UNIVERSITEIT VAN PRETORIA
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Faculty of Humanities

Audiovestibular Profile of HIV Positive Adults

By

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Submitted in the fulfilment of the requirements for the degree
MA AUDIOLOGY

In the Department of Speech-Language Pathology and Audiology
Faculty of Humanities
University of Pretoria

2018

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Acknowledgements

"My success is only by Allah" **Qur'an [11:88]**

First, and foremost, all praises and thanks are to my Creator, Sustainer, Nourisher, Cherisher and Provider, without Whom none of this would have been possible.

I would like to sincerely thank the following people who contributed towards the making and completion of this master's research project:

My parents, Nafisa Amod and Shabeer Mahomed, and my sister Zahra Mahomed, there are no words to thank you enough for all of your continued support, encouragement and love throughout this year. Thank you for always listening to me talk about my study more often than I should have and trying to understand all the technical terms I threw your way and expected you to be interested in. Thank you for always believing in me and never letting me give up as well as being my anchor and my sense of direction.

My supervisor and mentor, Dr Barbara Heinze, thank you so very much for your continued support, encouragement, guidance, analysing, reviewing and pep talks along the way. This research project would most definitely not have been possible without your guidance, expertise and enthusiasm. It helped to keep me motivated and dedicated. You have taught me a lot, and are an inspiration and an example that I am glad to have been given the chance to acquaint with.

Prof Anton Stoltz, my supervisor, thank you for your guidance and support. Thank you for always taking the time to help me in the best way possible. Thank you for all the arrangements that you helped to make, from acquiring the necessary signatures to securing patients and test rooms. Thank you for helping me recruit patients in the ID clinic as well as at the ARV clinic in Tshwane District Hospital. It was a privilege to be able to work under someone with your wealth of knowledge and expertise.

Prof Bart Vinck, my supervisor, thank you for your assistance in compiling this research project, especially in the reviewing of the statistics and data analysis. Your advice and expertise has been of the utmost help in the compilation of this research project.

My biostatistician, Dr Marien Graham, thank you for all of your assistance with the data analysis and running (and rerunning) of my statistics. Thank you for your patience and diligence.

My language editor, Aneesa Haffejee, thank you so much for all the effort and time that went into editing my dissertation. Your interest in my study was encouraging and helped to keep me motivated.

The staff at the ID clinic and the ARV clinic at TDH, thank so much for your support, helping me recruit patients and answering my countless questions. You definitely made data collection a much easier and bearable feat.

Thank you to all my friends, family, colleagues and acquaintances who volunteered to be participants as part of my control group in my study. Also, thank you to everybody who helped me acquire participants for my control group. Thank you to all the patients at the ID clinic and the ARV clinic who volunteered and allowed me to test them as part of my experimental group for my study. Your time, patience and interest in the study was appreciated. Without you, the current study would not have been possible.

A very big thank you to the rest of my family and friends who always supported and encouraged me. It means more to me than you will ever know.

Last, but not least, thank you to all my fellow “M” colleagues. This year would have been unbearable if not for the friendships that we have formed. Thank you for your support, shared experiences and true understanding throughout the year.

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Abstract

Despite HIV being a global challenge, sub-Saharan Africa continues to sustain the maximum share of the global burden of HIV. Auditory and otological manifestations is a common occurrence in individuals affected with HIV/AIDS as well as vestibular symptoms which have also been documented.

The main aim of the current study was to describe and compare the profile of auditory and vestibular function as well as health-related quality of life and risk for falls in adults with HIV. This was achieved by collecting results obtained from audio and vestibular testing as well as risk for falls assessments and responses from health-related quality of life (EQ-5D-5L) questionnaire.

The occurrence of hearing loss, as well as the mean threshold values obtained at all frequencies, were lower in the control group (23.3%) when compared to the HIV positive test group (41.7%) but with no statistical significance. A significantly larger occurrence of vestibular dysfunction was measured in the HIV positive test group (80%) when compared to the HIV negative test group (33.3%). There were three times more abnormal vHIT results in the HIV positive test group than the HIV negative test group as well as more absent oVEMPs in the HIV positive test group. Results obtained for fall risk assessments in all three test categories were within the norm and therefore not of clinical relevance as this indicated no impairment in balance in both test groups. It was observed that the HIV positive test group experienced more difficulty in all five health dimensions with statistically significant differences measured in four out of five health dimensions as well as in the VAS scores.

To conclude, there were significantly more HIV positive individuals identified with an auditory and vestibular dysfunction when compared to the HIV negative test group. Furthermore, results also indicated that participants with HIV presented with poorer HRQoL in comparison to the HIV negative test group. Lastly, even though, overall the functional balance assessments did not yield results indicative of a risk of falls in the HIV positive test group, the HIV positive test group did present with more participants that were at a risk for falls when compared to the HIV negative test group.

Keywords

HIV/AIDS

Audiovestibular

VEMP

vHIT

Health related quality of life

Risk for falls

List of abbreviations and Acronyms

3TC	Lamivudine
AAOSPFP	American Academy of Orthopaedic Surgeons Panel on Falls Prevention
ABC	Abacavir
AC	Air Conduction
AGS	American geriatric Society
AIDS	Acquired Immune Deficiency Syndrome
AR	Asymmetry Ratio
ART	Antiretroviral Therapy
ARV	Antiretroviral
AZT	Zidovudine
AZT/r	Atazanavir/ritonavir
BBS	Berg Balance Scale
BC	Bone Conduction
BGS	British Geriatrics Society
CD4+	Cluster of Differentiation 4+
cVEMP	Cervical Vestibular Evoked Myogenic Potential
CEO	Chief Executive Officer
DGI	Dynamic Gait Index
DHI	Dizziness Handicap Inventory
DPOAE	Distortion Product Otoacoustic Emission
DRV	Darunavir
EFV	Efavirenz
ENT	Ear, Nose and Throat Specialist
FDC	Fixed Dose Combination
FTC	Emtricitabine
HAART	Highly Active Antiretroviral Treatment
HL	Hearing Loss
HRQoL	Health Related Quality of Life
Hz	Hertz
HIV	Human Immunodeficiency Virus
ID	Infectious Disease
LARP	Left Anterior Right Posterior
LPV/r	Lopinavir/ritonavir
NNRTI	Non-nucleoside Reverse Transcriptase Inhibitor

NRTI	Nucleoside Reverse Transcriptase Inhibitor
NVP	Nevirapine
oVEMP	Ocular Vestibular Evoked Myogenic Potential
PLWHA	People Living with HIV/AIDS
PTA	Pure Tone Average
RALP	Right Anterior Left Posterior
SBAH	Steve Biko Academic Hospital
SCM	Sternocleidomastoid Muscle
SD	Standard Deviation
SNHL	Sensorineural Hearing Loss
SVV	Subjective Visual Vertical
TDF	Tenofovir
TDH	Tshwane District Hospital
TUG	Timed “Up & Go” Test
UNAIDS	The Joint United Nations Programme on HIV/AIDS
UNICEF	The United Nations Children’s Fund
VAS	Visual Analogue Scale
VCR	Vestibulocollic Reflex
VD	Vestibular Dysfunction
VEMP	Vestibular Evoked Myogenic Potential
vHIT	Video Head Impulse Test
VOR	Vestibular Ocular Reflex
WHO	World Health Organisation

CHAPTER 1: INTRODUCTION

1.1 Burdens of disease

The human immunodeficiency virus (HIV) and acquired immune deficiency syndrome (AIDS) is a global epidemic, and one of the leading contributors towards the development of significant health-related issues as well as the severely diminished quality of life (Swanepoel & Louw, 2010). According to the Joint United Nations Programme on HIV/AIDS, it was estimated that globally, there were 36.9 million 'People Living with HIV/AIDS' (PLWHA) in the year 2017, with 1.8 million new infections, of whom 940 000 died from AIDS-related illnesses in the very same year. Despite HIV being a global challenge, sub-Saharan Africa continues to sustain the maximum share of the global burden of HIV, responsible for 66% of all new infections in 2017**.** The area with the highest prevalence in the region would have to be South Africa, presenting with the highest incidence of new HIV infections (33%) and AIDS-related deaths (29%) (Joint United Nations Programme on HIV/AIDS [UNAIDS], 2018).

In South Africa, despite post-apartheid efforts to increase health spending in poverty-stricken areas, rural and African residents continue to endure the most substantial burden of illness (Chopra et al., 2009). Due to the poor socio-economic status of residents, the highest occurrence of HIV continues to present in informal urban areas. As a result, government departments have been urged to improve the circumstances of these areas by reducing poor housing conditions, poverty and unemployment which contribute towards an HIV-risk environment (Shisana et al., 2014). Furthermore, there is a lack of knowledge, regarding HIV/AIDS in Sub-Saharan Africa (UNAIDS, 2013a). Globally, discrimination and HIV/AIDS-related stigma has proven to be one of the main barriers to effective HIV prevention and provision of treatment thereof (UNAIDS, 2013b). However, despite the challenges faced, South Africa continues to monitor the epidemic and is continually assessing, strengthening and reviewing the efforts and response to HIV and AIDS (Shisana, Rehle, Simbayi, Zuma, Jooste, Zungu, Labadarios & Onoya, 2014).

1.2 The advancement of antiretroviral therapy (ART)

Globally, a massive expansion has occurred with regards to access to HIV treatment and has, in effect, not only transformed the HIV epidemic but also the health sector at large. This proves that despite circumstances being anything but ideal in regions most severely affected by HIV, e.g., South Africa, the right to adequate health care can be realized (World Health Organization[WHO], United Nations International Childrens Emergency Fund [UNICEF], & UNAIDS, 2013). In South Africa, ART usage has increased substantially and has thus lead to a decrease in AIDS-related deaths and therefore an increase in life expectancy (Johnson et al., 2013). As a result, this advancement in ART

has allowed for a shift in emphasis, currently focusing on quality of life (Ensink & Kuper, 2017). However, the primary objective of ART is the reduction of morbidity and the prevention of secondary manifestations, and even though the aforementioned has been achieved and has helped to increase these aspects of quality of life, other aspects such as hearing loss are being overlooked (Minhas, Iyengar, Thakur, J, & Azad, 2018).

In 2013 the first introduction of a fixed-dose combination (FDC) antiretroviral (ARV) medication was made (Davies, 2013). After that, South Africa had established and conducted the largest ART programme in the world, the benefits of which are evident in the reduction of AIDS-related deaths (Shisana et al., 2014). The ART guidelines followed in South Africa are specific to the issues present in Southern Africa, such as socioeconomic status and affordability, available treatment and diagnostic options, the gap in treatment between public and private healthcare and ensuring the best and most current practice for the circumstances present. For initial treatment, in accordance with international standards, it is recommended that a non-nucleoside reverse transcriptase inhibitor (NNRTI), either: Nevirapine (NVP) or Efavirenz (EFV) should be combined with two nucleoside reverse transcriptase inhibitors (NRTI), either: Lamivudine (3TC)/ Emtricitabine (FTC) plus Tenofovir (TDF), Zidovudine (AZT) or Abacavir (ABC), be used as the first-line ART regimen (Meintjes et al., 2012). This is because, the combination of an NNRTI and appropriate NRTI's are the most tolerable and effective long-term ART regime (Riddler et al., 2008). Only if presented with prolonged virological failure, will the clinician change a patient's ART regime to the second line ART. The second line ART consists of ritonavir-boosted Protease Inhibitors (PI): Atazanavir/ritonavir(ATZ/r), Lopinavir/ritonavir (LPV/r), Darunavir (DRV), and are recommended in combination with two NRTI's. However, it is much more difficult for patients to tolerate the drugs in the second-line ART, as it is more expensive and is usually more limited in options for further treatment due to the cost thereof. In the event of virological failure while on the drugs from the NNRTI, NRTI and PI classes, the patient is then put onto the third-line ART (Meintjes et al., 2012).

It is most definite that ART's aid in successfully controlling viral loads, however, it is likely to induce cellular stress responses, oxidative stress, inflammation and mitochondrial damage (Nooka & Ghorpade, 2017). Specifically, the NRTI component in ART’s may cause various toxicities (Canter et al., 2008), specifically otoxicity (when combined with other drugs) (Brits, Strauss, Eloff, Becker, & Swanepoel, 2012; WHO, 2013) and are the most probable cause of a sensorineural hearing loss (SNHL), either permanent or reversible (Harris & Heinze, 2013). According to a study conducted by Matas and colleagues (2014), the majority of the participants whom formed the test group exposed to ART's presented with hearing loss and 89% presented with hearing complaints. A study by Matas et al. (2014) showed that pure tone audiometry (PTA) results for participants exposed to ART's

presented with a higher proportion of hearing loss (48.1%) when compared to the group that was not on treatment (27.8%). It was concluded that the group exposed to ART was more susceptible to incidences of auditory alterations in comparison to the unexposed group and that these findings may have been due to the use of ART drugs which are ototoxic in nature and may result in a hearing loss (Matas et al., 2014).

1.3 HIV/AIDS and its effects on health-related quality of life

Various aspects are impacted upon when a person has been diagnosed with HIV, for example, deterioration of physical health, psychological and emotional distress as well as social isolation and the financial burden (Majumdar & Mazaleni, 2010). However, deterioration of physical health is the most crippling and life-altering adjustment experienced by an HIV infected individual. The virus may enter a host via various bodily fluids (i.e., blood, breast milk, semen, and vaginal fluid), after which it attacks and gradually damages the body's immune system as it enters cells responsible for controlling immunity against foreign pathogens (Evian, 2000). The virus belongs to a subgroup of retroviruses known as a lentivirus, which means that it takes a prolonged period, post-infection, to cause disease (Williamson & Martin, 2005). As a result, the body becomes increasingly susceptible to opportunistic infections, and due to the weakened state of the immune system, results in infections that would not typically occur in a healthy individual (Fan, Conner, & Villarreal, 2014). Deterioration in physical health due to illness results in affected individuals being unable to maintain the quality of their lifestyle before the diagnosis of infection and therefore results in a decline in their level of activity (Majumdar & Mazaleni, 2010).

1.4 HIV/AIDS and the effects on the auditory system

Diseases associated with regions of the head and neck are usually the first signs of an immune compromised body (Barzan, Tavio, Tirelli, & Comoretto, 1993; Lubbe, 2004; Marsot-Dupuch, Quillard, & Meyohas, 2004; Salzer, 1994; Somefun, Nwawolo, & Okeowo, 2001). Furthermore, according to Moayedi, (2010), these head-and neck-diseases may be due to the presence of opportunistic infections, as a result of the weakened immune system.

The HIV is neurotropic, influencing both the auditory and vestibular pathways (Mathews, Albert, & Job, 2012). Many studies have reported auditory and otological manifestations in association with HIV/AIDS (Assuiti et al., 2013; Heinze, Vinck, Hofmeyr, & Swanepoel, 2014; Khoza-Shangase, 2010; Swanepoel & Stearn, 2010; Teggi, Cesarani, Lira Luce, & Lazzarin, 2008; Van Der Westhuizen, Swanepoel, Heinze, & Hofmeyr, 2013). This is a common occurrence in individuals affected with HIV/AIDS and usually increases as the disease advances (Van Der Westhuizen et al., 2013), resulting in these individuals exhibiting symptoms of otalgia, tinnitus, vertigo, otorhea and hearing loss (Khoza & Ross, 2002; Swanepoel & Stearn, 2010; Teggi et al., 2008). Hearing loss can

be conductive, sensorineural or mixed in nature (Mathews et al., 2012); however, SNHL is more prevalent in the later more advanced stages of HIV (Van Der Westhuizen et al., 2013) and is usually irreversible (Ensink & Kuper, 2017). Hearing loss can result in poor communication, social isolation, withdrawal, depression, dementia, frustration, decreased functional status and maladaptive behaviour (Chew & Yeak, 2010; Dalton et al., 2003), all of which can contribute towards a diminished quality of life.

There are multiple factors associated with HIV/AIDS that may result in auditory dysfunction (Khoza-Shangase, 2010; Swanepoel & Stearn, 2010). The first is a high viral load as well as the direct impact of the virus on the cochleovestibular system and the central nervous system. Secondly, due to the use of ART, opportunistic infections (possibly bacterial and fungal in nature), associated with hearing loss and ototoxicity, may occur. Lastly, auditory dysfunction may also occur due to consumption of ototoxic medication used for the treatment of opportunistic infections, such as Tuberculosis (Assuiti et al., 2013; Khoza-Shangase, 2010; Moayedi, 2010; Swanepoel & Stearn, 2010).

HIV/AIDS may either directly or indirectly negatively effect the delicate structures of the ear, resulting in conductive, sensorineural or mixed hearing loss (Chan et al., 2008; Devaleenal, Ahilasamy, Solomon, & Kumarasamy, 2008; Matas et al.,2000; Palacios et al., 2008; Vincenti et al., 2005). A recent study by Ensink and Kuper (2017), found that one in three PLWHA present with a hearing impairment. Furthermore, they found that there was a statistically significant association between HIV and hearing loss in both adults and children, and that these findings corroborated with other studies conducted in high-income countries, proving that hearing loss is quite common in the HIV population (Chandrasekhar et al., 2000; Luque et al., 2014). Furthermore, the study was able to ascertain a positive association between a low CD4 count and hearing loss; however, the association between ART usage and hearing loss was unclear (Ensink & Kuper, 2017).

1.5 HIV/AIDS and the effects on the vestibular system

In addition to the auditory symptoms, vestibular symptoms have also been documented (Heinze et al., 2014; Heinze, Swanepoel, & Hofmeyr, 2011; Teggi et al., 2008). Taking into consideration the shared anatomy of the auditory and vestibular organs, i.e., the cochlear and vestibular organs, as Identifying the presence, severity, and nature of vestibular symptoms in PLWHA is of utmost importance to healthcare professionals, to ensure that the symptoms do not have any debilitating nor any adverse effects on the patient's quality of life (Holmes & Padgham, 2011).

A recent study indicated that HIV positive patients were 16.61 times more likely to develop a vestibular pathology than their HIV negative counterparts (Heinze et al., 2014). Furthermore, post-mortem studies have indicated that the virus results in deterioration of the vestibular anatomy and physiology (Pappas, Roland, Lim, Lai, & Hillman, 1995). Studies indicate an association between the HIV infection and a peripheral and central vestibular dysfunction together with related symptoms may occur, regardless of the progression of the disease (Cohen et al., 2012; Mathews, Albert, & Job, 2012; Heinze et al., 2014; Heinze, Swanepoel, & Hofmeyr, 2011; Teggi et al., 2008).

