), the noise-exposed population could be seen as “protected noise exposed”, following 2001. However, in the results, it is evident that the noise-exposed group’s hearing still deteriorates at a faster rate than their non-noise-exposed counterparts. A possible explanation for this may be attributed to findings by Basner et al. (2014), which indicate that despite the introduction of standards for hearing protection, reduction in occupational noise exposure in developed countries, as well as extensive public health efforts, hearing loss due to occupational noise remains a problem. Many countries enforce health and safety

legislation that specifies maximum exposure levels and requirements for action, which are intended to protect employees from excessive noise exposure. However, for legislation to work effectively, strict adherence to legislation should be enforced. In a study investigating hearing protection device usage at a South African mine by Hansia and Dickinson (2010), observed use of hearing protection devices (50%) was much lower than reported use (93%). It is therefore possible that the study population is still, to an extent, exposed to occupational noise, even with legislated hearing conservation programmes in place. These reports are concerning, as evidence exists that even a single synoptopathic exposure to high noise levels can accelerate cochlear aging (Fernandez et al., 2015). Therefore, even with partial adherence to noise protection strategies, there can still be negative long-term consequences in respect to hearing thresholds. From this, the importance of not only implementing a hearing conservation program, but also to monitor it effectiveness on a continues basis can be seen, Effort should be made on an ongoing basis to ensure adherance of mine workers to noise control programs and strategies, and should also monitor the effectiveness of specific types of hearing protection devices used.

Second, the classic view of NIHL has been that the primary damage areas are the hair cells, and that auditory nerve loss is mostly secondary to hair cell loss. Much evidence cited in support of this view is based on audiometric thresholds, measured with a pure tone audiogram, which are good at reflecting damage to hair cells, but not to the sensory cells innervating them (Fernandez et al., 2015). More recent evidence by Fernandez et al. (2015) and Liberman (2017) suggests that in both NIHL and ARHL synaptic connections between the hair cells and cochlear neurons can be destroyed even before hair cell damage occurs. These destroyed synaptic connections will form the basis for further damage, either by more noise or from aging.

The finding that early synaptic damage can form a basis for future damage challenges the traditional view that the influence of noise on hearing is time-limited, meaning the progression of NIHL ceases when noise exposure stops (Fernandez et al., 2015). In the sample, it is therefore possible that even after the introduction of annual testing and noise hygiene programmes in 2001 (COIDA, 2001), the hearing thresholds of the noise-exposed group still increased at a faster pace than their non-noise-exposed counterparts due to previous damage, not only at hair cell level, but also at synaptic level. In recent attempts to explain this complex interaction between NIHL and ARHL,

two possible models of interaction have emerged (Aarhus et al., 2016). A possible super-additive interaction follows the notion that an already damaged hair cell is more susceptible to further damage from additional factors. When describing the interaction between NIHL and ARHL as a less than additive effect, the assumption is based on the premise that when a number of hair cells were previously damaged, there is a decreased risk of further damage. Simply stated, hair cells lost from one cause cannot be lost again from a second cause (Gallo & Gloring, 1964; Gates et al., 2000; Dobie, 2008).

Although the specific mechanism for the accelerated increase in hearing thresholds seen in these analyses cannot be identified accurately, it seems possible that the noise-damaged ear does not age at the same rate as an ear without known noise damage. This points to a possible super-additive interaction between NIHL and ARHL. These findings can be compared to findings that suggest pathological changes from early noise exposure to substantially increase the risk of inner-ear aging and related hearing loss in later years (Gates et al., 2000; Campo et al., 2011; Kujawa & Liberman, 2006; Meneses-Barriviera, Melo, & De Moraes Marchiori, 2013). As previously discussed, this is supported by recent evidence by Fernandez et al. (2015) and Liberman (2017), that both noise exposure (even noise exposure causing only TTS) and aging cause early synaptic damage, which will not be picked up by a standard audiogram, but will form a basis of damage that will greatly influence the progression of hearing loss in later years.