According to various studies, vestibular involvement in HIV infected individuals may result in episodes of dizziness and vertigo or a sense of spinning, disequilibrium and/or nausea and vomiting (Heinze et al., 2014; Heinze, Swanepoel, & Hofmeyr, 2011; Scherz, Kallail, Downs, & Scherz, 2013; Teggi et al, 2008). The origin of vestibular dysfunction associated with HIV/AIDS is multifaceted, encompassing direct effects as well as indirect effects of the virus via the presence of and medications taken for opportunistic infections (Heinze et al., 2014; Teggi et al., 2008). Furthermore, aminoglycosides and medications used in the ART regimes are vestibulocochleotoxic, and the simultaneous use thereof (commonly seen in South African HIV patients) may result in a sensorineural hearing loss, tinnitus and vestibular damage (Harris & Heinze, 2013). Overall, an individual with HIV may consequently experience diminished quality of life as they may present with persistent symptoms of vestibular dysfunction such as dizziness, vertigo and/or imbalance (Heinze, Vinck, & Swanepoel, 2011).

Vestibular symptoms may be overshadowed by more fatal illnesses and disorders occurring as a result of HIV/AIDS (Teggi et al., 2008). As a result, there is a dearth of published evidence detailing the impact of HIV/AIDS and ARV on the vestibular system, particularly in South Africa (Heinze, Vinck, & Swanepoel, 2011). Even though vestibular symptoms in HIV/AIDS have been confirmed, the presentation and nature of these manifestations throughout the progression of the disease are yet to be established (Heinze, Vinck, & Swanepoel, 2011).

1.6 HIV/AIDS and risk for falls

In addition to the auditory and vestibular manifestations in HIV infected individuals, these individuals exhibit a high occurrence of several comorbidities and physical impairments associated with an elevated fall risk (Effros et al., 2008). As many as 75% of HIV infected individuals are prescribed at least one other medication in addition to ART, where prescriptions associated with a high-fall risk (cardiovascular and psychoactive medications) are among the most common (Marzolini et al., 2010). Based on previous studies, it was established that HIV infected individuals present with low bone density, increased fracture risk, and premature frailty (Deeks, 2009; Desquilbet et al., 2007;

Effros et al., 2008; Mccomsey et al., 2018; Onen et al., 2009; Terzian et al., 2009), indicating an increased risk for susceptibility of falls and consequently an increased risk of morbidity when falls do occur (Erlandson et al., 2012).

Self-motion perception, otherwise known as the various aspects that help us to perceive and navigate our movements through space, are dependent on a combination of auditory cues and other sensory inputs, i.e., visual, vestibular and proprioceptive. The inputs mentioned above provide essential information that helps to optimize self-motion perception and effective, safe mobility. Previous research indicates that there is a correlation between hearing loss and increased difficulty in walking, poorer overall physical functioning and a significantly increased risk for falls in the elderly (Campos & Pichora-Fuller, 2018). Degeneration of the central nervous system, a consequence of the natural process of aging, is responsible for the impairment of the processing of vestibular, visual and proprioceptive information, all of which is needed to maintain balance and the ability to modify adaptive reflexes (Paiva et al., 2017). As a result of this degenerative process, dizziness and/or vertigo and imbalance may occur in the elderly as well (Ruwe, Rossi, & Simon, 2005). Unlike normal circumstances where aging would not usually cause significant problems, when faced with the additional strain of a disease, a pathological condition may ensue (Lima & Delgado, 2010). Additionally, ototoxicity causes significant and usually permanently irreversible damage to hearing and/or balance. Ototoxic medications usually lead to various auditory impairments and/or symptoms of bilateral vestibular hypofunction such as oscillopsia, and general postural instability accompanied by a higher risk of falls, especially if accompanied by compromised vision and proprioception (Al-Malky, 2016).

1.7 HIV/AIDS subtypes and global distribution

The global distribution and type of HIV/AIDS vary in different parts of the world (AVERT, 2017). This is due to the fact that every time HIV replicates, minute changes or mutations may occur in the newly infected cell (Smyth & Davenport, 2012), resulting in the formation of several variations/subtypes of HIV/AIDS, not only in different parts of the world but also within the host themselves (AVERT, 2017).

Looking at the different geographical regions, it was found that HIV subtype B is the predominant HIV subtype found in the Americas, western and central Europe and Australia, where majority of clinical research has been conducted, despite the fact that the aforementioned population accounts for only 12% of global HIV infections (AVERT, 2017; Buonaguro, Tornesello, & Buonaguro, 2007). HIV subtype C, which is found in high occurrences in countries of southern Africa, India & Asia, accounts for almost half of all people living with HIV (Abdool Karim, Churchyard, Abdool Karim, & Lawn, 2009; AVERT, 2017; Buonaguro et al., 2007). As mentioned previously, South Africa has

been categorized amongst those countries with the highest prevalence of HIV and TB (Abdool Karim et al., 2009). However, despite the statistics, very little research is available for HIV subtype C (AVERT, 2017). Clinical research as well as the data obtained in the West, i.e., regions such as America and the United Kingdom, far exceeds the research and data obtained from developing countries such as South Africa (AVERT, 2017).

1.8 Rationale

Most of what is known and been reported about HIV/AIDS and its effects on the auditory system has stemmed from international and developed countries with minimal information from developing countries in which the presentation and treatment of the virus may differ (Khoza-shangase, 2011). Even though the causes may be multifaceted, i.e. either a direct effect of the virus or indirect due to opportunistic infections and/or the treatment thereof with ototoxic medication or the use of ART drugs, various studies clearly depict associations between hearing loss and HIV (Ensink & Kuper, 2017; Matas et al., 2014; Van Der Westhuizen et al., 2013).

It has also been established that there is there is a relationship between HIV/AIDS and the vestibular symptoms; however, the nature and severity of these vestibular symptoms are unknown (Heinze, Vinck, & Swanepoel, 2011). Furthermore, there is a paucity of published information regarding the impact of HIV/AIDS and the use of ART medications on the auditory-vestibular system (Heinze, Vinck, & Swanepoel, 2011).

The current study therefore aimed to describe and compare the profile of auditory and vestibular function as well as health-related quality of life and risk for falls in adults with HIV.

CHAPTER 2: METHODOLOGY

2.1 Aim

The current research study aimed to describe and compare the profile of auditory and vestibular function as well as health-related quality of life and risk for falls in adults with HIV.

2.2 Research design and setting

This research study was conducted using a descriptive research design and data was collected in a cross-sectional manner and was quantitative in nature. According to Yin (2003), a descriptive study describes a phenomenon in a specific context. Furthermore, a descriptive study aims to systematically and accurately portray characteristics within a specified population or area of interest (Isaacs & Michael, 1995), as well as to report on the frequency and occurrence of the variables being researched (Polit & Beck, 2004). The current study was quantitative in nature, as measurable variables predicted the outcome (Leedy & Ormrod, 2005). All HIV positive participants who were tested were approached at a tertiary health care facility; the Infectious Diseases (ID) Clinic at Steve Biko Academic Hospital (SBAH) and the ARV clinic at Tshwane District Hospital (TDH). The HIV negative healthy age and gender-matched group (control group) consisted of friends, family, acquaintances, and colleagues of the researcher. Testing of the HIV negative participants took place at the Department of Speech-Language Pathology and Audiology, University of Pretoria. All testing, for both groups, was conducted in a quiet and controlled environment. The current research study was conducted in accordance with the Declaration of Helsinki: World Medical Association, (2013)(Appendix A).

2.3 Ethical considerations and informed consent

Before commencing with data collection, permission from the Deputy Chief Executive Officer (CEO) of SBAH, Dr. Mangwang (Appendix B), the Head of the ID Clinic at SBAH (Appendix C), as well as from the CEO of TDH was obtained (Appendix D). After that, clearance was obtained from the Research Ethics Committee of the Faculty of Health Sciences (Appendix E & F) followed by Research Ethics Committee of the faculty of Humanities (Appendix G), University of Pretoria. The current study fully complied with local research and ethical requirements.

2.3.1 Permission

Prof Anton Stoltz, Head of the ID Clinic at SBAH, gave written permission for the researcher to invite their patients to participate in the current research study (Appendix B). Permission was also obtained from the Deputy Chief Executive Officer of SBAH, Dr. Mangwang, to proceed with the current research study and to access the patient's files (Appendix C). Additionally, permission was also granted by Dr. Sasha Nkusi, the CEO of Tshwane District Hospital so that patients from the ARV clinic at TDH could be approached and their files accessed (Appendix D).

2.3.2 Voluntary and informed consent

Both the HIV positive group as well as the HIV negative group of participants were required to complete and sign a written informed consent form (Appendix H & I) before the research procedure was conducted. Participants were first informed regarding the aim of the current study and what was required of them before they agreed to participate. The tests and testing procedure that was followed as well as the duration of testing was also explained to them in detail. It was explained to participants that there are no risks associated with the current study, nor any direct benefits, however, the study would aid in research that would improve the overall healthcare treatment for people with HIV. It was also explained to participants that even though their test results would be used in the current research study and possibly published in a scientific journal, all of their identifying information was to be kept confidential. Furthermore, the identity of participants will only be known to the researcher and all identifying information will be stored and reported anonymously through the use of an alphanumeric code. Contact details for the researchers involved and information regarding ethical clearance acquired for the current study were also provided to the participants should they wish to inquire about the study. Furthermore, participants were assured that they had the right to withdraw at any stage of the research process without any consequences (Leedy & Ormrod, 2014) and that their participation was entirely voluntary.

Participants were then required to complete and sign the written informed consent to participate in the current study (Appendix H & I).

2.3.3 Risks and safety

There were no risks involved for participants. For the HIV positive group, participation did not hinder or interfere with their medication or their visit at both the clinics. After their appointment with the doctor, patients who volunteered to take part in the current study were tested by the researcher. Participants were however expected to complete a series of physical activities that belong under the fall risk tests battery (Appendix J: Dynamic Gait Index; Appendix K: The Berg Balance Scale and Appendix L: Timed ‘Up & Go’ Test). Rest time was given to the participants as needed, as well as continued physical support (tester offered assistance to participants if it was needed) during the testing.

2.3.4 Anticipated benefits

The participants of the current study did not benefit directly from the study; however, the results assisted researchers to determine the occurrence and nature of the hearing, vestibular and balance impairments, as well as risk for falls and overall quality of life that individuals with HIV/AIDS presented with. Participants that were diagnosed with any possible vestibular deficits during the testing were referred to the Department of Speech-Language Pathology and Audiology at the

University of Pretoria where further diagnostic testing could be done, and rehabilitation may be provided for the identified vestibular problem. Participants who were diagnosed with any possible auditory deficits were referred to, depending on their preference, the Audiologist at SBAH, TDH or the Department of Speech-Language Pathology and Audiology at the University of Pretoria for further diagnostic testing and management (Appendix M). Thereafter, participants who passed were then given a pass letter (Appendix N)

2.3.5 Confidentiality

Participants were guaranteed that all information will be kept confidential and that anonymity was assured (Leedy & Ormrod, 2014; Mouton & Babbie, 2007). Confidentiality was achieved by allocating each participant a unique and random code, e.g., B001, to their data collection and questionnaire sheets, once the informed consent form had been completed and signed. This code was then used to replace the name of the participant. Only the researcher was aware of the identity of participants, however anonymity and privacy of research participants were ensured, maintained and protected during the reporting and storage of results by using the alphanumeric codes assigned to each participant. Therefore, no personal information was identifiable or published at any stage of the research process.

2.3.6 Plagiarism

The current study was carried out following the University of Pretoria's guidelines on plagiarism. A declaration of originality has been signed and included.

2.3.7 Reliability and Validity

All participants were tested in similar environments with similar surrounding conditions using the same calibrated equipment. All participants were given the same instructions before testing, and if needed, instructions were supplemented with demonstrations. Furthermore, the same test battery was conducted on all participants. However, the order of the test battery sequence, where possible (i.e., for video head impulse test (vHIT), cervical vestibular evoked myogenic potentials (cVEMP), ocular vestibular evoked myogenic potentials (oVEMP) and functional balance assessments), as well as the ear on which testing begun was varied from participant to participant. This was done to ensure randomization and accuracy. Additionally, to compensate and correct for tester bias and/or error, a second professional's opinion was employed when marking waveforms for the cVEMP and oVEMP.

2.3.6 Data storage

According to the policy of the University of Pretoria, the data obtained from the research project will be archived at the Department of Speech-Language Pathology and Audiology, University of Pretoria

(Appendix O). The data will be archived in digital form and hard copy format for 15 years. Furthermore, this data will be kept for researchers to be used for future research.

2.4 Participants

2.4.1 Participant selection criteria

- All participants were required to be aged 18 years and older to provide consent independently and legally (Strode, Slack, & Essack, 2010). Furthermore, previous research indicated that participants aged 60 years and older achieved VEMP results with decreased amplitudes and response rates (Su, Huang, Young, & Cheng, 2004). Similarly, there is an increased occurrence of presbycusis in persons aged 55 years and older (Kovalova et al., 2016). An age category of 18-45 years was therefore utilized in the current study to ensure that the effects of HIV/AIDS were observed independently without any influence as a result of age.
- Research has indicated that it is unlikely for opportunistic infections to occur in HIV-infected individuals with a CD4+ cell count >200-250 cells/µL (Masur, Ognibene, Yarchoan, & Al., 1989). Therefore, all HIV positive participants were required to have a CD4+ cell count of >200 cells/µL to reduce the risk of opportunistic infections being present.
- The friends and family who were approached and invited to participate (control group- HIV negative), voluntarily underwent HIV screening at their local clinic such as, Dischem or Clicks. If the HIV screening test indicated a positive result, the clinic staff provided counselling. To successfully and accurately compare the results, age and gender-matched adult participants were utilized in the current study to determine the extent to which HIV/AIDS affects the audiovestibular functioning in the experimental group (HIV positive) participants.

Table one provides a rationale for the exclusion criteria of both the experimental group and the control group in the current research study, as many co-morbid factors may influence the current study's findings**.** Any participant who presented with or whose files documented history or presence of the following was not tested.

Table 1*: Exclusion criteria for both test groups*

EXCLUSION CRITERIA:	RATIONALE:
Participants with a history of chronic alcohol abuse.	According to a study conducted by (Popelka et al., 2000), alcohol consumption and/or smoking neither prevents nor causes initial hearing damage, instead, it may slow down or exacerbate the mechanisms involved in the decline of hearing function. Additionally, in another study it was observed that post consumption of a moderate quantity of alcohol, both the ocular motor system as well as the vestibular system were both affected (Tianwu et al., 2009). The impaired function of the vestibular system, post alcohol consumption, may also result in postural instability (Tianwu et al., 2009). For these reasons, participants with a history of alcohol abuse was excluded from the current study as the results obtained would not have been due to the effects of HIV exclusively.
Participants who have a history of occupational and recreational noise exposure.	One of the most common contributors towards the development of a hearing loss is noise (Rabinowitz, 2000), more specifically occupational noise(Nelson, Nelson, Concha-Barrientos, & Fingerhut, 2005) . Long term occupational or recreational noise exposure can cause hearing loss and is due to a combination of mechanical and metabolic factors (Ferrite & Santana, 2005). Sustained and extreme noise exposure results in damage to the cochlear hair cells and as a result metabolic changes due to hypoxia (reduced oxygen supply to organs and tissues in the body) which ultimately is caused by noise induced capillary vasoconstriction (Ferrite & Santana, 2005). Therefore, participants who had long term occupational or recreational noise exposure was excluded from the current study as this ensured that the effects of the HIV virus on the audiovestibular functioning was examined as independently as possible.
Participants who smoke.	An association between cigarette smoking and hearing loss in adults has been found in some clinical studies (Cruickshanks et al., 1998). According to a study conducted by Popelka et al. (2000), alcohol consumption and/or smoking neither prevents nor causes the initial hearing damage, instead, it may slow down or exacerbate the mechanisms involved in the decline of hearing function. Furthermore, according to Ferrite & Santana, (2005) tobacco affects the blood supply to the cochlear, i.e. a reduction of blood supply to the cochlea may be due to the impact of current smoking on the vascular system or the anti-oxidative mechanisms of the inner ear and consequently the impaired hearing function (Cruickshanks et al., 1998; Zelman, 1973). Furthermore, current smokers have shown a significant susceptibility for the risk of acquiring a hearing loss in comparison to that of non-smokers (Itoh et al., 2001). In the current study, the effects of HIV/AIDS on the audiovestibular function needed to be tested independently from any other damage that was subsequently caused due to smoking. Therefore, potential participants identified as 'smokers' were excluded from the current study.
Participants with a middle ear pathology.	An intact and fully functioning outer and middle ear is needed for reliable VEMP responses. Previous research has indicated that persons with an air-bone-gap larger than 10 dB HL presented with reduced or absent responses (Bath, Harris, Mcewan, & Yardley, 1999). Therefore, participants who presented with an air-bone gap on behavioural audiometric test results, and acoustic immittance measurements that indicated tympanometry results that fell outside of normal Type A tympanogram, were excluded from the current study. Middle ear pathologies and conductive hearing loss could result in absent recordings or significantly delayed wave latencies (Wang & Lee, 2007; Yang & Young, 2007). As a result, middle ear infections hinders the reliability of audiometric test results as well as the VEMP test results due to the presence of a conductive component.

Participants with a hearing loss >60 dB HL at 250 Hz-8000 Hz.	Previous studies have indicated reduced cVEMP amplitudes in participants with a SNHL (Akin et al., 2012; Hong et al., 2008). Additionally, present but reduced c- and oVEMP responses were found in participants with severe to profound SNHL (Bansal, Sahni, & Sinha, 2013) and only 39% of participants with a profound SNHL presented with oVEMP responses (Xu et al., 2016).
Participants with a history of ototoxic medication use.	Participants with a history of ototoxic medication use, e.g. gentamycin, were excluded from the current study; as ototoxic medication may have influenced auditory function negatively (Assuiti et al., 2013; Khoza-Shangase, 2010; Moayedi, 2010; Swanepoel & Stearn, 2010).
Participants who do not present with mobility and physical stability.	Any participant who was identified with a mobility disability, e.g. bound by a wheelchair or made use of assistive devices to walk independently, was excluded from the current study. Furthermore, participants who presented with poor ankle range of motion were also excluded. Such factors would have hindered the participants from partaking in the 'risk for falls' tests.
Participants who have previously experienced a traumatic brain injury (TBI)	A study by Scherer and Schubert (2009) found an 80% prevalence of vestibular dysfunction in participants with TBI. This was further confirmed by results obtained through caloric irrigation where seven out of 10 participants had a unilateral vestibular hypo-function and one out of the 10 participants had a bilateral vestibular hypo-function (Scherer & Schubert, 2009). Therefore, participants who presented with TBI were excluded from the current study to ensure that the effect of HIV on the fall risk assessments and health related quality of life was measured independently.
Participants with Diabetes and peripheral neuropathy.	A study by Kim et al. (2012) indicated that within their study 80% of their participants with diabetes presented with peripheral neuropathy. Patients who have severe neuropathy may present with ulcers under their feet, paresis, muscle weakness or heat dysfunction (Kim et al., 2012). Therefore, participants who presented with Diabetes or peripheral neuropathy were excluded from the study as participation in the fall risk assessments would not have been possible.
Participants with opportunistic infections.	There are various opportunistic infections that may affect the outer and middle ear and this could result in conductive or mixed hearing losses (Harris & Heinze, 2013). Some examples may include: middle ear effusions, acute otitis media, chronic suppurative otitis media, TB otitis media, malignant otitis externa and pneumocystis carinii otitis externa (Harris & Heinze, 2013). Furthermore, opportunistic infections may compromise the function of the sensory and neural components of the inner ear, thus causing SNHL (Harris & Heinze, 2013). Some examples may include: otitis media, cholesteotoma, otosyphillis, cytomegalovirus, herpes zoster virus and meningitis (Zuniga, 1999).

2.4.2 Study population

A power analysis (Appendix P), calculated using an online calculator (https://www.danielsoper.com/statcalc/calculator.aspx?id=47), indicated that a minimum of 26 participants was needed per test group, i.e. the experimental group and the control group, should be tested. The study group consisted of 60 participants in total: 30 participants in the HIV positive group and 30 participants in the HIV negative group. A percentage of 85% were female and 15% were male participants. Data collection took place between February and June 2018.

2.5 Data collection procedure

A detailed description of the test methods and procedure that was followed in the current study is schematically represented in Figure 1. Testing was conducted in single sessions lasting 60-90 minutes each.

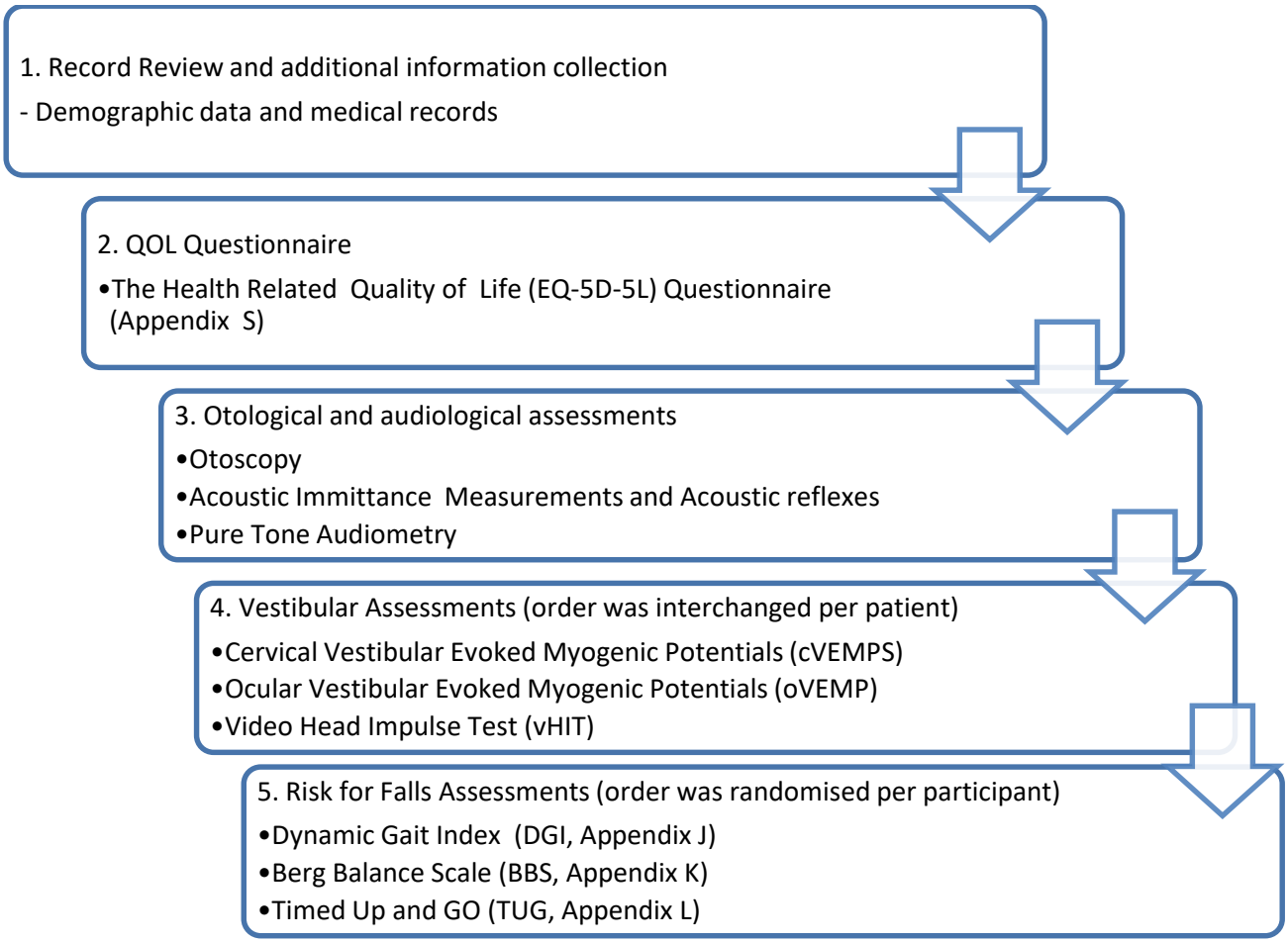

***Figure 1**:* Summarised data collection protocol according to test sequence

2.5.1 Record review and additional information collection

Record review for HIV positive participants

Once the HIV positive participants provided written consent to the researcher to participate in the current study as well as to access their files (Appendix H), the following information was extracted (Appendix Q) from their files at the clinic:

a) Date of Birth
b) Duration of ART since diagnosis
c) CD4+ cell count
d) Use of ototoxic medication
e) Any concomitant diseases
f) Any indication of alcohol abuses or smoking
g) History of occupational or recreational noise exposure

Demographic data for the HIV negative participants

Participants in the control group were age and gender-matched to the HIV positive participants. After volunteers agreed to participate by signing the written consent form (Appendix I), participants were asked to visit their local clinic or Dischem/Clicks to undergo an HIV screening test. Thereafter, if the results obtained were negative, participants were tested. Testing commenced with a structured interview and documented the following information (Appendix R):

a) Age
b) Gender
c) History of ototoxic medications
d) History of alcohol abuse or smoking
e) History of occupational or recreational noise exposure

2.5.2 Questionnaire for data collection

Before testing, data was collected via a self-administered questionnaire regarding the participant's health-related quality of life. The EQ-5D-5L Health questionnaire developed by the EuroQol Group, (1987) (Appendix S), is a standard and easy to use self-administered questionnaire that has been used as a patient-reported health-related outcome measure. It is a 2-page questionnaire that consists of an EQ-5D-5L descriptive system and also has an EQ Visual Analogue Scale (EQ-VAS). The descriptive system of the Questionnaire has five dimensions: i.e. mobility, self-care, usual activities, pain/discomfort, and anxiety/depression and has five levels of severity for each health dimension, i.e. no problems, slight problems, moderate problems, severe problems, and extreme problems (Herdman et al., 2011). Participants were asked to indicate their health state by ticking/placing a cross in the corresponding box next to the most appropriate statement in each of the five dimensions. This decision results in a 1-digit number expressing the level selected for that dimension.

The EQ VAS records the participant's self-rated health on a 20 cm vertical, visual analog scale with the two endpoints labelled: ‘the best health you can imagine" and "the worst health you can imagine" (Herdman et al., 2011). The VAS can be used as a quantitative measure of health as rated by the participants themselves (Herdman et al., 2011). Participants had to quantitatively measure their health state on the EQ Visual Analogue Scale (VAS) out of 100, based on how they felt on the day of testing. Their best health state imaginable was marked as 100 and zero indicated the worst health state imaginable.

2.5.3 Otologic and audiologic assessments

Otoscopy

Otoscopic examination of the outer ears and tympanic membranes was conducted using a Welch Allyn Pocketscope™ with reusable specula. Non-occluding ear canals were required for the audiologic and vestibular tests. All the participants' ear canals were clear of obstructions, and auditory-vestibular tests could continue. However, for those who were identified with occluding ear wax, the researcher referred them for ear cerumen management to the Department of Speech Therapy and Audiology in either SBAH or TDH.

Tympanometry and stapedial reflexes

Tympanometry was performed using a screener Y-226 Hz probe tone (GSI Tympstar, Grason-Stadler. Eden Prairie, MN, USA). Normal middle ear functioning was classified following Jerger, (1970) and was categorized as follows: ear canal volume (0.8 to 2.0 ml), static compliance (0.3 to 1.8 ml), and middle ear pressure (-100 to +50 daPa). Otoscopy and tympanometry were performed to rule out the presence of any conductive pathologies that could negatively affect vestibular testing (Jerger, 1970).

Additionally, screening stapedial reflexes were measured at 500, 1000, 2000 and 4000 Hz. Reflexes were regarded as present and normal if elicited and measured at 70-90 dB SPL. Participants who were identified with a middle ear pathology were excluded from the current study and the researcher referred them to the Department of E.N.T at SBAH, for further management with and Ear, Nose, and Throat specialist (ENT).

Pure tone audiometry

To determine and confirm the hearing status of participants, automated diagnostic pure tone audiometry was performed using a KUDUwave Type 2 Clinical Audiometer (IEC 60645-1/2) manufactured by eMOYOdotNET, Johannesburg, South Africa, and was operated via a notebook computer (Acer Aspire E1532, running Microsoft Windows 8), as validated by Swanepoel, Maclennan-Smith and Hall, (2013). The audiometer hardware was encased within each circumaural ear cup and was powered by the notebook computer. The transducers used were insert earphones (ER3A-Insert earphones, Etymotic Research, Elk Grove Village, IL, USA) covered by the circumaural cups after insertion into the external auditory canal. A response button was connected to the KUDUwave device to record the participant’s response to the acoustic stimuli presented (Mahomed-Asmail, Swanepoel, & Eikelboom, 2016). Ambient noise levels were also measured while testing through a microphone located on the circumaural ear cups.

Pure tone audiometry, a behavioural hearing test, was conducted to determine the presence, degree, and type of hearing loss. Pure tone hearing thresholds were obtained using air conduction

(AC) across the frequency range 250 Hz to 8000 Hz. Bone conduction (BC) was performed automatically, via the bone oscillator attached to the circumaural headband, if the participant's AC score was ≥20 dB HL and masking was automatically applied where necessary. A four-tone pure tone average was calculated for 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz. The type and degree of hearing loss were based on the participant's 4-tone pure tone average in accordance with the American Speech-Language-Hearing Association (Clark, 1981). The hearing was classified as either normal hearing: Pure tone average (PTA) of ≤15 dB HL, or as presenting with a hearing loss: PTA of ≥16 dB HL (Clark, 1981). Unilateral hearing losses were classified by normal hearing of the better ear (PTA of ≤15 dB HL) and by the hearing status of the poorer ear (PTA of ≥16 dB HL), and PTA of ≥16 dB HL classified bilateral hearing losses for both ears. (Clark, 1981). Furthermore, the degree of hearing loss was classified as follows: normal ≤15 dB HL, slight hearing loss 16 dB HL to 25 dB HL, mild hearing loss 26 dB HL to 40 dB HL, moderate hearing loss 41 dB HL to 55 dB HL, moderately severe 56 dB HL to 70 dB HL, severe 71 dB HL to 90 dB HL and profound ≥91 dB HL. Participants who presented with an air-bone gap of ≥10 dB HL or with severe-profound hearing losses, as indicated by pure tone thresholds of >60 dB HL, were excluded from further procedures.

2.5.4 Vestibular assessments

Vestibular Evoked Myogenic Potential (VEMP) testing was done to measure the integrity and function of the otolith organs as well as the vestibular nerve. Two different types of VEMPs can be distinguished, i.e., Cervical vestibular evoked myogenic potential (cVEMP) and ocular vestibular evoked myogenic potential (oVEMP). Air conduction (AC) cVEMPs are utilized specifically when assessing the function of the saccule and the inferior vestibular nerve and AC oVEMPs is used to assess the function of the utricle and the superior vestibular nerve (Bansal et al., 2013). Both the cVEMP and oVEMP are evoked by acoustic stimulation, and a response is measured in the presence of a myogenic response (Felipe & Kingma, 2013).

Cervical vestibular evoked myogenic potentials

Participants were seated on a standard chair for both cVEMP and oVEMPs (Isaradisaikul, Navacharoen, Hanprasertpong, & Kangsanarak, 2012). The VEMPs were performed using the Bio-logic Navigator® Pro, manufactured by Natus Medical, USA, and was connected to an Acer Laptop, programmed with software version 7.2.1. Stimuli comprised of air conduction 500 Hz toneburst presented at an intensity of 95 dBnHL using alternating polarity with at a rate of 5.1 Hz. Insert earphones (ER3AInsert earphones, Etymotic Research, Elk Grove Village, IL, USA) with disposable ear tips were used. Participants' skin was prepared with alcohol wipes and Nuprep® gel to ensure that the impedances were kept under 5kΩ. After that, reusable gold cup electrodes were positioned

onto the skin with Ten20® conductive paste. To ensure that the electrodes were kept securely in place on the skin, Micropore tape was used.

The VEMP asymmetry ratio (AR) was calculated as follows: [(AL - AS) / (AL+ AS)] x 100, where AL=the larger P1-N1 amplitude and AS= the smaller P1-N1 amplitude (Akin & Murnane, 2008). To ensure that VEMP responses were considered present and subsequently labelled, it was required for the responses to be repeated (immediately after obtaining the first response), to ensure wave reproducibility as well as to eliminate potential artefacts. The VEMP responses were interpreted in accordance with the following guidelines: (i) the presence of identifiable P1and N1 waveforms; (ii) Latencies above the upper limits of the waveform latencies were considered present yet delayed, and considered abnormal; and (iii) the presence of an amplitude asymmetry ratio (AR) of ≥40% was considered abnormal as it indicates amplitude differences between the ears (Akin & Murnane, 2008).

During cVEMP testing, ipsilateral electromyography recordings were performed. Testing required participants to obtain sufficient tonicity of the sternocleidomastoid (SCM) muscle with minimum discomfort to acquire accurate responses (Isaradisaikul et al., 2012). During testing, neck flexion of the SCM muscle was achieved by instructing the participant to turn their head contralateral to the side of stimulation, ensuring a cVEMP response with robust amplitudes and without early fatigability (Isaacson, Murphy, & Cohen, 2006; Isaradisaikul et al., 2012). Participants were also instructed to tilt their heads forward, when turned towards the contralateral side of stimulation, to achieve maximum flexion of the SCM. The active (inverting) electrode was placed on the ipsilateral mid-portion of the SCM muscle of the test ear, the reference (non-inverting) electrode was placed on the sternoclavicular junction, and the ground electrode was placed on the forehead (Isaradisaikul et al., 2012; Konukseven et al., 2015). For the cVEMP waveform, the first positive peak of the waveform was marked as P1, and the first negative deflection (trough) was marked as N1. Zapala & Brey, (2004) as well as Isaradisaikul et al. (2012) state that, a latency of ≤19 msec was considered normal for P1 and a latency of ≤28 msec was considered normal for N1. The peak-to-peak (inter-peak) amplitude was the sum of the amplitudes of these repeated responses. After obtaining the initial and repeated response, both response waves were averaged using the "weighted average" function. Lastly, using the raw, averaged and labelled waveform (P13 and N23), the prestimulus rectification algorithm was calculated on the selected waveform.

Ocular vestibular evoked myogenic potential

During oVEMP testing, participants were instructed to keep their head level while maintaining an upward gaze during the stimulation and recording, focusing their gaze on a stationary target on the

ceiling. Electromyography recordings from the extra-ocular muscles in the infraorbital region were recorded while the stimulus was presented in the contralateral test ear. The active (inverting) electrode was placed on the inferior oblique muscle, on the opposite eye from the test ear, the reference (non-inverting) electrode was placed on the side of the nose bridge, and the ground electrode was placed on the forehead (Leyssens et al., 2016). For the oVEMP waveform, the first negative deflection on the waveform was marked as N1, and the first positive peak was marked P1 (Leyssens et al., 2016; Sandhu, George, & Rea, 2013; Vanspauwen, Wuyts, Krijger, & Maes, 2017). Sandhu et al. (2013), Leyssens et al. (2016) and Vanspauwen et al. (2017) state that a latency of ≤11.1 msec was considered within the norm for N1 and a latency of ≤17.6 msec was considered normal for P1. The peak-to-peak amplitude was the sum of the amplitudes of these repeated responses.

Video Head Impulse Testing (vHIT)

Measuring the function of individual semicircular canals allows for the collection of invaluable information that is needed for diagnosing peripheral vestibular loss (McGarvie et al., 2015). The Video head impulse test is an objective measure that can be used to achieve this purpose and can assess the individual function of each of the six semicircular canals (Halmagyi et al., 2017; McGarvie et al., 2015). The vHIT makes use of a quick and simple procedure to quantify the functioning of the vestibular ocular reflex (VOR) (Curthoys, 2012). This objective measure displays the gain values achieved as well as the presence of covert and overt corrective saccades (Curthoys, 2012). The vHIT procedure was conducted with the Otometrics ICS Impulse® version 4.10 using the Video Frenzel goggles manufactured by Natus Medical, Denmark, connected to an Acer Laptop. Participants were seated on a standard fixed armchair with an eye-level target at a distance of 1.5 meters in front of them.

Furthermore, to obtain reliable results, calibration was performed for each participant before commencing with the testing. Values >27 Delta were re-calibrated as suggested by the manufacturing company Otometrics. Lastly, the goggles were secured tightly to the head to minimize goggles slippage.

During the head impulse test, the researcher stood behind the patient, while he/she was instructed to stare at the fixation dot placed on the wall in front of them. The tester began with lateral vHIT where quick, but small horizontal head impulses were performed in an unexpected manner (Guinand et al., 2017; Halmagyi et al., 2017) abrupt and unpredictable manner making sure to vary the direction of the turns. The researcher placed both thumbs on the sides of the participant's face, and both index fingers were placed on the lower jaw of the participant and the remaining three fingers

placed on the side of the participant's neck. After that, the vertical vHIT tests were performed in which the researcher delivered small, abrupt movements in the direction of the planes left anterior right posterior (LARP) and right anterior left posterior (RALP) as described by McGarvie et al. (2015) and Halmagyi et al. (2017). During the movements for LARP and RALP, the researcher placed one hand on top of the participant's head, and the other hand cupped the underneath of participants' chin. The researcher ensured that her hands were placed away from the goggles strap to avoid any interference during the head movements. When eliciting the vHIT, the goggles collect both head and eye data. Simultaneous displays of the data recorded for both head and eye movement allowed the clinician to determine if the response was within normal limits or not. Furthermore, the software system displayed the gain values obtained in each canal as well as if there were any catch-up saccades recorded. It was observed that in healthy subjects, the exact measures of eye movements in response to the passive head impulses show that after a very short latency of about 10 seconds, there is a smooth compensatory eye movement opposite in direction and equal in velocity to that of the head velocity (Cremer et al., 1998; Halmagyi et al., 1990).

The interpretation of test results was considered abnormal if: (i) the VOR gain value was <0.8 for the lateral canals and <0.7 for vertical canals, or (ii) either covert or overt catch-up saccades were present (Curthoys, 2012; McGarvie et al., 2015).