The existence of cochlear synaptopathy in humans will have major implications for audiological practice, specifically in health surveillance and noise exposure regulations. An obstacle to the quantification of cochlear synaptopathy, and to the eventual incorporation thereof into audiological practice, is the absence of a reliable and validated diagnostic test for the disorder (Plack et al., 2016). Wave I of the transient-evoked auditory brainstem response is a non-invasive electrophysiological measure of auditory nerve function that have been validated in animal studies, however in humans, wave I amplitude shows high inter in inner-subject variability. Another test, called the frequency-following response is a sustained evoked potential reflecting synchronous neural activity in the rostral brainstem, and can potentially be a more robust test that the auditory brainstem response wave I. The frequency-following test however is a measure of central activity, and may be dependent on

individual differences in central processing. Despite the obstacles, a diagnostic test for cochlear synaptopathy is a worthwhile goal, with important implications for both for clinical practice and health surveillance (Plack et al., 2016).

This study suggests that noise-exposed individuals can potentially have a basis of damage, comprised of previous synaptic loss and hair cell loss that negatively impacts the progression of their hearing loss over time. Interacting with this, with further noise exposure possibly due to non-compliance to hearing conservation programmes, their hearing can continue to deteriorate at a faster pace than their non-noise-induced counterparts. In view of the above statement, the complexity of the interaction between noise exposure and aging, together with contributions from other intrinsic and extrinsic variables that could not be accounted for in this study, should not be disregarded. These variables can include but should not be limited to genetic predisposition to hearing loss, such as race and gender, or factors like medical conditions directly associated with hearing loss, as well as non-occupational noise exposure.

4.2 Strengths of the study

The major strength of this study can be found in its longitudinal nature. For years it was assumed that NIHL develops more rapidly in the first years of noise exposure than in the later years of exposure, but serial audiograms that could assist in diagnosis are often unavailable (Dobie, 2008). In this study, the main strength was to have available audiograms over nine years for a large group of individuals, making it possible to have a large enough cohort to analyse four serial audiograms for each participant within that timeframe. This is important, as recent studies suggest that it is possible that the noise-damaged ear does not age at the same rate as an ear without known noise damage (Fernandez et al., 2015; Libeman, 2017). The current research is therefore valuable as it could add to these findings because of its ability to look at the decline of hearing thresholds over time, as opposed to a cross-sectional view.

The above calls into question assumptions that have been made on the relative contributions of ARHL and NIHL in cross-sectional analysis. Cross-sectional data can overestimate the relevant contribution of age because the accelerated time-related degeneration would be attributed only to age, rather than to previous noise damage. Gates (2000) supported this notion from a study looking at longitudinal threshold changes in older men. In a cross-sectional study of 40,123 gold miners in South Africa,

employing the same data as the current study, it was found that age was the most important influence on hearing thresholds for both noise-exposed and non-noise-exposed mine workers (Strauss et al., 2014). In the mentioned study, it is therefore possible that this conclusion could over-state the relative contribution of age, as in its cross-sectional nature, to the accelerated time-related degeneration since an interaction between noise and age was not taken into consideration. It should, however, also be noted that the mentioned study made use of a much larger cohort of the total data set (40,123 mine employees) compared to the current study (2,536 mine employees). Caution should therefore be taken when making direct comparisons between the two studies.

4.3 Limitations of the study

While noise exposure and aging can be seen as the main contributors to the total decrease in average hearing thresholds over time for both exposure groups in this sample, caution should be taken to disregard other possible contributions to the increase in hearing thresholds in these groups. Hearing loss in the sample should be seen as multifactorial, with contributions from as well as potential interactions between numerous intrinsic and extrinsic variables (Kujawa et al., 2006; Yamasoba et al., 2013). Unfortunately, certain factors that may affect the audiological outcome of the study participants could not be considered, for example:

- Genetic predisposition in terms of race and gender (sample sizes for Caucasian and female participants were small for statistical analysis);
- Health co-morbidities (no data were available for health conditions known to influence hearing thresholds, such as Diabetes and Tuberculosis);
- Environmental influences on hearing, such as non-occupational noise exposure and chemical exposures.

The participants in this study, however, were all from the same occupational background, with similar socio-economic status, living conditions, health exposures and leisure activities. Therefore, comparisons between noise-exposed groups in this study could be made without fear of one group having substantial other hearing risks above a second group. Caution should, however, be taken when comparing these results to that of other groups that are not exposed to the same health co-morbidities and environmental factors.

Secondly, no data were available regarding previous work history or noise exposure. Together with this, there was also limited insight regarding the employee's adherence to noise-limiting strategies, such as their compliance to wearing hearing protection. It was therefore difficult to make assumptions pertaining to whether the noise-exposed group is no longer noise-exposed, partly noise-exposed or still noise-exposed. With legislation and noise exposure limits now enforced, it has become more difficult to access data of truly noise-exposed subjects.

Thirdly, the data was gathered between 2001 and 2008, and therefore does not take into consideration the advances in both legislation and modernization of hearing protection devices in recent years. If this study could be duplicated with data following 2008, it would give significant insight into the effectiveness of continues evolvement of hearing protection adherence and advances.

Lastly, the study was able to analyse only four serial audiograms, although data were available for nine years. As a limitation of a mixed effects regression analysis, serial audiograms were required without skipping years (for example 2001, 2002, 2003, 2004 or 2003, 2004, 2005 and 2006). To increase the internal validity of the study, two homogeneous noise exposure groups were selected for comparison. Within these homogeneous exposure groups, only 2,853 employees from a total of 6,610 employees fulfilled the requirement of four serial audiograms. Although this diminished the sample size, 11,412 audiograms were still available for analysis. The analyses would have been of a higher value if more than four serial audiograms could be analysed, but this would have decreased the sample size, which would have limited the statistical analysis and in return decreased the external validity of the study.

4.4 Future research

Three areas for potential research have been identified:

Firstly, it is known that hair cell damage is a key contributor to NIHL and ARHL and therefore most evidence gathered with regard to the interaction between NIHL and ARHL is based on audiometric thresholds as defined by the audiogram (Fernandez et al., 2015; Libberman, 2017). The same holds true for this study. Recent research, however, demonstrates that in both NIHL and ARHL, synaptic connections between the hair cells and cochlear neurons can be destroyed even before hair cell damage occurs (Liberman,2017). This should be taken into consideration in future research. The relative contributions of noise exposure and aging on hearing over time should be explored by comparing findings from audiometric threshold data with recent work where the effects of noise and aging on a synaptic (neural) level are explored.

Secondly, the effectiveness of noise management programmes and how these influence progression of NIHL and ARHL over time should be investigated. In the current study, there was a noise-exposed group with damage to their hearing prior to the commencement of the annual audiological testing represented in this data. From 2001, when the first data were gathered, legislative annual screening and noise management programmes were implemented. What is not known is to what extent mine employees adhere to noise management protocols. As evidence in this study suggests, hearing in the noise-exposed group continued to deteriorate at a faster pace than their non-noise-exposed counterparts. Further research, with data newer that that utilized in this study is therefore necessary to establish adherence to noise management programmes, and how non-adherence will influence future outcomes. A repeat study with newer data will give us insight into the effectiveness of modernization and development of hearing protection strategies over time.

Lastly, ARHL and NIHL in humans are both multifactorial, with contributions from and interactions between numerous intrinsic as well as extrinsic variables that can shape its final outcome (Kujawa & Liberman, 2006; Yamasoba et al., 2013). The effects of additional mediating factors such as gender, race, health co-morbidities and environmental exposures (e.g. non-occupational noise exposure and chemical exposure) should be explored to quantify them as additional contributors to the total decrease in hearing thresholds above that of noise exposure and age.

4.5 Conclusion

Both age and occupational noise exposure influence hearing thresholds over time. Noise exposure stays a definite contributor to hearing loss, even in a setting where occupational noise exposure levels are controlled. This continued increase in hearing thresholds of the noise-exposed group above that of the non-noise-exposed group was seen predominantly in the high frequencies, but also to a lesser extent in the low frequencies. The continued increase in hearing thresholds of the noise-exposed group above that of the non-noise-exposed group can possibly be related to ineffective noise management programme implementation. It could also support the fact that early noise exposure leads to a higher burden of hearing loss in later life, even after noise exposure has stopped.