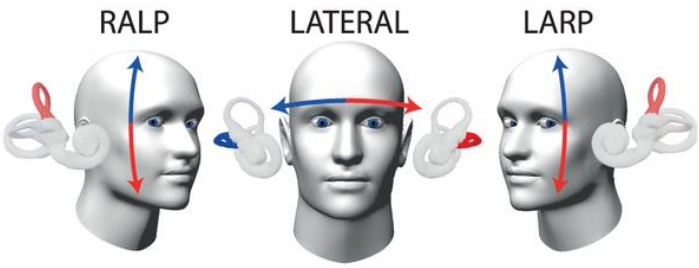

Figure 2: Procedure of performing the head impulses for RALP, lateral canal stimulation and LARP- as viewed from the fixation point (MacDougall, McGarvie, Halmagyi, Curthoys, & Weber, 2013).

A participant was classified as having a vestibular dysfunction if the vHIT results and/or VEMP results were found to be abnormal. The vHIT results were classified and described as abnormal if the gain was found to be abnormally low (< 0.7) and/or covert or overt saccades were present. The cVEMP and oVEMP results were classified and described as abnormal if results were obtained under the following conditions: (i) the presence of an identifiable P1 and N1 waveforms; (ii) Latencies above the upper limits of the waveform latencies were considered present yet delayed, and considered abnormal; and (iii) the presence of an amplitude AR of ≥40% was considered abnormal as it indicates amplitude differences between the ears (Akin & Murnane, 2008).

2.5.5 Risk for falls assessments

The Timed Up and Go (TUG)

The TUG test by Podisadlo and Richardson, (1991), is an easy, quick and well known used clinical performance-based measure of lower extremity function and mobility (Herman, Giladi, & Hausdorff, 2011); and due to its ease of application, quick administrative time and association for risk of falling and sensitivity thereof, it has been recommended by the American Geriatrica Society, British Geriatrics Society, & American Academy of Orthopedic Surgeons Panel on Falls Prevention [AAOSPFP], 2001 and Sletvold et al., 1996 that the TUG be used as a screening test for risk of falling (Herman et al., 2011).

Participants were instructed to stand up from a standard chair, with a seat height between 44 and 47 cm, after that walk a distance of 3 m at a comfortable pace, turn, walk back and sit down (Herman et al., 2011). Participants were allowed to use walking aids if they had one but were instructed not to use their arms when standing up (Herman et al., 2011). No physical assistance was given during the task (Herman et al., 2011). The duration of the task was measured when the command “go” was given and ceased when the subject’s back was positioned against the back of the chair after sitting down again (Herman et al., 2011). The duration of the task completion was measured using a stopwatch on the researcher's phone, and a cut-off point of 13.5 s was used as a threshold for identifying persons with an increased risk of falling (Shumway-cook, Brauer, & Woollacott, 2000; AGS et al., 2001). Participants who took longer than 13.5 s were identified as being at high risk for falling (Herman et al., 2011; Podisadlo & Richardson, 1991; Whitney, Marchetti, Schade, & Wrisley, 2004).

The Dynamic Gait Index (DGI)

The DGI has been developed to assess an individual’s ability to adapt their gait in response to various task demands and can be used to assess the gait of older adults (Shumway-Cook & Woollacott, 1995) as well as persons with a vestibular disorder (Whitney, Hudak, & Marchetti, 2000)., 2000). The DGI may be applied in various conditions, for example when examining the ability of older adults with dizziness or balance problems (Boulgarides, Mcginty, Willett, & Barnes, 2003; Chiu, Fritz, Light, & Velozo, 2006). Gait instability, as measured by the DGI, is a good predictor of risk for falls in both the elderly and young individuals with vestibular disorders (Whitney et al., 2004; Whitney et al., 2000).

The test is comprised of eight functional walking tasks and is varied in complexity. Participants were assessed in the following eight functional walking tasks: (i) gait on level surface, (ii) change in gait speed, (iii) gait with horizontal head turns, (iv) gait with vertical head turns, (v) gait and pivot turn,

(vi) step over obstacle, (vii) step around obstacles, and (viii) going up steps (Herdman, 2000; Shumway-Cook & Woollacott, 1995). The abovementioned functional tasks on the DGI were graded on a four-point scale from 'normal performance' (3) to 'severely impaired' (0) making a maximum score of 24 that could be obtained by participants (Herman, Inbar-Borovsky, Brozgol, Giladi, & Hausdorff, 2009). A Score of 19/24 or less may be indicative to an increased risk of falls in older adults (Shumway-Cook, Woollacott, Kerns, & Baldwin, 1997) as well as in people with vestibular dysfunction (Whitney et al., 2000)

The Berg Balance Scale (BBS)

The BBS (Berg, Wood-Dauphinee, Williams, & Gayton, 1989) is a well-established clinical measure that was designed to measure balance in elderly individuals (Whitney, Wrisley, & Furman, 2003). The BBS is a relatively inexpensive test of balance and does not require any specific equipment. Participant's balance was assessed by examining their performance in 14 functional tasks while being timed in a clinical setting. The participants were requested to complete the following 14 functional tasks: (i) sitting to standing, (ii) standing unsupported, (iii) sitting unsupported, (iv) standing to sitting, (v) transfers from one chair to another, (vi) standing with eyes closed, (vii) standing with feet together, (viii) reaching forward with an outstretched arm, (ix) retrieving an object from the floor, (x) turning to look behind, (xi) turning 360 degrees, (xii) placing alternate feet on a stool, (xiii) standing with one foot in front of the other, and (xiv) standing on one foot (Berg, Wood-Dauphine, Williams, & Gayton, 1989). The 14 functional tasks on the BBS varied in complexity and was scored on a 5-point scale from 0 to 4 (Andersson, Kamwendo, & Appelros, 2006), where 0 was indicative of the subject being unable to perform the task required, and four indicated that the subject was able to have fully met the most demanding criteria for the required task. Scores yielded were graded accordingly: 41 to 56 indicated a low risk of falling, 21 to 40 indicated a medium risk of falling and less than 20 indicated a high risk of falling (Berg, Wood-Dauphinee, et al., 1989).

2.6 Data analysis

All data was run and analysed by a biostatistician, Dr. Marien Graham. (Appendix T)

The current study utilized descriptive statistics, i.e., means, frequencies, percentages, and standard deviations as well as inferential statistics to determine whether there was a significant difference in the audiovestibular profile between the experimental group (HIV positive participants) and the control group (healthy age and gender-matched participants). As the data was not normally distributed, nonparametric tests were used. The Kolmogorov-Smirnov statistic test was used to test for normality. The Chi-Square test of independence was used to determine whether there was a significant relationship between two nominal (categorical) variables. If the expected count was less than 5, then the Fisher's Exact test was used. The Mann-Whitney U test was used to determine if

there were statistically significant differences between the two groups for all the continuous variables. A two proportion z-test allowed for comparison between two proportions (percentage: % and the number of ears: n) and to determine whether there was a statistically significant difference and the Fisher's Exact test was used for small samples. A level of significance of 5% was used, i.e., if the *p*-value is less than 0.05, there were statistically significant differences between the groups. Data was analysed in SPSS version 25.

CHAPTER 3: RESULTS

Results were obtained from audio and vestibular testing as well as risk for falls assessments and responses from health-related quality of life (EQ-5D-5L) questionnaire. The results were obtained from 30 HIV positive participants, i.e., the experimental group, and 30 HIV negative participants, i.e., the control group, who were age and gender matched.

3.1 Study Participants

Table 2 provides a summary of the demographic features presented by the 60 participants tested in the current study. There were no statistically significant differences in the mean age between the two test groups. Both groups had more female participants with 83.3% and 86.7% in the HIV positive and HIV negative groups respectively. For the antiretroviral therapy (ART) duration, a mean of 8.6 (SD=4.6) years, a minimum of 4 months and a maximum of 19 years were documented. All participants except one in the HIV positive group were on the 1st line fixed dose ART regime (Tenofovir (300mg), Emtricitabine (200mg) and Efavirenz (600mg)) and the remaining participant was on the second line fixed dose ART regime (Zidovudine (300mg), Lamivudine (150mg) and Lopinavir/Ritonavir (400mg/100mg)). With regard to the cluster of Differentiation 4+ ($CD4^+$) cell count, a mean value of 580.5 cells/µL (SD=321.7 cells/µL), a minimum of 235 cells/µL and a maximum of 1473 cells/µL were documented.

Table 2: *Demographic features of study participants*

		Mean (SD)	Mean (SD)	Mean (SD)	
		ALL(n=60)	HIV positive (n=30)	HIV negative (n=30)	p-value
		Mean (SD)	Mean (SD)	Mean (SD)	
Age (years)		36.8 (±6.8)	37.6 (±6.8)	36.6 (±6.8)	0.720
ART duration (years)		-	8.6 (±4.6)	NA	
$CD4^+$ cell count (cells/µL)		-	580.5 (±321.7)	NA	
		n (%)	n (%)	n (%)	
Gender (%)	**Female**	n=51 (85%)	n=25 (83.3%)	n=26 (86.7%)	0.799
	Male	n=9 (15%)	n=5 (16.7%)	n=4 (13.3%)	
ART Regime	**1st line fixed dose combination**	-	n=29 (96.7%)	NA	
	2nd line	-	n=1 (3.3%)	NA	

Note: ART= antiretroviral therapy, CD4+= cluster of differentiation 4+, cells/µL= cells per micro litre, n=number of participants, ± = Standard deviation (SD).

3.2 Audiological Assessments

Table 3 describes the Air Conduction (AC) pure tone audiometry, using mean and standard deviation (SD), across the test frequency spectrum 250 to 8000 Hz, per ear, and per test group. A 4-tone pure-tone average (PTA) was calculated for each participant at 0.5, 1, 2 and 4 kHz per ear and degree of the hearing was classified following guidelines by Clark, (1981).

Table 3: *Pure tone audiometry thresholds (dB HL) of study participants*

	Mean (SD) thresholds in dB HL for the left ears (n=60)			Mean (SD) thresholds in dB HL for the right ears (n=60)		
Frequency	HIV positive	HIV negative	*p*-value[a]	HIV positive	HIV negative	*p*-value[a]
250 Hz	22.5 (±14.3)	11.5 (±10)	0.002*	19 (±12.9)	10.5 (±7.4)	0.003*
500 Hz	22.2 (±11.7)	11.5 (±8.9)	0.000**	19.2 (±13.8)	12 (±8.6)	0.036*
1000 Hz	14.5 (±8.3)	9.7 (±9)	0.039*	16.3 (±12.1)	13.5 (±12.7)	0.257
2000 Hz	14 (±8.6)	12 (±9.3)	0.554	13.2 (±11.5)	10.2 (±8.3)	0.385
4000 Hz	9.7 (±10.2)	3.2 (±6.9)	0.001*	7.8 (±11.9)	7.8 (±8.1)	0.594
8000 Hz	8.8 (±11.4)	3.5 (±6)	0.008*	7.5 (±11.9)	2 (±4.1)	0.008*
4-Tone PTA	15.2 (±7.3)	9 (±7.3)	0.002*	14.2 (±11.2)	10.9 (±8.6)	0.177

Note: *= Significant difference at a 5% level of significance, [a=] The Mann-Whitney test was run for differences between two independent samples, ±= Standard deviation (SD), dB HL= decibel hearing level, Hz= Hertz, n= number of ears, PTA= pure tone average.

In reference to the 4-tone PTA, the Mann Whitney test was utilised and results obtained in the left ear indicated significantly higher (p=0.002) mean thresholds in the HIV positive group when compared to the HIV negative group. The HIV positive group had a mean value of 15.2 (SD=7.3) while the HIV negative group had a lower mean value of 9.0 (SD=7.3). Furthermore, the mean values at all frequencies were significantly higher in the HIV positive group in comparison to the HIV negative group, except at 2000 Hz.

In the right ear, with regard to the 4-tone PTA, the HIV positive group had a mean value of 14.2 (SD=11.2) in comparison to the HIV negative group with a lower mean value of 10.9 (SD=8.6). However, despite the difference between the aforementioned mean values, this was not of statistical significance. Similarly, when looking at the mean values at all frequencies, results obtained indicate higher mean thresholds in the HIV positive group in comparison to the HIV negative group. However, statistically significant differences between both test groups were measured only at 250 Hz, 500 Hz and 8000 Hz.

Furthermore, based on their calculated 4-Tone PTA, participants' hearing was also described in terms of normality and lateralization, i.e., bilateral normal hearing (PTA ≤ 15 dB HL in both ears), or unilateral hearing loss (poorer ear= PTA ≥16 dB HL) or bilateral hearing loss (both ears= PTA ≥16 dB HL). Regarding bilateral normal hearing, the HIV negative group presented with an occurrence of 66.7% (n=40), and the HIV positive group with 46.7% (n=28). However, even though there is a difference of 20% between both test groups, the difference is not statistically significant (p=0.110).

The classification and occurrence of the different types of hearing loss in the HIV positive group and the HIV negative group are illustrated below in Figures 3 and 4.

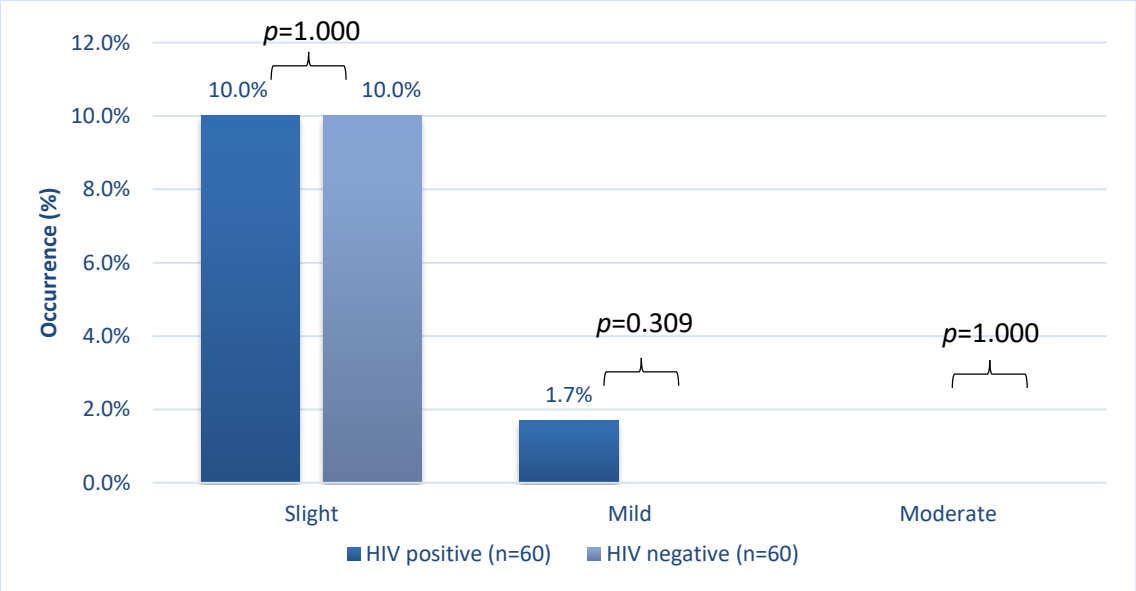

***Figure 3**:* Classification and presentation of unilateral hearing loss in both test groups

Slight unilateral hearing loss, for both the HIV positive and HIV negative test groups, had an equal occurrence of 10% (n=6) each. The mild unilateral hearing loss was prevalent in 1.7% (n=1) of the HIV positive group while the HIV negative test group had a 0% occurrence. Neither the HIV positive test group nor the HIV negative test group presented with moderate unilateral hearing loss. There were no statistically significant differences measured for all three types of unilateral hearing abilities.

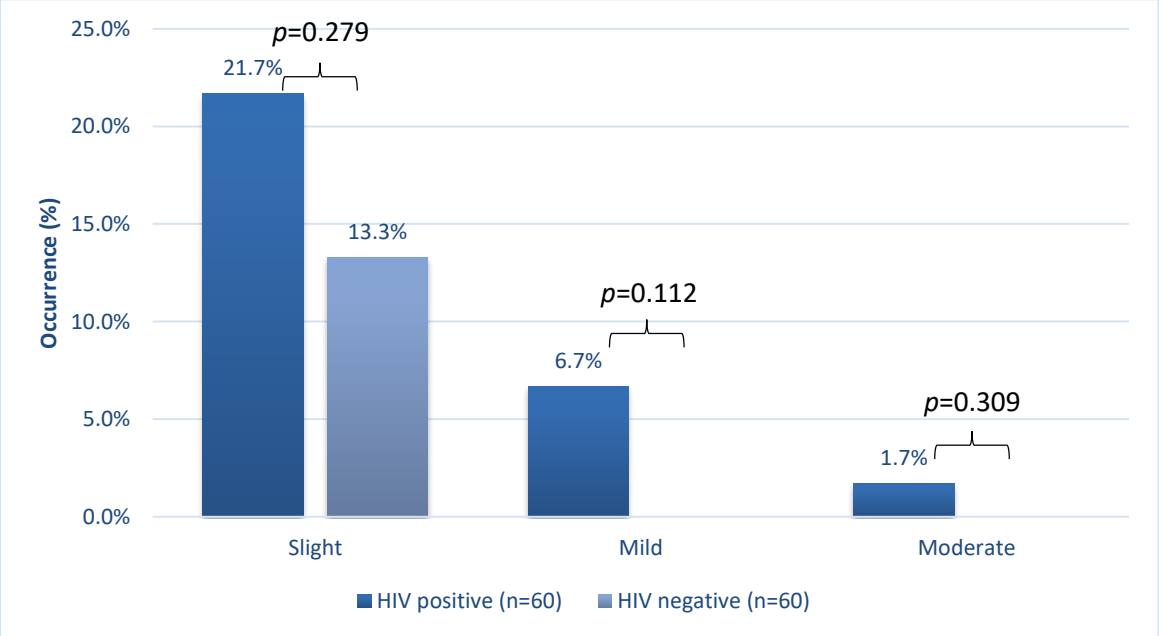

Figure 4: Classification and presentation of bilateral hearing loss in both test groups

Regarding slight bilateral hearing loss, the HIV positive test group presented with a prevalence of 21.7% (n=13) whilst the HIV negative test group presented with a lower prevalence of 13.3% (n=8). A mild bilateral hearing loss was prevalent in 6.7% (n=4) of the HIV positive test population in comparison to the HIV negative test group who had 0% occurrence. A moderate bilateral hearing loss was prevalent at 1.7% (n=1) in the HIV positive test group in comparison to the HIV negative

test group who had 0% occurrence. There were no statistically significant differences measured for all three types of bilateral hearing loss.

A total occurrence of 41.7% (n=25) and of 23.3% (n=14) hearing loss was found in the HIV positive and HIV negative test group respectively. It was found that predominantly, unilateral and bilateral slight hearing loss was the most prevalent type of hearing loss in both test groups.

3.3. Vestibular Assessments- Video Head Impulse Test (vHIT) and Cervical/Ocular vestibular evoked myogenic potential (c/oVEMP) testing

A vestibular dysfunction was classified if a participant presented with abnormal vHIT results and/ or abnormal VEMP results. Within the HIV positive test group, 80% (n=24), presented with abnormalities in vHIT and/or VEMP in comparison to a much lower 33.3% (n=10) of the HIV negative test group.

Video Head Impulse Test (vHIT)

Table 4 details the vHIT gain results for the HIV positive group vs. the HIV negative group in both the right and left ears respectively. Furthermore, both overt and/or covert saccades were also documented if present.

Table 4: *Description of vHIT results- Gain and saccades*

vHIT gain				**vHIT saccades**			
Right ears (n=60)				*Right ears (n=60)*			
Median (25, 75 percentile)				% (n)			
Canal	HIV positive	HIV negative	*p*-value[a]	Canal	HIV positive	HIV negative	*p*-value[b]
Lateral	1	1	0.651	Lateral	26.7%	0.00%	0.005*
	(0.90,1.07)	(0.97, 1.01)			(8)	(0)	
Anterior	0.85	0.97	0.146	Anterior	3.3%	0.00%	1.000
	(0.71, 1.04)	(0.78, 1.10)			(1)	(0)	
Posterior	0.87	0.90	0.264	Posterior	13.3%	13.3%	1.000
	(0.80, 1.02)	(0.88, 0.98)			(4)	(4)	
Left ears (n=60)				*Left ears (n=60)*			
Lateral	0.92	0.91	0.903	Lateral	16.7%	0.00%	0.052
	(0.86, 0.99)	(0.86, 1.00)			(5)	(0)	
Anterior	1.01	0.96	0.200	Anterior	10.0%	0.00%	0.237
	(0.88, 1.07)	(0.84, 1.02)			(3)	(0)	
Posterior	0.86	0.91	0.193	Posterior	10.0%	0.0%	0.237
	(0.78, 0.98)	(0.84, 1.00)			3	(0)	

Note: [a]= The Mann-Whitney test was run for differences between two independent samples, [b]= The Chi-square test is used to determine differences between dichotomous variables for independent samples, *=Significant difference at 5% level of significance, n= number of ears.

Regarding the gain, using the Mann-Whitney test, results indicated no statistically significant differences (all *p*- values >0.05) measured in both the HIV positive and HIV negative test groups. The median gain values obtained for both test groups, in both ears for all six vHIT testing conditions were within the normative data range used in the current study. However, a total of 33.3% (n=10)

HIV positive participants presented with abnormally low gain values in one or more of the six semicircular canals with three of these values found in the lateral canals, eight in the anterior canals and five in the posterior canals. Furthermore, in the HIV negative population, a total of 10% (n=3) of participants presented with abnormally low gain values in one or more of the six semicircular canals with one participant presenting one value in the anterior canal and the second and third participants having one value each in the anterior and lateral canals.

For saccades to be considered 'present', it needed to appear more than 50% of the time during the 10-15 HITs elicited per semicircular canal. If a saccade/s appeared it was documented as 'present' regardless of the number of saccades. All head impulses were carried out at a high velocity of >100 deg/sec. Therefore, any and all saccades would be indicative of a possible peripheral vestibular dysfunction.

With regard to catch up saccades, in the HIV positive test group, there was a total occurrence of 36.7% (n=11). This percentage constituted thirteen traces measured in both lateral canals, four traces measured in both the anterior canals and lastly, seven traces measured in both posterior canals. However, only 6.7% (n=2) presented with low gain values together with catch up saccades.

In contrast, within the HIV negative test group, a total of 13.3% (n=4) of participants presented with catch up saccades.

Table 5: *Catch up saccades in the HIV positive group and the HIV negative group*

	Lateral canals		**Anterior canals**		**Posterior canals**	
	Left	Right	Left	Right	Left	Right
HIV positive	Four traces of overt saccades + one trace of a covert saccade	Eight traces of overt saccades	One trace of an overt saccade + one trace of a covert saccade + one trace of a combined overt and covert saccade	One trace of a covert saccade	Two traces of overt saccades + one trace of a covert saccade	Two traces of overt saccades + two traces of covert saccades
HIV negative						Four traces of combined overt and covert saccades

Results obtained for both the gain and catch up saccades indicated that HIV positive participants were three times more likely to present with abnormally low gain values when compared to HIV negative participants. Therefore, HIV positive participants are three times more likely to be at risk of a possible peripheral vestibular pathology.

Vestibular evoked myogenic potential (VEMP)

Within the HIV positive test group, regarding the cVEMP test, 13.3% (n=4), and 16.7% (n=5) presented with absent responses in the left and right ear respectively. Furthermore, for the oVEMP test, 16.7% and 23.3% presented with absent responses in the left and right ear respectively. In contrast, for both cVEMP and oVEMP testing, the HIV negative test group presented with 0% absent responses bilaterally. The VEMP responses (present) are included in a detailed description of the findings below. Table 5 describes the cVEMP and oVEMP results, detailing the presence, latencies (ms) and the Inter-peak amplitudes (µV)

Table 6: *cVEMP and oVEMP presence, latencies and inter-peak amplitudes of study participants*

VEMP	**Left ears**			**Right ears**		
cVEMP	HIV positive	HIV negative	*p*-value [a/b]	HIV positive	HIV negative	*p*-value [a/b]
	% (n)			% (n)		
Present	86.7% (26)	100% (30)	0.112[b]	83.3% (25)	100% (30)	0.052[b]
	Mean (SD) thresholds			Mean (SD) thresholds		
P1 (ms)	15.60 (±2.75)	14.88 (±1.84)	0.245[a]	14.96 (±1.63)	15.18 (±1.33)	0.525[a]
N1 (ms)	24.58 (±3.33)	23.30 (±2.17)	0.246[a]	22.97 (±2.9)	23.49 (±1.48)	0.152[a]
I-P amplitude (µV)	23.75 (±17.98)	21.55 (±9.18)	0.810[a]	17.11 (±10.04)	32.64 (±13.77)	0.001*
Minimum and Maximum values for P1-N1 latencies						
	Left Ears			Right ears		
	HIV positive	HIV negative		HIV positive	HIV negative	
P1 Minimum (ms)	12.72	12.3		11.89	12.93	
P1 Maximum (ms)	26.67	18.13		21.05	17.72	
N1 Minimum (ms)	19.8	18.76		17.51	19.8	
N1 Maximum (ms)	36.25	27.71		29.59	26.05	
oVEMP	HIV positive	HIV negative	*p*-value [a/b]	HIV positive	HIV negative	*p*-value [a/b]
	% (n)			% (n)		
Present	83.3% (25)	100% (30)	0.052[b]	76.7% (23)	100% (30)	0.011[b]
	Mean (SD)			Mean (SD)		
N1 (ms)	9.64 (±0.51)	9.60 (±0.52)	0.464[a]	10.50 (±2.22)	9.88 (±0.88)	0.371[a]
P1 (ms)	14.10 (±0.96)	14.42 (±1.27)	0.374[a]	15.18 (±2.61)	14.46 (±1.17)	0.659[a]
I-P amplitude (µV)	17.14 (±10.64)	15.61 (±12.11)	0.432[a]	11.63 (±9.91)	14.99 (±7.17)	0.082[a]
	Minimum and Maximum values for N1-P1 latencies					
	Left ears			Right ears		
	HIV positive	HIV negative		HIV positive	HIV negative	
N1 Minimum (ms)	8.78	8.99		8.78	8.78	

N1 Maximum (ms)	10.86	10.86	19.6	13.57
P1 Minimum (ms)	12.94	12.32	12.94	12.73
P1 Maximum (ms)	15.65	16.9	25.23	16.48

Note: *= Significant difference at a 5% level of significance, [a]=The Mann-Whitney test was run for differences between two independent samples, [b] = The Chi-square test is used to determine differences between dichotomous variables for independent samples, I-P= inter-peak, µV= microvolt, ms= milliseconds, n= number of ears, ±= standard deviation (SD).

The Mann-Whitney test was used to calculate the *p*-values for the P1/N1 latencies and the Chi-Square test was used to calculate the *p*-values the 'present' category. Regarding the cVEMP test, within the HIV positive test group, there was one right unilateral and four bilateral absent responses recorded. Furthermore, for the oVEMP test, there were five bilateral and two right unilateral absent responses recorded.

For the cVEMP test, there were no statistically significant differences measured between the two test groups in the mean P1-N1 latency values measured in both the left and right ears (all *p*-values >0.05). Overall, both test groups presented with mean P1-N1 latency values that were within the clinical norm. However, in the results recorded for the left ears, even though of no statistically significant difference, the mean values for the P1-N1 latencies measured in the HIV positive test group were obtained slightly later than those of the HIV negative test group. In contrast, all P1-N1 latencies in the results recorded for the right ears indicated that the HIV positive test group obtained latencies earlier in comparison to the HIV negative test group.

Furthermore, regarding the cVEMP, there was no statistically significant difference found in the mean inter-peak amplitude value between both test groups in the left ear. However, in the right ear, the HIV positive group presented with a smaller mean value than the HIV negative group and a highly statistically significant difference (*p*= 0.001) was measured between both test groups.

Despite the lack of statistically significant differences and apart from the absent cVEMP's, there were 16.7% (n=5) of HIV positive participants who presented with delayed P1-N1 latencies. Three participants presented with delayed N1 latencies, with two of the three delayed latencies obtained in the left ear and one in the right ear. The fourth participant had a delayed P1 latency in the right ear and bilaterally delayed N1 latencies. The fifth participant had delayed P1-N1 latencies in the left ear.

In the HIV negative population, there were 10% (n=3) of participants presenting with delayed N1 latencies in the left ear.

For the oVEMP results, there were no statistically significant differences measured in both the left and right ears for the N1-P1 latencies (all *p*-values >0.05). Overall, both test groups presented with mean N1-P1 latency values that were within the clinical norm. However, even though there were no statistically significant differences, bilaterally, the mean values for the N1 latencies and the mean

P1 value in the right ears measured in the HIV positive test group were obtained slightly later than those of the HIV negative test group. In contrast, the mean P1 latency value in the left ear indicated that the HIV positive test group obtained a mean latency value that was earlier in comparison to the HIV negative test group.

Furthermore, there were no statistically significant differences found in the mean inter-peak amplitude values between both test groups in both ears.

Despite the lack of statistically significant differences and apart from the absent oVEMP's, there were 3.3% (n=1) of HIV positive participants who presented with delayed N1-P1 latencies. One participant presented with delayed N1-P1 latencies in the left ear.

3.4 Occurrence of hearing loss (HL) and vestibular dysfunction (VD)

Figure 5 displays the occurrence of hearing loss and vestibular dysfunction in the HIV positive test group versus HIV negative test group.

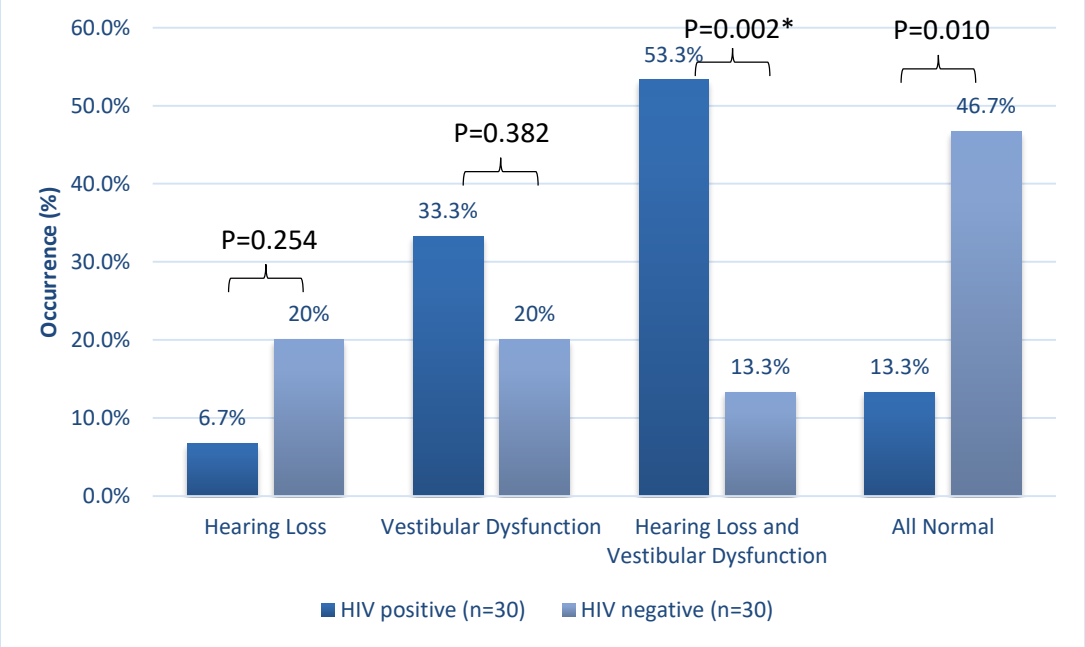

Figure 5: Occurrence of hearing loss and vestibular dysfunction in both test groups

A two proportion z-test allowed for comparison between two proportions (percentage: % and the number of ears: n) and to determine whether there was a statistically significant difference and the Fisher's Exact test was used for small samples. Despite the occurrence of hearing loss being higher in the HIV negative test group when compared to the HIV positive test group, no statistically significant difference was found (p=0.254). Likewise, even though the occurrence of vestibular dysfunction is higher in the HIV positive test group when compared to the HIV negative test group, there was no statistically significant difference measured (p=0.382). In contrast, concerning 'Hearing Loss and Vestibular Dysfunction,' a statistically significant difference was measured (p=0.002) with a higher occurrence recorded in the HIV positive group. This therefore indicates that an HIV positive

person is more likely to have both a hearing loss and a vestibular dysfunction when compared to a HIV negative participant. Lastly, in the 'All Normal' category, even though the HIV negative group presented with a much higher occurrence in comparison to the HIV positive group, there was no statistically significant difference measured (p=0.010).

3.4 Fall risk assessment results

Table 6 lists and describes three fall risk assessments, i.e., the Dynamic gait index (DGI), Berg Balance Scale (BBS) and The Timed Up and Go (TUG) was used to assess the functional balance and risk for falls in both the HIV positive and HIV negative test groups.

Table 7: *Risk for falls assessments*

	HIV positive (n=30)	**HIV negative (n=30)**	
	Mean (SD)	Mean (SD)	*p*-value
DGI	23.4 (±1.4)	23.8 (±0.6)	0.044*
BBS	54.9 (±2.0)	55.8 (±0.4)	0.028*
TUG	10.0 sec(±1.9sec)	8.3sec (±1.6sec)	0.001*

Note: The Mann-Whitney test was used, ±= standard deviation (SD), n= number of participants, DGI=Dynamic Gait Index, BBS=Berg Balance Scale, TUG= Timed Up and Go.

Using the Mann-Whitney test, results obtained indicated statistically significant differences (all p-values <0.05) in all three functional assessments between both test groups. However, even though statistically significant differences were measured, all three test categories yielded results within the norm and is therefore not indicative of any clinical relevance.

The HIV positive group yielded results that were better than the HIV negative group in each functional balance assessment. For the DGI, results indicated that two HIV positive participants presented with an increased risk of falling whilst none of the HIV negative participants presented with a risk of falling. For the BBS ten HIV positive participants presented with a low risk for falls whilst there was no HIV negative participant who presented with a risk for falls. During the TUG there was only one HIV positive participant identified with an increased risk for falls whilst there were no HIV negative participants with a risk for falls.

3.5 Health-Related Quality of Life (EQ-5D-5L) Questionnaire

Table 7 describes and rates the health-related quality of life for both test groups according to the EQ-5D-5L.

Table 8: *Health Related Quality of Life (EQ-5D-5L) Questionnaire*

		HIV positive (n=30)		HIV negative (n=30)		*p*-value[a]
Health Dimensions	Levels	Number	Percentage	Number	Percentage	
Mobility	L1	26	86.7%	30	100.0%	0.006*
	L2	2	6.7%			
	L3	1	3.3%			
	L4	1	3.3%			
	L5					
Self-care	L1	24	80.0%	30	100.0%	0.001*
	L2	5	16.7%			
	L3					
	L4	1	3.3%			
	L5					
Usual activities	L1	24	80.0%	27	90.0%	0.127
	L2	5	16.7%	3	10.0%	
	L3	1	3.3%			
	L4					
	L5					
Pain/discomfort	L1	23	76.7%	30	100.0%	0.000*
	L2	3	10.0%			
	L3	4	13.3%			
	L4					
	L5					
Anxiety/depression	L1	20	66.7%	25	83.3%	0.021*
	L2	7	23.3%	5	16.7%	
	L3	2	6.7%			
	L4					
	L5	1	3.3%			
	Mean (SD)			Mean (SD)		
VAS		88.5% (±11.9%)		92.3% (±12.3%)		0.015*

Note: ±= standard deviation (SD), [a] The Mann-Whitney test was run for differences between two independent samples, * Significant difference at a 5% level of significance, VAS= Visual Analogue Scale.

Using the Mann-Whitney test, a statistically significant difference between the test groups in four health dimensions, i.e., mobility (p=0.006), self-care (p=0.001), pain/discomfort (p=0.000), anxiety and depression (p=0.021) were measured. However, it was observed that the HIV positive test group experienced more difficulty in all five health dimensions than the HIV negative group. The HIV positive group provided more responses fitting in L2, L3, L4 and L5 in comparison to the HIV negative group who provided most of their responses fitting in L1. Concerning the four previously mentioned health dimensions, it would appear that the HIV negative group presents with a better health-related quality of life than the HIV positive group. However, no statistically significant differences were measured between the test groups for the health dimension: usual activities, indicating that both groups felt equal about their ability therein. Additionally, there was a statistically significant difference measured in the Visual Analogue Scale (VAS) (p=0.015) with a higher mean

value measured in the HIV negative group. This indicates that the HIV positive group (mean=88.5, SD=11.9), indicated a poorer health-related quality of life in comparison to the HIV negative group (mean=92.3 SD=12.3).

4. CHAPTER 4: DISCUSSION

4.1 Discussion

The main aim of the current study was to describe the profile of auditory and vestibular function in participants with HIV versus HIV negative participants. Furthermore, functional balance, as well as their health-related quality of life (HRQoL), was also described and compared. Despite the lack of statistically significant differences between the HIV positive and HIV negative groups, results from the current study indicated that there were significantly more HIV positive participants who presented with auditory and vestibular dysfunction in comparison to the HIV negative participants. Furthermore, when looking at HRQoL and risk for falls, there were significant differences measured between the HIV positive group when compared to the HIV negative group, which could be of clinical relevance.