While trying to explain the findings of this research on the level of the above statement, it should be remembered that a high probability exists that both of these scenarios can be interplaying in the final outcome together with other intrinsic (e.g. genetic predisposition) and extrinsic (e.g. non-occupational noise exposure) factors that can impact on an individual's total hearing loss over their lifetime. Ongoing effort is necessary to increase the effectiveness of noise management programmes to counter the unending negative effects of noise exposure on hearing thresholds, as well as the possible additive interaction between noise exposure and age-related hearing loss.

5. REFERENCES

Aarhus, L., Tambs, K., Nafstad, P., Bjorgan, E., & Engdahl, B. (2016). Childhood sensorineural hearing loss: Effects of combined exposure with aging or noise exposure in later life. European Archives of Oto-Rhino-Laryngology, 273(5), 1099-1105.

Agrawal, Y., Niparko, J. K., & Dobie, R. A. (2010). Estimating the effect of occupational noise exposure on hearing thresholds: The importance of adjusting for confounding variables. Ear & Hearing, 31(2), 234-237.

AngloGold Ashanti. Company. (2018). Overview. Retrieved from: http://www. anglogoldashanti.com/company/overview/

Basner, M., Babisch, W., Davis, A., Brink, M., Clark, C., Janssen, S., & Stansfeld, S. (2014). Auditory and non-auditory effects of noise on health. Lancet, 383(9925), 1325-1332.

Campo, P., Venet, T., Rumeau, C., Thomas, A., Rieger, B., Cour, C., Cosnier, F., & Parietti-Winkler, C. (2011). Impact of noise on styrene exposure on the kinetics of presbycusis. Hearing Research, 280(1-2), 122-132.

Checkoway, H., Pearce, N. E., & Kriebel, D. L. (2004). Research methods in occupational epidemiology. International Journal of Epidemiology, 33(5), 1155-1156.

COIDA. (2001). Compensation for Occupational Injuries and Diseases Act, No. 130 of 1993. Circular Instruction No. 171. South Africa Government Gazette, no. 22296, A61311, A10/4/3/4.

DeForge, B. R. (2010). Research design principles. In N. J. Salkind, (Ed.), Encyclopedia of research design, v. 3. Thousand Oaks, CA: Sage.

Dias, R. C., Cordeiro, R., Corente, J. E., & Gonçalves, C. G. O. (2006). Association between noise-induced hearing loss and tinnitus. Cadernos de Saúde Pública, 22(1), 63-68.

Dobie, R. A. (2008). The burdens of age-related and occupational noise-induced hearing loss in the United States. Ear & Hearing, 29(4), 565-577.

Edwards, A., Dekker, J., & Franz, A. M. (2011). Profiles of noise exposure levels in South African mining. Journal of the Southern African Institute of Mining and Metallurgy, 111(5), 315-322.

Engdahl, B., & Tambs, K. (2010). Occupation and the risk of hearing impairment-results from the Nord-Trøndelag study on hearing loss. Scandinavian Journal of Work, Environment & Health, 36(3), 250-257.

Eriksson, H. P., Andersson, E., Schiőler, L., Sőderberg, M. S., Rosengren, A., & Torén, K. (2018). Longitudinal study of occupational noise exposure and joint effects with job strain and risk for coronary heart disease and stroke in Swedish men. BMJ Open, 8(4), e019160. doi: 10.1136/bmjopen-2017-019160

Fernandez, A., Jeffers, W. C., Lall, K., Libberman, M. C., & Kujawa, S. G. (2015). Aging after noise exposure: Acceleration of cochlear synaptopathy in "recovered" ears. Journal of Neuroscience, 35(19), 7509-7520.

Field, A. (2009). Discovering statistics using SPSS. (3rd ed.). London: Sage Publications.

Gallo, R., & Gloring, A. (1964). Permanent threshold shift changes produced by noise exposure and aging. American Industrial Hygiene Association Journal, 25(3), 237-245.

Gates, G. A., Schmid, P., Kujawa, S. G., Nam, B., & D'Agostino, R. (2000). Longitudinal threshold changes in older men with audiometric notches. Hearing Research, 141(1-2), 220-228.

Hansia, M. R., & Dickinson, D. (2010). Hearing protection device usage at a South African gold mine. Occupational Medicine, 60(1), 72-74.

Hermanus, M. A. (2007). Occupational health and safety in mining-status, new developments, and concern. Journal of the Southern African Institute of Mining and Metallurgy, 107(8), 531-538.