4.1.1 Hearing Loss and HIV/AIDS

A systematic literature review reported findings from previous studies that have emphasized a need to monitor HIV-related hearing loss as well as to incorporate the screening thereof into HIV/AIDS-related routine medical care (Assuiti et al., 2013; Van Der Westhuizen et al., 2013). With the advancement in ART medications and the resultant shift in emphasis, now being on quality of life, it is now possible to address this urgent need (Ensink & Kuper, 2017). The HIV is a global epidemic that affects millions of people and in combination with hearing loss, an invisible pandemic, it is proving to be one of the most significant challenges faced today (Swanepoel & Louw, 2010; Wilson, Tucci, Merson, & O'Donoghue, 2017).

Previously, statistics indicated that one in three people living with HIV/AIDS presented with a hearing impairment as well as a statistically significant association between HIV and hearing loss (Ensink & Kuper, 2017). This was further recognized by a cross-correlation established between different studies, comparing HIV positive to HIV negative individuals, which indicated hearing loss as a common occurrence in PLWHA, regardless of socioeconomic status (Chandrasekhar et al., 2000; Luque et al., 2014). In this current study, the criteria used for classification of hearing loss followed that of Clark (1981). Therefore, if any four tone pure tone average (PTA) value was ≥16 dB HL, then a hearing loss was identified. The occurrence of hearing loss (23% versus 41.7%) as well as the mean threshold values (HIV negative= 9 (±7.3) and 10.9 (±8.6) versus HIV positive=15.2 (±7.3) and 14.2 (±11.2)), were lower in the control group when compared to the HIV positive test group respectively but with no statistical significance. Agreeing with a previous study (Matas, Filha, Juan, Pinto, & Gonçalves, 2010), the current study showed that despite the increased occurrence of hearing loss in the HIV positive test group, normal hearing was obtained for the majority (46.7%) of the HIV positive test group within the current study.

Despite the above, agreeing with another similar cross-sectional study that investigated hearing loss in HIV positive adults, where the criteria used for hearing loss was twofold, i.e. ≥16 dB HL PTA and >25 dB HL, and the occurrence of hearing loss was indicated as 39% and 14% respectively (Van Der Westhuizen et al., 2013). Other studies that utilized a >20dB PTA as the criteria for hearing loss indicated an occurrence of 27% (Fokouo et al., 2015) and 40% (Matas et al., 2014) in their sample of HIV positive participants. Furthermore, another study that utilized >25dB PTA as the criteria for hearing loss presented with a 10% occurrence of hearing loss in their HIV test population (Khoza-Shangase, 2011). The strict criteria used for classifying hearing loss in the current study could be the reason for the decreased occurrence of hearing loss observed (Khoza-Shangase, 2011). Even though there are conflicting views (Assuiti et al., 2013; Makau, Ongulo, & Oburra, 2010; Minhas et al., 2018), another possible reason for a lower occurrence of hearing loss in the study by Khoza-Shangase, (2011), in which participants were not on ART, is the absence of the ototoxic nature associated with ART usage by participants utilised as indicated by Matas et al. (2014). As a result, the occurrence of hearing loss was higher in other studies when compared to that of Khoza-Shangase, (2011). In the current study, all participants were required to have a CD4+ cell count above 200 cells/µL so as to eliminate the possibility of a compromised immune system that is associated with a low CD4+ cell count. Therefore, the lowest CD4+ count was 235 cells/µL and the maximum was 1473 cells/µL. For majority of participants, the duration of ART usage and the duration of disease was one and the same. Findings from the current study indicated that participants with an ART usage of and/or duration of disease >10 years presented with fewer auditory and vestibular dysfunction in comparison to participants with an ART usage/disease duration of <10 years. This could indicate a possible suppression of the virus. Lastly, 29 out of 30 HIV positive participants tested were on the 1st line fixed dose ART regime whilst only one participant was on the 2nd line ART regime. This allowed for a homogenous test group in which results could be favourably fairly.

Additionally, there were also studies that did not make mention of their criteria used for the classification of hearing loss and reported much higher occurrences of hearing loss 68% (Sulyman et al., 2012) and 53% (Mathews et al., 2012). The current study is in agreement with Van Der Westhuizen et al. (2013) and Ongulo & Oburra (2010) regarding the difficulty in drawing a direct comparison with other studies. This is because, not all studies used the same classifications to determine hearing loss nor were the sample sizes equal in number in each study. However, irrespective of the criteria used for the classification of hearing loss and/or the sample size, the current study is in agreement with the abovementioned studies concerning the higher occurrence of hearing loss in the HIV positive group when compared to the HIV negative control group.

The occurrence and type of hearing loss observed in the current study may have been higher and varied if not for the deliberate exclusion of participants presenting with a conductive component. This was done to ensure accurate and reliable vestibular evoked myogenic potential (VEMP) recordings. As a result, the only type of hearing loss examined in this current study was sensorineural in nature. From amongst those that presented with a hearing loss (41.7%) in the current study, 28% presented with a unilateral hearing loss and the remaining 72% presented with a bilateral hearing loss. In the study by Van Der Westhuizen et al. (2013) where participants had a hearing loss with a PTA greater than 15 dB HL (39%), 17% were unilateral whilst 22% were bilateral in nature; and the participants that had a hearing loss >25 dB HL PTA (14%) presented with an occurrence of 8% and 6% unilateral and bilateral hearing loss respectively. Within their respective HIV positive test group that presented with a hearing loss, Fokouo et al. (2015) reported bilateral hearing loss to be 43%, Khoza-Shangase (2011) reported an occurrence of 47% and 53% of unilateral and bilateral hearing loss respectively and Mathews et al. (2012) reported a 31.3%% unilateral and 68.8% bilateral hearing loss occurrence. The studies mentioned above are in agreement with the current study where reports indicate that bilateral hearing loss accounts for the majority of the hearing loss occurrence in each of their respective HIV positive test groups that present with a hearing loss.

Previous studies, even though inclusive of all types of hearing loss, indicated sensorineural hearing loss (SNHL) to be the most prevalent type of hearing loss in the HIV positive adult test populations (Ensink & Kuper, 2017; Fokouo et al., 2015; Khoza and Ross, 2002; Makau et al., 2010; Van Der Westhuizen et al., 2013). In accordance with the present study, a study by Van Der Westhuizen et al. (2013), who utilized the same criteria for hearing loss, >15 dB HL PTA, reported a 64% occurrence of SNHL. Furthermore, other studies that utilized different criteria for the classification of hearing loss, i.e.,>20dB PTA, reported that 62% (Fokouo et al., 2015) and 61% (Matas et al., 2014) within their test populations with a hearing loss, presented with a SNHL. Lastly, a study that utilized a hearing loss classification of >25dB PTA reported a 60% (Khoza & Ross, 2002) occurrence of SNHL in their test population presenting with a hearing loss.

The mean threshold values obtained in the higher frequencies were much lower in comparison to the lower frequencies, thus indicating better hearing thresholds were obtained in the higher frequencies. The current study found that 10% of HIV positive participants presented with abnormal thresholds (thresholds >15 dB HL) at 8000 Hz and 18.3% at 4000 Hz in comparison to the 40% at 2000 Hz, 33.3% at 1000 Hz, 55% at 500 Hz and 45% at 250 Hz. These findings are in contrast to previous studies which found 4000 Hz and 8000 Hz to be the most affected frequencies (Chandrasekhar et al., 2000; Makau et al., 2010; Minhas et al., 2018; Rey, L'Heritier, & Lang, 2002). Furthermore, the mean threshold values at all frequencies, including the PTA value obtained in the

right ear was lower (better) in comparison to the left ear. A similar finding by Fokouo et al. (2015) and Khoza-Shangase (2011) indicated a left-sided predominance in hearing loss which cannot be explained.

4.1.2 Vestibular dysfunction and HIV/AIDS

The current study demonstrated a significantly higher occurrence of vestibular dysfunction in the HIV positive test group (80%) when compared to the HIV negative test group (33.3%). These findings agreed with previous studies that also demonstrated the aforementioned phenomenon (Castello, Baroni, & Pallestrini, 1998; Dellepiane, Medicina, Mora, & Salami, 2005; Hausler, Vibert, Koralnik, & Hirschel, 1991; Heinze, Vinck, Hofmeyr, & Swanepoel, 2014; Johnston, Miller, & Nath, 1996; Teggi et al., 2008). Previous studies indicated a definite central nervous system involvement as indicated by various results obtained in the oculomotor, visual suppression, saccades and pursuit tracking (Castello et al., 1998; Hausler et al., 1991; Heinze, Swanepoel, & Hofmeyr, 2011; Johnston et al., 1996). These studies also made use of caloric irrigation to assess peripheral vestibular function; however, results obtained were quantitatively within normal limits, and due to the lack of further and more comprehensive testing, peripheral vestibular involvement could not be excluded completely (Castello et al., 1998; Heinze, Vinck, & Swanepoel, 2011). The current study included the Video Head Impulse Test (vHIT), cervical vestibular evoked myogenic potential (cVEMP) and ocular vestibular evoked myogenic potential (oVEMP) to assess further and provide a holistic overview on the peripheral vestibular functioning in the HIV positive population.

Results obtained in the current study for the vHIT did not yield any statistically significant differences. However, the occurrence of abnormality when examining the gain values indicated a higher occurrence in the HIV positive group (33.3%) when compared to the HIV negative group (10%). In the current study, there were three times more abnormal vHIT results obtained in the HIV positive test group when compared to the HIV negative test group. Furthermore, the presence of catch up saccades was also much higher (36.7%) in occurrence in the HIV positive test group in comparison to the HIV negative test group (13.3%). To date, there are no studies that have utilized the vHIT when investigating vestibular function in a study of this nature with an HIV positive population. There is only one previous study (Jung, Kim, & Kim, 2017), based on the case of a 46-year HIV positive man who was also diagnosed with Fisher's syndrome, that utilized the vHIT was to assess semicircular canal function. Results measured were positive in both horizontal canals and the left vertical canal. Previously, a study by Heinze et al. (2014) used the bedside equivalent, i.e., the horizontal head impulse test (HIT), where the investigator relied on simple observation to determine the presence and absence of catch up saccades. Results by Heinze et al. (2014) indicated that there was a larger occurrence (20.8%) of abnormalities in the HIV positive test group when compared to

the HIV negative test group (10.5%) suggesting the involvement of the superior vestibular nerve and the semicircular canals.

Another study by Cohen et al. (2012) that also utilized the horizontal HIT reported a 5% occurrence in the HIV positive population and a 17,7% occurrence in the HIV negative test group. The findings from the current study were not dependant on simple observation by the investigator, but rather, obtained through an objective record of eye movements during the head impulses (Halmagyi et al., 2017). This therefore allowed for the function of each canal to be measured individually in terms of gain and catch up saccades (Halmagyi et al., 2017). The current study was thus able to quantify gain and measure covert saccades which the previous studies were unable to do and could, as a result, justify the higher occurrences reported presently. Therefore, the occurrences reported by Heinze et al. (2014) and Cohen et al. (2012) may be lower in comparison due to the horizontal HIT being limited to human assessment and examination of the horizontal canals and overt saccades only. However, despite the differences in the medium of testing, i.e., the studies agreed that there is a significant occurrence of peripheral vestibular involvement, affecting the semicircular canals and superior vestibular nerve, in the HIV positive test group. Furthermore, the reduction in gain and amplitude values in conjunction with the presence of saccades indicates the involvement of pons-cerebellar pathways and supratentorial areas, i.e., a neural component (Castello et al., 1998).

Results obtained in the current study for cVEMP testing indicated a larger occurrence (20%) of absent responses bilaterally in the HIV positive test group while the HIV negative group had a 0% occurrence. Studies by Heinze et al. (2014) and Heinze, Vinck, and Swanepoel (2011) reported a 35.8% and 66% respectively indicating a much larger occurrence in their HIV positive test group when compared to their HIV negative test groups. Despite this, in the current study, all the mean P1 and N1 latency values measured were within the clinical norm. Furthermore, in the right ear, the HIV positive group presented with a smaller mean interpeak amplitude value than the HIV negative group and a statistically significant difference (p= 0.001) was measured between both test groups indicating more robust responses were obtained in the HIV negative group. Additionally, the HIV positive test group presented with a larger (16.7%) occurrence of delayed P1-N1 latencies in comparison to the HIV negative test group (10%). Likewise, Heinze et al. (2014) also indicated a higher (17%) occurrence of delayed latencies in the HIV positive test group in comparison to the HIV negative test group (0%). In the case report by Jung et al. (2017), cVEMP results obtained were indicated to be "symmetric," but no further detail was given. Heinze, Swanepoel, & Hofmeyr (2011) and Heinze et al. (2014) are the only two studies that made use of the cVEMP to describe the vestibulocollic reflex pathway and to investigate the occurrence of vestibular involvement in HIV positive adults in a similar manner to the present study.

Results obtained in the current study for the oVEMP indicated a larger occurrence (40%) of absent responses in the HIV positive test group in comparison to the HIV negative test group (0%). Like the cVEMP, all mean N1 and P1 latency values for the oVEMP were within the clinical norm (Sandhu et al., 2013; Leyssens et al., 2016; Vanspauwen et al., 2017) . However, the mean N1 and P1 latencies were obtained earlier in the HIV negative test group when compared to the HIV positive test group. Furthermore, there was only one HIV positive participant who presented with delayed N1-P1 latencies. Aside from the case report by Jung et al. (2017), wherein results obtained indicated no wave formations, there are no studies that have utilized the oVEMP to assess utricular and superior vestibular nerve function in an HIV positive test group. However, previous studies did make use of test procedures such as caloric irrigation, the headshake, head impulse and positional tests to determine semicircular canal and superior vestibular nerve function (Castello et al., 1998; Heinze et al., 2014; Heinze, Swanepoel, & Hofmeyr, 2011; Heinze, Vinck, & Swanepoel, 2011).

Furthermore, the study by Heinze et al. (2014) made use of the subjective visual vertical test as a bedside tool to assess for abnormal subjective tilt and effectively utricular function in their HIV positive test group. Results indicated a 3.8% occurrence of an abnormal subjective tilt, and therefore utricular involvement in the HIV positive test group while the HIV negative test group did not present with any occurrence of abnormality (Heinze et al., 2014). Results from these studies agreed with the current study and indicated a peripheral vestibular involvement in their HIV positive test groups.

4.1.3 Risk of falling and HIV

Results obtained in all three tests of functional balance, i.e., dynamic gait index (DGI), Berg balance scale (BBS) and timed up and go (TUG), indicated statistically significant differences between both test groups. However, the results obtained in all three test categories were within normal limits and therefore not of clinical relevance as this indicated no impairment in balance in both test groups. Concerning the DGI and BBS, the statistically significant differences obtained indicated higher mean values in the in the HIV negative group in comparison to the HIV positive group; however, a significantly lower mean value was obtained in the HIV negative test group in comparison to the HIV positive group when looking at the TUG. This finding indicates that participants who were HIV negative performed better (achieving higher scores) in the risk for falls assessments in comparison to the HIV positive group. Despite the aforementioned and although the scores obtained were within normal clinical limits, other factors may be taken into account. Firstly, persons presenting with unilateral vestibular dysfunction, in conjunction with associated symptoms such as vertigo, are more susceptible to the risk of falls (Herdman, Blatt, Schubert, & Tusa, 2000). In the current study, within the HIV positive test group, 23.3% of participants expressed complaints of vertigo and/or dizziness. In accordance with the report by Herdman et al. (2000), the current study indicated that 3.3% (n=1) of participants presented with an absent cVEMP on the right side and another 3.3.% (n=1) with an

absent oVEMP on the right side together with an increased latency in the TUG, and both presented with lower DGI and BBS scores in comparison to the other HIV positive participants. Furthermore, both of the participants mentioned above expressed complaints of persistent episodes of vertigo. Secondly, persons presenting with a bilateral vestibular dysfunction are at an increased risk for falls, more so than those with unilateral vestibular dysfunction (Herdman et al., 2000). In the current study, 10% (n=3) of participants presented with bilateral vestibular dysfunction (VEMP and/or vHIT) together with increased latency in the TUG as well as lower scores in the DGI and BBS in comparison to other HIV positive participants. Another 3.3% (n=1) did not present with any vestibular dysfunction but did present with increased latency in the TUG and lower scores in the DGI and BBS. A previous study by Teggi et al. (2006) utilised the DGI to assess equilibrium in their HIV positive test group and results indicated that 23.3% in the HIV positive test group achieved a score of <21 but >19 indicating a balance disturbance and another 13.3% achieved a score of <19 indicating a high risk for falls. The study concluded that there was a correlation between the patient's balance as assessed by the DGI and the number of years infected. Additionally, in agreement with the current study, there were two other studies (Richert et al., 2011, 2014) that utilized the TUG and BBS to assess dynamic balance in which results indicated normal balance function in PLWHA. Furthermore, Richert et al. (2014) reported that central sensorimotor components might play a role in the locomotion of PLWHA. Also, another study (Meyerhoff, 2001) indicated that PLWHA presented with certain neurological symptoms before their death that included problems with movement and balance. As mentioned previously, reduced gain and amplitude values, as well as the presence of saccades in vHIT results, indicate neural involvement (Castello et al., 1998). In agreement with Castello et al. (1998), the current study indicates that 23.3% of participants presented with reduced gain values and/or the presence of saccades together with an increased latency in the TUG and/or lower scores in the BBS and/or DGI in comparison to the other HIV positive participants tested. This suggests that neurological involvement in vestibular dysfunction may contribute towards an increased risk of falls. The current study therefore concluded that based on the current test population, that there was a significant difference measured between the HIV negative test group (performed better) when compared to the HIV positive test group (performed poorer).

4.1.4 Health-Related Quality of life (HRQoL) and HIV

The HRQoL was assessed using the Health-Related Quality of Life (EQ-5D-5L) Questionnaire. It was observed that the HIV positive test group experienced more difficulty in all five health dimensions than the HIV negative group with statistically significant differences measured in four out of five health dimensions. Furthermore, the mean Visual analog scale (VAS) score was higher in the HIV negative group (92.3, ±12.3) in comparison to the HIV positive test group (88.5, ±11.9). Based on these findings it was concluded that the HIV positive test group presents with a diminished

HRQoL in comparison to the HIV negative test group. The current study is in agreement with a study conducted by Tran, Ohinmaa and Nguyen, (2012), who also used the EQ-5D-5L questionnaire and found that results indicated a high occurrence of anxiety/depression and pain/discomfort among PLWHA. In another study (Hays et al., 2000), results obtained via the 36-Item Short Form Survey (SF-36) indicated that physical functioning and emotional well-being was worse in PLWHA than others with a chronic disease. These findings are in agreement with the current study which concluded that a significant difference as measured between both test groups where the HIV positive test group presented with a lower HRQoL when compared to the HIV negative test group.