Hong, O., Kerr, M. J., Poling, G. L., & Dhar, S. (2013). Understanding and preventing noise-induced hearing loss. Disease-a-Month, 59(4), 110-118.

Jonsson, R., & Rosenhall, U. (1998). Hearing in advanced age. A study of presbycusis in 85-, 88- and 90-year-old people. Audiology, 37(4), 207-218.

Kerns, E., Masterson, E. A., Themann, C. L., & Calvert, G. M. (2018). Cardiovascular conditions, hearing difficulty, and occupational noise exposure within US industries and occupation. American Journal of Industrial Medicine, 61(6), 477-491.

Kujawa, S. G., & Liberman, M. C. (2006). Acceleration of age-related hearing loss by early noise exposure: Evidence of a misspent youth. Journal of Neuroscience, 26(7), 2115-2123.

Leedy, P. D., & Omrod, J. E. (2001). Practical research: Planning and design. Englewood Cliffs, N.J.: Prentice Hall.

Liberman, M. C. (2017). Noise-induced and age-related hearing loss: New perspectives and potential therapies. Version 1. F1000 Research, 6, 927.

Lie, A., Skogstad, M., Johannessen, H. A., Tynes, T., Mehlum, I. S., Nordby, K., Engdahl, B., & Tambs, K. (2016). Occupational noise exposure and hearing: A systematic review. International Archives of Occupational and Environmental Health, 89(3), 351-372.

Masterson, E., Deddens, J., Themann, C. L., Bertke, S., & Calvert, G. M. (2015). Trends in worker hearing loss by industry sector, 1981-2010. American Journal of Industrial Medicine, 58(4), 392-401.

Meneses-Barriviera, C. L., Melo, J. J., & De Moraes Marchiori, L. L. (2013). Hearing loss in the elderly: History of occupational noise exposure. International Archives of Otorhinolaryngology, 17(2), 179-183.

Mineral Council of South-Africa. (2018). Mining in SA. Retreived from http://www.mineralscouncil.org.za/sa-mining.

Nelson, D. I., Nelson, R. Y., Concha-Barrientos, M., & Fingerhut, M. (2005). The global burden of occupational noise-induced hearing loss. American Journal of Industrial Medicine, 48(6), 446-458.

Neuman, W. L. (2012). Basics of social research: Qualitative and quantitative approaches (3rd ed.). Upper Saddle River, N.J., Pearson Education.

Phillips, J.I. (2007). Rock Drills used in South-African Mines: a Comparative Study of Noise and Vibration Levels. Annals of Occupational Hygiene, 54 (3), 305-310.

Plack, C.J., Léger, A., Prendergast, G., Kluk, K., Guest, H., & Munro, K.J. (2016). Toward a Diagnostic Test for Hidden Hearing Loss. Trends in Hearing, 20, 1-9.

Robson, C. (2011). Real world research (3rd ed.). Chichester, UK: Wiley.

Rosenhall, U. (2003). The influence of ageing on noise-induced hearing loss. Noise & Health, 5(20), 47-53.

Sliwinska-Kowalska, M., & Davis, A. (2012). Noise-induced hearing loss. Noise & Health, 14(61), 274-280.

South Africa. Department of Health. (2000). A policy on quality in health care for South Africa. Government Gazette. Pretoria: Government Printer. Retrieved from www.doh.gov.za/docs/policy/qhc.pdf

South Africa. Department of Health. (2007). National Health Act, 2003. Regulations relating to research on human subjects. Government gazette. Retrieved from: http://www.info.gov.za/view/DownloadFileAction?id=72155.

South African National Standards. 2013. SANS10083:2004. The measurement and assessment of occupational noise for hearing conservation purposes. Pretoria: South African National Standards.

Strauss, S. (2012). Noise-induced hearing loss: Prevalence, degree and impairment criteria in South African gold miners. Pretoria: University of Pretoria. (Thesis - PhD.)

Swanepoel, D. W., & Hall III, J. W. (2010). Football match spectator sound exposure effect on hearing: A pretest-post-test study. SAMJ, South African Medical Journal, 100(4), 239-242.