5. CHAPTER 5: CLINICAL IMPLICATION AND CONCLUSION

5.1 Clinical Implications of the current study

The current study, in conjunction with numerous previous studies has established a clear association between hearing loss and HIV/AIDS (Chandrasekhar et al., 2000; Fokouo et al., 2015; Katijah Khoza-Shangase, 2011; Luque et al., 2014; Matas et al., 2014; Mathews et al., 2012; Sulyman et al., 2012; Van Der Westhuizen et al., 2013b). Audiologists should be aware of their patients' HIV status and, as previous research states, monitor HIV-related hearing loss as well as incorporate the screening thereof into HIV/AIDS-related routine medical care (Assuiti et al., 2013; Van Der Westhuizen et al., 2013b). This can be done via mHealth using the hearZA application, as it is cost effective, requires minimal equipment and does not need extensive training to use the application (Swanepoel, 2017). Furthermore, annual audiological routine testing or a retest at any time should be encouraged and emphasized especially if the physician or patient recognize changes regarding hearing/hearing loss. Risk for falls has also been highlighted as a presenting factor in PLWHA and must be monitored and managed carefully. Therefore, patients should also be screened for any symptoms indicative of vestibular dysfunction as well as risk for falls. This can be done via the physician attending to the patient, by asking questions that are specific indicators as well as advising patients on what to look out for regarding possible vestibular dysfunction and risk for falls. After that, if needed, bedside assessments can be conducted and may include the three functional balance assessments, i.e. DGI (Shumway-Cook & Woollacott, 1995), BBS (Berg, Wood-Dauphine, et al., 1989), and TUG (Podisadlo & Richardson, 1991) and SVV, the horizontal HIT, pursuit tracking, etc. If based on the results obtained, vestibular dysfunction and/or risk for falls is indicated, a referral for diagnostic testing should be made and if necessary vestibular rehabilitation to ensure an improved HRQoL in those patients.

Audiological and vestibular test results don't help to diagnose HIV/AIDS. However, the information obtained, i.e., regarding hearing, vestibular function and balance, may be of importance in the management and treatment of the disease. These findings can help a clinician to make appropriate referrals, avoid the prescription of cochleototoxic and/or vestibulotoxic medications and assist in informing healthcare personnel on what to look out for and effectively provide a more holistic approach to treatment.

5.2 Critical evaluation of the current study

The strengths and limitations of the current research study were critically considered and can aid in directing future research projects. The strengths and limitations are discussed below:

5.2.1 Strengths of the current study

- The research design employed in the current study controlled for age and gender with a matched experimental (HIV positive group) and control group (HIV negative group) thereby minimizing any possible confounding influences.
- Participants aged 18-45 years old were utilized in the current study to ensure no involvement of presbycusis.
- The present study was a comprehensive study, in that it included a full test protocol that helped to determine and describe the audiovestibular function, risk of falling, and health-related quality of life in HIV positive adults compared to HIV negative adults. Previous research does not include a synthesised study like the current study, instead the results from the abovementioned tests were reported separately in different studies.
- This is the first study, conducted using a larger HIV test population, that includes the oVEMP in conjunction with the cVEMP, and also the vHIT in the test protocol and therefore details information that was not previously reported. Previously, there has only been one study utilizing these tests that details the results from one patient only (Jung et al., 2017).
- All participants were screened and cleared of any conductive component to ensure accurate and reliable VEMP responses were obtained.
- The current study consists of a homogenous HIV positive test group as twenty-nine out of the thirty participants tested were on the first line fixed dose ART regime. This allowed for consistency in the results obtained and reported.

5.2.2 Limitations of the current study

- A possible limitation of the current study was the small sample size of both groups (n=30). Further studies should aim to test and compare larger samples sizes.
- The researcher acquired data from patients that were all based in one hospital, and this could, therefore, make it difficult to generalize the results obtained for all PLWHA.
- In the current study, 10% of HIV positive participants were found to have abnormal thresholds (>15 dB HL) at 8000 Hz and 18.3% at 4000 Hz. High-frequency Audiometry (HFA) should be conducted as HIV positive individuals receiving ART are susceptible to HFA alterations that may be due to otoxicity (Khoza-Shangase, 2010; Matas et al., 2014).
- Distortion Product Otoacoustic emissions (DPOAE's) was not performed, which could help to further characterize changes in hearing as well as describe the functioning of the cochlea. (Khoza-Shangase, 2010). Future studies should include DPOAE's as part of the test protocol to obtain more information on the functioning of the cochlea.
- Further investigations need to be conducted to investigate the left side predominance in hearing loss that was observed in the current study.

- Furthermore, the full vestibular frequency spectrum was not tested. Caloric testing, for low frequency testing, and rotary chair testing, for the middle frequencies, were not tested as this equipment is not mobile. However, the vHIT (high frequency test) was mobile. Thus our examination of vestibular function was limited to high and very high (VEMP) frequency testing

5.3 Conclusion

There were significantly more HIV positive individuals with auditory and vestibular dysfunction identified than HIV negative individuals. Furthermore, significant differences were also obtained in the HRQoL which indicated that HIV negative participants experience a better HRQoL in comparison to HIV positive participants. Lastly, during the risk for falls assessments, despite values obtained being within the clinical norm, a significant difference was measured between both test groups where the HIV negative test group performed better than the HIV positive test group.

In accordance with previous studies, hearing loss is most definitely associated with HIV and is the most common symptom of audiological dysfunction. Additionally, SNHL was found to be the most prevalent type of hearing loss observed in the HIV positive test group. Hearing loss was observed to be unilateral and bilateral in nature and ranged from slight to moderate in degree. The majority of HIV positive participants within this test group presented with normal hearing. Monitoring HIV positive patients should be implemented into HIV-related routine medical care to ensure early identification, and appropriate intervention is implemented.

Furthermore, within this current study, vestibular dysfunction, both central and peripheral in nature is also more prevalent in the HIV positive population in comparison to the HIV negative test group. The vast majority of HIV positive participants presented with an abnormality in VEMP and/or vHIT results. With the advancement in vestibular testing technologies now including tests such as the oVEMP, cVEMP, and vHIT, it is now possible for further investigation regarding the site of lesion, nature, and extent of vestibular symptoms, and as a result, utilize a more comprehensive test battery when examining vestibular dysfunction. In the current study, it was found that there were more HIV positive individuals with auditory and vestibular dysfunction as well as absent oVEMPs. Furthermore, there three times more abnormal vHIT results obtained in the HIV positive group when compared to the HIV negative test group. Questions regarding vestibular function as well as screening thereof should be implemented into HIV-related routine medical care to ensure early identification and appropriate management will be implemented.

Even though statistically, the values obtained in the current study did not indicate risk for falls in the HIV positive test population, previous research has indicated the opposite. Therefore, HIV-related medical care should ensure routine screening of risk for falls and appropriate management after that.

References

Abdool Karim, S., Churchyard, G. J., Abdool Karim, Q., & Lawn, S. D. (2009). Health in South Africa 3 HIV infection and tuberculosis in South Africa : an urgent need to escalate the public health response. *The Lancet*, *374*(9693), 921–933. https://doi.org/10.1016/S0140-6736(09)60916-8

American Geriatric Society, British Geriatic Society, & American Academy of Orthopaedic Surgeons Panel on Falls Prevention. (2001). Guideline for the Prevention of Falls in Older Persons. *Jags*, *49*(5), 664–672. https://doi.org/10.1046/j.1532-5415.2001.49115.x

Akin, F. W., & Murnane, O. D. (2008). Vestibular evoked myogenic potentials. In *G. P. Jacobson, & N. T. Shepard (Eds.), Balance function assessment and management* (pp. 405–434).

Akin, F. W., Murnane, O. D., Tampas, J. W., Clinard, C., Byrd, S., & Kelly, J. K. (2012). The effect of noise exposure on the cervical vestibular evoked myogenic potential. *Ear & Hearing*, *33*(4), 458–465. https://doi.org/10.1097/AUD.0b013e3182498c5f

Al-malky, B. Y. G. (2016). Audiological monitoring in ototoxicity . *Ent and Audiology News*, *25*(5).

Andersson, G., Kamwendo, K., & Appelros, P. (2006). How to Identify Potential Fallers in a Stroke Unit : Validity Indexes of Four Test Methods, 186–191. https://doi.org/10.1080/16501970500478023

Assuiti, L. F. C., Marcellino, G., Lanzoni, D. M., Cristine, F., Erdmann, A. L., Hörner, B., & Meirelles, S. (2013). Hearing loss in people with HIV/AIDS and associated factors: an integrative review. *Brazilian Journal of Otorhinolaryngology*, *79*(2), 248–255. https://doi.org/10.5935/1808-8694.20130042

AVERT. (2017). Global HIV and AIDS statistics. Retrieved from https://www.avert.org/global-hiv-and-aids-statistics

Bansal, S., Sahni, S., & Sinha, S. K. (2013). Cervical and ocular vestibular evoked myogenic potentials in individuals with severe to profound hearing loss. *Journal of Hearing Science*, *3*(4), 56–63.

Barzan, L., Tavio, M., Tirelli, U., & Comoretto, R. (1993). Head and neck manifestations during HIV infection. *The Journal of Laryngology & Otology*, *107*(2), 133–136. https://doi.org/10.1017/S0022215100122418

Bath, A. P., Harris, N., Mcewan, J., & Yardley, M. P. (1999). Effect of conductive hearing loss on the vestibulo-collic reflex. *Clinical Otolaryngology*, *24*(3), 181–183.

Berg, K., Wood-Dauphine, S., Williams, J. I., & Gayton, D. (1989). Measuring balance in the elderly: preliminary development of an instrument. *Physiotherapy Canada, 41*(6), 304–311.

Berg, K., Wood-Dauphinee, S., Williams, J., & Gayton, D. (1989). Measuring balance scale: Reliability assessment with an elderly population. *Archives of Physical Medicine and Rehabilitation*, *73*, 1073–1080.

Boulgarides, L. K., Mcginty, S. M., Willett, J. A., & Barnes, C. W. (2003). Research Report Use of Clinical and Impairment- Based Tests to Predict Falls by Community-Dwelling Older Adults. *Physical Therapy*, *83*(4), 328–339.

Brits, J., Strauss, S., Eloff, Z., Becker, P. J., & De Swanepoel, W. (2012). Hearing profile of gold miners with and without tuberculosis. *Occupational and Environmental Medicine*, *69*(4), 243–249. https://doi.org/10.1136/oemed-2011-100106

Buonaguro, L., Tornesello, M. L., & Buonaguro, F. M. (2007). Human Immunodeficiency Virus Type 1 Subtype Distribution in the Worldwide Epidemic: Pathogenetic and Therapeutic Implications. *Journal of Virology*, *81*(19),

10209–10219. https://doi.org/10.1128/JVI.00872-07

Campos, J., & Pichora-Fuller, M. K. (2018). Hearing, self-motion perception, mobility and aging. *Hearing Research, 369* (2018), 42-55.

Canter, J. A., Haas, D. W., Kallianpur, A. R., Robbins, G. K., Shafer, R. W., & Hulgan, T. (2008). The mitochondrial pharmacogenomics of haplogroup T : MTND2 * LHON4917G and antiretroviral therapy-associated peripheral neuropathy, (June 2007). *The Pharmacogenomics Journal,* 71–77. https://doi.org/10.1038/sj.tpj.6500470

Castello, E., Baroni, N., & Pallestrini, E. (1998). Neurotological and Auditory Brain Stem Response Findings in Human Immunodeficiency Virus – Positive Patients Without Neurologic Manifestations. *Annals of Otology, Rhinology & Laryngology*, *107*(12), 1054–1060.

Chan, S. Y., Medhi, M., Ekbote, A., Moses, S., Sibtain, N., Andrews, T., … Kulasegaram, R. (2008). Syphilis causing hearing loss. *International Journal of STD & AIDS*, *19*(10), 721–722. https://doi.org/10.1258/ijsa.2008.008124

Chandrasekhar, S. S., Connelly, P. E., Brahmbhatt, S. S., Shah, C. S., Kloser, P. C., & Baredes, S. (2000). Otologic and audiological evaluation of human immunodeficiency virus-infected patients. *American Journal of Otolaryngology*, *21*(1), 1–9.

Chew, H. S., & Yeak, S. (2010). Quality of life in patients with untreated age-related hearing loss. *The Journal of Laryngology & Otology*, *124*(8), 835–841. https://doi.org/10.1017/S0022215110000757

Chiu, Y.-P., Fritz, S. L., Light, K. E., & Velozo, C. A. (2006). Use of item response analysis to investigate measurement properties and clinical validity of data for the dynamic gait index. *Physical Therapy*, *86*(6), 778–787.

Chopra, M., Lawn, J. E., Sanders, D., Barron, P., Abdool Karim, S. S., Bradshaw, D., … Coovadia, H. (2009). Health in South Africa 6 Achieving the health Millennium Development Goals for South Africa : challenges and priorities. *The Lancet*, *374*(9694), 1023–1031. https://doi.org/10.1016/S0140-6736(09)61122-3

Clark, J. G. (1981). Uses and abuses of hearing loss classification. *ASHA: A Journal of the American Speech-Language-Hearing Association*, *23*(7), 493–500.

Cohen, H. S., Cox, C., Springer, G., Hoffman, H. J., Young, M. A., Margolick, J. B., & Plankey, M. W. (2012). Prevalence of Abnormalities in Vestibular Function and Balance among HIV-Seropositive and HIV-Seronegative Women and Men. *PLos ONE*, *7*(5), 5–12. https://doi.org/10.1371/journal.pone.0038419

Cremer, P. D., Halmagyi, G. M., Aw, S. T., Curthoys, I. S., McGarvie, L. A., Todd, M. J., … Hannigan, I. P. (1998). Semicircular canal plane head impulses detect absent function of individual semicircular canals. *Brain*, *121*(4), 699–716. https://doi.org/10.1093/brain/121.4.699

Cruickshanks, K. J., Klein, R., Klein, B. E. K., Wiley, T. L., Nondahl, D. M., & Tweed, T. S. (1998). Cigarette Smoking and Hearing Loss The Epidemiology of Hearing Loss Study, *279*(21), 1715–1719.

Curthoys, I. S. (2012). The interpretation of clinical tests of peripheral vestibular function. *The Laryngoscope*, *122*(6), 1342–1352. https://doi.org/10.1002/lary.23258

Dalton, D. S., Cruickshanks, K. J., Klein, B. E. K., Klein, R., Wiley, T. L., & Nondahl, D. M. (2003). The Impact of Hearing Loss on Quality of Life in Older Adults. *Gerontologist*, *43*(5), 661–668. https://doi.org/10.1093/geront/43.5.661

Davies, N. E. C. G. (2013). Fixed-dose combination for adults accessing antiretroviral therapy: advice document. *Southern African Journal of HIV Medicine*, *14*(1), 41–43.

Deeks, S. G. (2009). Immune dysfunction, inflammation, and accelerated aging in patients on antiretroviral therapy. *International AIDS Society*, *17*(4), 118–123.

Dellepiane, M., Medicina, M. C., Mora, R., & Salami, A. (2005). Static and dynamic posturography in patients with asymptomatic HIV-1 infection and AIDS. *Acta Otorhinolaryngologica Italica*, *25*(6), 353.

Desquilbet, L., Jacobson, L. P., Fried, L. P., Phair, J. P., Jamieson, B. D., Holloway, M., & Margolick, J. B. (2007). HIV-1 Infection Is Associated With an Earlier Occurrence of a Phenotype Related to Frailty. *The Journals of Gerontology*, *62*(11), 1279–1286.

Devaleenal, D. B., Ahilasamy, N., Solomon, S., & Kumarasamy, N. (2008). Ramsay hunt syndrome in a person with HIV disease. *Indian Journal of Otolaryngology and Head and Neck Surgery : Official Publication of the Association of Otolaryngologists of India*, *60*(2), 171–173. https://doi.org/10.1007/s12070-008-0041-x

Effros, R. B., Fletcher, C. V, Gebo, K., Halter, J. B., Hazzard, W. R., Horne, F. M., … High, K. P. (2008). Workshop on HIV Infection and Aging: What Is Known and Future Research Directions. *NIH Public Access*, *47*(4), 542–553. https://doi.org/10.1086/590150.Workshop

Ensink, R. J. H., & Kuper, H. (2017). Is hearing impairment associated with HIV ? A systematic review of data from low- and middle-income countries. *Tropical Medicine and International Health*, *22*(12), 1493–1504. https://doi.org/10.1111/tmi.12993

Erlandson, K. M., Allshouse, A. A., Jankowski, C. M., Mawhinney, S., Kohrt, W. M., & Campbell, T. B. (2012). *NIH* Public Access, *61*(4), 484–489. https://doi.org/10.1097/QAI.0b013e3182716e38.Risk

EuroQol Group. (1990). EuroQol--a new facility for the measurement of health-related quality of life. EuroQol Group1. *Health Policy*, *16*(3), 199–208.

Evian, C. (2000). *Primary AIDS Care* (3rd ed.). Houghton: Jcana Media.

Fan, H. Y., Conner, R. F., & Villarreal, L. P. (2014). *AIDS: Sceince and Society* (7th ed.). Burlington: Jones & Bartlett Learning.

Felipe, L., & Kingma, H. (2013). Ocular vestibular evoked myogenic potentials. *International Archives of Otorhinolaryngology*, *18*(1), 77–79. https://doi.org/10.1055/s-0033-1352503

Ferrite, S., & Santana, V. (2005). Joint effects of smoking, noise exposure and age on hearing loss. *Occupational Medicine*, *55*(1), 48–53. https://doi.org/10.1093/occmed/kqi002

Fokouo, J. V. F., Vokwely, J. E. E., Noubiap, J. N. N., Nouthe, B. E., Zafack, J., Minka Ngom, E. S., … Njock, R. (2015). Effect of HIV infection and highly active antiretroviral therapy on hearing function: A prospective case-control study from Cameroon. *JAMA Otolaryngology - Head and Neck Surgery*, *141*(5), 436–441. https://doi.org/10.1001/jamaoto.2015.125

Guinand, N., Van de Berg, R., Cavuscens, S., Ranieri, M., Schneider, E., Lucieer, F., … Fornos, A. P. (2017). The video head impulse test to assess the efficacy of vestibular implants in humans. *Frontiers in Neurology*, *8*. https://doi.org/10.3389/fneur.2017.00600

Halmagyi, G., Curthoys, I., Cremer, P., Henderson, C., Todd, M., & Al., E. (1990). The human horizontal vestibulo-ocular reflex in response to high-acceleration stimulation before and after unilateral vestibular neurectomy. *Experimental Brain Research*, *81*(3), 479–490.

Halmagyi, G. M., Chen, L., MacDougall, H. G., Weber, K. P., McGarvie, L. A., & Curthoys, I. S. (2017). The video head impulse test. *Frontiers in Neurology*, *8*(258), 1–23. https://doi.org/10.3389/fneur.2017.00258

Harris, T., & Heinze, B. (2013). OPEN ACCESS GUIDE TO AUDIOLOGY AND HEARING AIDS FOR OTOLARYNGOLOGISTS.

Hausler, R., Vibert, D., Koralnik, I. J., & Hirschel, B. (1991). Neuro-otological Manifestations in Different Stages of HIV Infection. *Acta Oto-Laryngologica*, *111*, 515–521.