Strauss, S., Swanepoel, D. W., Becker, P., Eloff, Z., & Hall III, J. W. (2012). Prevalence and degree of noise-induced hearing loss in South African gold miners. Occupational Health Southern Africa, 18(6), 20-25.

Strauss, S., Swanepoel, D. W., Becker, P., Eloff, Z., & Hall III, J. W. (2014). Noise and age-related hearing loss: A study of 40 123 gold miners in South Africa. International Journal of Audiology, 53(Sup2), S66-S75.

Tak, S., & Calvert, G. M. (2008). Hearing difficulty attributable to employment by industry and occupation: An analysis of the National Health Interview Survey - United States, 1997-2003. Journal of Occupational and Environmental Medicine, 50(1), 46-56.

Teles, R. M., & Medeiros, M. P. H. (2007). Audiometric profile of Maracanau's industrial district workers. Revista da Sociedade Brasileira de Fonoaudiologia, 12(3), 233-239.

Thiese, M. S. (2014). Observational and interventional study design types; an overview. Biochemia Medica, 24(2),199-210.

Wang, D., Zhou, M., Li, W., Kng, W., Wang, Z., Guo, Y., Zhang, X., He, M., Guo, H. & Chen, W. (2018). Occupational noise exposure and hypertension: The Dongfeng-Tongji Cohort Study. Journal of the American Society of Hypertension, 12(2), 71-79.

Xiong, M., Yang, C., Lai, H., & Wang, J. (2013). Impulse noise exposure in early adulthood accelerates age-related hearing loss. European Archives of Oto-Rhino-Laryngology, 271(6), 1351-1354.

Yamasoba, T., Lin, F. R., Someya, S., Kashio, A., Sakamoto, T., & Kondo, K. (2013). Current concepts in age-related hearing loss. Epidemiology and mechanistic pathways. Hearing Research, 303, 30-38.

6. APPENDICES

Appendix A: Ethical clearance, Faculty of Humanities, University of Pretoria

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Humanities
Research Ethics Committee

09 September2014

Dear Prof Vinck

Project:	**A regression model for the prediction on noise-induced hearing loss over time, as a function of age, race and gender**
Researcher:	**L M Grobler**
Supervisor:	**Prof DeWet Swanepoel**
Department:	**Speech-Language Pathology and Audiology**
Reference number:	**26123445**

Thank you for your response to the Committee's letter of 3 September 2014.

I am pleased to inform you that the above application was **approved** by the **Research Ethics Committee** at an *ad hoc* meeting on 8 September 2014. Data collection may therefore commence.

Please note that this approval is based on the assumption that the research will be carried out along the lines laid out in the proposal. Should the actual research depart significantly from the proposed research, it will be necessary to apply for a new research approval and ethical clearance.

The Committee requests you to convey this approval to the researcher.

We wish you success with the project.

Sincerely

Prof Karen Harris
Acting Chair: Research Ethics Committee
Faculty of Humanities
UNIVERSITY OF PRETORIA
e-mail:karen.harris@up.ac.za

Appendix B: Collaborative research on hearing and hearing loss at AngloGold Ashanti

ANGLOGOLDASHANTI
AngloGold Ashanti Health Proprietary Limited

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18 February 2014

Professor De Wet Swanepoel
Senior Lecturer
Department of Communication Pathology
University of Pretoria
South Africa

Re: Collaborative research on hearing and hearing loss at AngloGold Ashanti

AngloGold Ashanti again welcomes the opportunity to engage in collaborative research with the University of Pretoria. In the first instance the two main areas of research was the prevalence and degree of hearing loss in South African gold miners, after which followed the effects of TB treatment on hearing loss. This proposed study will be an extension of the first study, and will aim to establish a model for the prediction of noise induced hearing loss over time, as a function of age, race and gender.

It is understood that the support offered is conditional upon:

1. Ethical approval, sought by the respective university.
2. The usual confidentiality that applies to medical research will be maintained by all involved in the projects.
3. Close liaison will be maintained with Dr Eloff – who is keen to be co-author of the paper.

We look forward to assisting you with this study.

Yours faithfully

Dr J.Z. Eloff
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AngloGold Ashanti Health
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C.c. Dr J Steele