Hays, R. D., Cunningham, W. E., Sherbourne, C. D., Wilson, I. B., Wu, A. W., Cleary, P. D., … Bozzette, S. A. (2000). Health-related quality of life in patients with human immunodeficiency virus infection in the United States: Results from the HIV cost and services utilization study. *American Journal of Medicine*, *108*(9), 714–722. https://doi.org/10.1016/S0002-9343(00)00387-9

Heinze, B. M., Vinck, B. M., Hofmeyr, L. M., & Swanepoel, D. W. (2014). Vestibular involvement in adults with HIV / AIDS. *Auris Nasus Larynx*, *41*(2), 160–168.

Heinze, B. M., Vinck, B. M., Hofmeyr, L. M., & Swanepoel, D. W. (2014). Vestibular involvement in adults with HIV / AIDS. *Auris Nasus Larynx*, *41*(2), 160–168. https://doi.org/10.1016/j.anl.2013.08.003

Heinze, B., Swanepoel, D. W., & Hofmeyr, L. M. (2011). Systematic review of vestibular disorders related to human immunodeficiency virus and acquired immunodeficiency syndrome. *The Journal of Laryngology & Otology*, *125*(9), 881–890. https://doi.org/10.1017/S0022215111001423

Heinze, B., Vinck, B. M., & Swanepoel, D. W. (2011). Does the human immunodeficiency virus influence the vestibulocollic reflex pathways ? A comparative study. *The Journal of Laryngology & Otology*, *128*(9), 772–779.

Herdman, M., Gudex, C., Lloyd, A., Janssen, M., Kind, P., Parkin, D., … Badia, X. (2011). Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Quality of Life Research*, *20*(10), 1727–1736. https://doi.org/10.1007/s11136-011-9903-x

Herdman, S. J. (2000). *Vestibular Rehabilitation* (2nd ed.). Philadelphia: F.A Davis Co.

Herdman, S. J., Blatt, P., Schubert, M. C., & Tusa, R. J. (2000). Falls in patients with vestibular deficits. *The American Journal of Otology*, *21*(6), 847–851.

Herman, T., Giladi, N., & Hausdorff, J. M. (2011). Properties of the “Timed Up and Go” test: More than meets the eye. *Gerontology*, *57*(3), 203–210. https://doi.org/10.1159/000314963

Herman, T., Inbar-Borovsky, N., Brozgol, M., Giladi, N., & Hausdorff, J. (2009). The Dynamic Gait Index in healthy older adults: the role of stair climbing, fear of falling and gender. *Gait & Posture*, *29*(2), 237–241.

Holmes, S., & Padgham, N. D. (2011). A review of the burden of vertigo. *Journal of Clinical Nursing, 20*(19–20), 2690–2701.

Hong, S. M., Byun, J. Y., Park, C. H., Lee, J. H., Park, M. S., & Cha, C. Il. (2008). Saccular damage in patients with idiopathic sudden sensorineural hearing loss without vertigo. *Otolaryngology - Head and Neck Surgery*, *139*(4), 541–545. https://doi.org/10.1016/j.otohns.2008.07.003

Isaacs, S., & Michael, W. B. (1995). *Handbook in research and evaluation: A collection of principles, methods, and strategies useful in the planning, design, and evaluation of studies in education and the behavioral sciences, 3rd ed.* (3rd ed.). San Diego, CA: EDITS.

Isaacson, B., Murphy, E., & Cohen, H. (2006). Does the method of sternocleidomastoid muscle activation affect the

vestibular evoked myogenic potential response? *Journal of Vestibular Research*, *16*(4,5), 187–191.

Isaradisaikul, S., Navacharoen, N., Hanprasertpong, C., & Kangsanarak, J. (2012). Cervical Vestibular-Evoked Myogenic Potentials: Norms and Protocols. *International Journal of Otolaryngology*, *2012*, 1–7. https://doi.org/10.1155/2012/913515

Itoh, A., Nakashima, T., Arao, H., Wakai, K., Tamakoshi, A., Kawamura, T., & Ohno, Y. (2001). Smoking and drinking habits as risk factors for hearing loss in the elderly. *Public Health*, *115*(3), 192–196.

Jerger, J. (1970). Clinical Experience With Impedance Audiometry. *Archives of Otolaryngology*, *92*(4), 311–324.

Johnson, L. F., Mossong, J., Dorrington, R. E., Schomaker, M., Hoffman, C. J., Keiser, O., & Al., E. (2013). Life expectancies treatment: antiretroviral starting adults of South African Collaborative analysis of cohort studies. *PLoS Medicine*, *10*(4), e.1001418.

Johnston, J. L., Miller, J. D., & Nath, A. (1996). Ocular motor dysfunction in HIV-1-infected subjects A quantitative oculographic analysis. *Neurology*, *46*(2), 451–457.

Jung, I., Kim, H. J., & Kim, J. S. (2017). Fluctuating ataxia and nystagmus in association with anti-GQ1b antibody in HIV infection. *Journal of the Neurological Sciences*, *382*, 123–125. https://doi.org/10.1016/j.jns.2017.09.044

Khoza-shangase, K. (2010). Is there a need for ototoxicity monitoring in patients with HIV / AIDS ? *African Journal of Pharmacy and Pharmacology*, *9*(April 2004), 1–9. https://doi.org/10.2989/16085906.2010.484531

Khoza-shangase, K. (2011). Highly active antiretroviral therapy : Does it. *Journal of Pharmacology and Bioallied Sciences*, *3*(1), 142–153. https://doi.org/10.4103/0975-7406.76494

Khoza-shangase, K. (2017). VESTIBULAR FUNCTION IN A GROUP OF ADULTS WITH HIV/AIDS ON HAART. *Afr., J., Infect., Dis.*, *12*(1), 7–14.

Khoza-Shangase, K. (2010). HIV/AIDS and auditory function in adults: the need for intensified research in the developing world. *African Journal of AIDS Research*, *9*(1), 1–9. https://doi.org/10.2989/16085906.2010.484531

Khoza-Shangase, K. (2011). An analysis of auditory manifestations in a group of adults with aids prior to antiretroviral therapy. *African Journal of Infectious Diseases*, *5*(1), 11–22.

Khoza-Shangase, K., & Jade Van Rie, K. (2017). Pathological vestibular symptoms presenting in a group of adults with HIV/AIDS in Johannesburg, South Africa. *Southern African Journal of Infectious Diseases*, *32*(2), 43–53. https://doi.org/10.1080/23120053.2016.1216816

Khoza, K., & Ross, E. (2002). Auditory Function in a Group of Adults Infected with HIV/AIDS in Gauteng, South Africa. *The South African Journal of Communication Disorders= Die Suid- Afrikaanse Tydskrif Kommunkasieafwykings*, *49*, 17–27.

Kim, S. K., Lee, K. J., Hahm, J. R., Lee, S. M., Jung, T. S., Jung, H. J., … Chung, S. (2012). Clinical relevance of the presence of autonomic and vestibular dysfunction in diabetic patients with peripheral neuropathy. *Diabetes & Metabolism Journal*, *36*(1), 64–69.

Konukseven, O., Polat, S. B., Karahan, S., Konukseven, E., Ersoy, R., Cakir, B., … Aksoy, S. (2015). Electrophysiologic vestibular evaluation in type 2 diabetic and prediabetic patients: Air conduction ocular and cervical vestibular evoked myogenic potentials. *International Journal of Audiology*, *54*(8), 536–543. https://doi.org/10.3109/14992027.2014.971887

Kovalova, M., Mrazkova, E., Sachova, P., Vojkovska, K., Tomaskova, H., Janoutova, J., & Janout, V. (2016). Hearing Loss in Persons Exposed and not Exposed to Occupational Noise. *The Journal of International Advanced Otology*, *12*(1), 49–54. https://doi.org/10.5152/iao.2016.1770

Leedy, P. D., & Ormrod, J. E. (2005). *Practical Research Planning and Design* (9th ed.). Pearson.

Leedy, P. D., & Ormrod, J. E. (2014). A*nd Design Ninth Edition*. Essex: Pearson Education Limited.

Leyssens, L., Hei nze, B., Vinck, B., Van Ombergen, A., Vanspauwen, R., Wuyts, F., & Maes, L. (2016). 'Standard' versus 'nose reference' electrode placement for measuring oVEMPs with air-conducted sound: Test–retest reliability and preliminary patient results. *Clinical Neurophysiology*, *128*(2), 312–322. https://doi.org/10.1016/j.clinph.2016.11.023

Lima, A. P., & Delgado, E. L. (2010). The Best Age in Brazil: biopsychosocial aspects arising from the aging process. *Ulbra and Movement (REFUM)*, *1*(2), 76–91.

Lubbe, D. E. (2004). HIV AND ENT HIV and ENT, *22*(5), 2002–2005.

Luque, A. E., Orlando, M. S., Cheng Leong, U., Allen, P. D., Guido, J. J., Hongmei, Y., & Wu, H. (2014). Hearing function in people living with HIV/AIDS. *Ear Hear*, *35*, 282–290.

MacDougall, H. G., McGarvie, L. A., Halmagyi, G. M., Curthoys, I. S., & Weber, K. P. (2013). The Video Head Impulse Test (vHIT) Detects Vertical Semicircular Canal Dysfunction. *PLoS ONE*, *8*(4).

Mahomed-Asmail, F., Swanepoel, D. W., & Eikelboom, R. H. (2016). Diagnostic Hearing Assessment in Schools: Validity and Time Efficiency of Automated Audiometry. *Journal of the American Academy of Audiology*, *27*(1), 42–48.

Majumdar, B., & Mazaleni, N. (2010). The experiences of people living with HIV / AIDS and of their direct informal caregivers in a resource-poor setting, (2003), 1–9.

Makau, S. M., Ongulo, B. A., & Oburra, H. O. (2010). The Pattern of Hearing Disorders in HIV Positive Patients on Anti - retrovirals at Kenyatta National Hospital. *East African Medical Journal*, *87*(10), 425–429. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/23457817

Marsot-Dupuch, K., Quillard, J., & Meyohas, M. C. (2004). Head and neck lesions in the immunocompromised host. *European Radiology Supplements*, *14*(3), 155–167.

Marzolini, C., Elzi, L., Gibbons, S., Weber, R., Fux, C., Furrer, H., … Battegay, M. (2010). Prevalence of comedications and effect of potential drug-drug interactions in the Swiss HIV cohort study. *Antiviral Therapy*, *15*(3), 413–423. https://doi.org/10.3851/IMP1540

Masur, H., Ognibene, F. P., Yarchoan, R., & Al., E. (1989). CD4 counts as predictors of opportunistic pneumonias in human immunodeficiency virus (hiv) infection. *Annals of Internal Medicine*, *111*(3), 223–231.

Matas, C. G., Angrisani, R. G., Cristina, F., Magliaro, L., Augusto, A., & Segurado, C. (2014). Audiological manifestations in HIV-positive adults. *Clinics*, *69*(7), 469–475. https://doi.org/10.6061/clinics/2014(07)05

Matas, C. G., Filha, V. A. V. S., Juan, K. R., Pinto, F. R., & Gonçalves, I. C. (2010). Audiological manifestations in children and adults with AIDS. *Pro-Fono : Revista de Atualizacao Cientifica*, *22*(3), 269–274. https://doi.org/10.1590/S0104-56872010000300019

Matas, C. G., Sansone, A. P., Iorio, M. C. M., & Succi, R. C. M. (2000). Audiological Evaluation in Children Born to HIV

Positive Mothers. *Brazilian Journal of Otorhinolaryngology*, *6*(4), 317–324.

Mathews, S. S., Albert, R. R., & Job, A. (2012). Audio-vestibular function in human immuno deficiency virus infected patients in India. *Indian Journal of Sexually Transmitted Diseases and AIDS*, *33*(2), 98–101. https://doi.org/10.4103/0253-7184.102115

Mccomsey, G. A., Tebas, P., Shane, E., Yin, M. T., Overton, E. T., Huang, J. S., … Brown, T. T. (2018). Bone Disease in HIV Infection : A Practical Review and Recommendations for HIV Care Providers, *51*(February), 937–946. https://doi.org/10.1086/656412

McGarvie, L. A., MacDougall, H. G., Halmagyi, G. M., Burgess, A. M., Weber, K. P., & Curthoys, I. S. (2015). The video head impulse test (vHIT) of semicircular canal function - age-dependent normative values of VOR gain in healthy subjects. *Frontiers in Neurology*, *6*(154), 1–11. https://doi.org/10.3389/fneur.2015.00154

Meintjes, G., Maartens, G., Committee, G., Boulle, A., Conradie, F., Goemaere, E., … Panel, E. (2012). Guidelines for antiretroviral therapy in adults, *13*(3), 36–45. https://doi.org/10.7196/SAJHIVMED.862

Meyerhoff, D. J. (2001). Effects of alcohol and HIV infection on the central nervous system. *Alcohol Research & Health: The Journal of the National Institute on Alcohol Abuse and Alcoholism*, *25*(4), 288–298. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11910707

Minhas, R. S., Iyengar, D. A., Thakur, J, S., & Azad, R. K. (2018). Effect of HIV and Antiretroviral Treatment on Auditory Functions. *International Archives of Otorhinolaryngology*, *22*(04), 378–381.

Moayedi, S. (2010). H e a d , N e c k an d Ophthalmologic Manifestations of HIV in the Emergency. *Emergency Medicine Clinics of NA*, *28*(2), 265–271. https://doi.org/10.1016/j.emc.2010.01.006

Mouton, J., & Babbie, E. (2007). *The Practice of Social Research (11th ed.)* (11th ed.). Belmont , CA: Thomson Higher Education.

Nelson, D. I., Nelson, R. Y., Concha-Barrientos, M., & Fingerhut, M. (2005). The global burden of occupational noise-induced hearing loss. *Am J Ind Med*, *48*(6), 446–458. https://doi.org/10.1002/ajim.20223

Nooka, S., & Ghorpade, A. (2017). No TitleInterleukin-1B and Abacavir Induce Astrocyte Endoplasmic Reticulum Stress During HIV-1-Associated Neurocognitive Disorders.

Onen, N. F., Agbebi, A., Shacham, E., Stamm, K. E., Onen, A. R., & Overton, E. T. (2009). Frailty among HIV-infected persons in an urban outpatient care setting. *Journal of Infection*, *59*(5), 346–352.

Ongulo, B. A., & Oburra, H. O. (2010). Hearing disorders in HIV positive adult patients not on anti-retroviral drugs at Kenyatta National Hospital. *East African Medical Journal*, *87*(9), 385–388.

Paiva, S. F. de, Mercia, C., Silva, B., Brito, O. E. de O., Soares, A. C. S., & Fraga, W. S. (2017). The Risk of Falling Associated to Dizziness in Elderly. *Journal of Otolaryngology- ENT Research*, *9*(4), 12–14. https://doi.org/10.15406/joentr.2017.09.00293

Palacios, G. C., Montalvo, M. S., Fraire, M. I., Leon, E., Alvarez, M. T., & Solorzano, F. (2008). Audiologic and vestibular findings in a sample of Human Immunodeficiency Virus type-1-infected Mexican children under Highly Active Antiretroviral Therapy. *International Journal of Pediatric Otorhinolaryngology*, *72*(11), 1671–1681. https://doi.org/10.1016/j.ijporl.2008.08.002

Pappas, J. D., Roland, J. J., Lim, J., Lai, A., & Hillman, D. E. (1995). Ultrastructural findings in the vestibular end-organs

of AIDS cases. *The American Journal of Otology*, *16*(2), 140–145.

Podisadlo, D., & Richardson, S. (1991). The Timed “Up & Go”: A Test of Basic Functional Mobility for Frail Elderly Persons. *Journal of the American Geriatrics Society*, *39*(2), 142–148.

Polit, D. F., & Beck, C. T. (2004). *Nursing Research: Principles and Methods* (7th ed.). Connecticut: Lippincott Williams & Wilkins.

Popelka, M. M., Cruickshanks, K. J., Wiley, T. L., Tweed, T. S., Klein, B. E. K., Klein, R., & Nondahl, D. M. (2000). Moderate Alcohol Consumption and Hearing Loss: A Protective Effect. *Journal of the American Geriatrics Society*, *48*(10), 1273–1278.

Rabinowitz, P. M. (2000). Noise-induced hearing loss. *American Family Physician*, *61*(9), 2749–2756. https://doi.org/10.1017/CBO9781107415324.004

Rey, D., L’Heritier, A., & Lang, J. M. (2002). Severe Ototoxicity in a Health Care Worker Who Received Postexposure Prophylaxis with Stavudine, Lamivudine, and Nevirapine after Occupational Exposure to HIV. *Clinical Infectious Diseases*, *34*(3), 418–419.

Richert, L., Brault, M., Mercié, P., Dauchy, F. A., Bruyand, M., Greib, C., … Dehail, P. (2014). Decline in locomotor functions over time in HIV-infected patients. *Aids*, *28*(10), 1441–1449. https://doi.org/10.1097/QAD.0000000000000246

Richert, L., Dehail, P., Mercié, P., Dauchy, F. A., Bruyand, M., Greib, C., … Chêne, G. (2011). High frequency of poor locomotor performance in HIV-infected patients. *Aids*, *25*(6), 797–805. https://doi.org/10.1097/QAD.0b013e3283455dff

Riddler, S. A., Haubrich, R., DiRienzo, G., Peeples, L., Powderly, W. G., Klingman, K. L., … Mellors, J. W. (2008). Class-Sparing Regimens for Initial Treatment of HIV-1 Infection. *The New England Journal of Medicine*, *358*(20), 2095–2106.

Ruwe, S. L., Rossi, A. G., & Simon, L. F. (2005). Balance in the elderly. *Rev Bras Otorhinolaryngolol*, *71*(3).

Salzer, T. A. (1994). Neurotologic Manifestations of HIV infection. Retrieved from http://www.bcm.edu/oto/grand/32494.html

Sandhu, J. S., George, S. R., & Rea, P. A. (2013). The effect of electrode positioning on the ocular vestibular evoked myogenic potential to air-conducted sound. *Clinical Neurophysiology*, *124*(6), 1232–1236.

Scherer, M. R., & Schubert, M. C. (2009). Traumatic Brain Injury and Vestibular Pathology as a Comorbidity After Blast Exposure. *Journal of the American Physical Therapy Association*, *89*(9), 1–13.

Scherz, J., Kallail, K. J., Downs, D., Sweet, D., & Zackula, R. E. (2013). Prevalence of Communication Disorders in HIV-Infected Adults Prevalence of Communication Disorders in HIV-Infected Adults, (November). https://doi.org/10.1177/2325957413510608

Shisana, O, Rehle, T, Simbayi LC, Zuma, K, Jooste, S, Zungu N, Labadarios, D., & Onoya, D. et al. (2014). *South African National HIV Prevalence, Incidence and Behaviour Survey, 2012*.

Shumway-cook, A., Brauer, S., & Woollacott, M. (2000). Predicting the Probability for Falls in Community-Dwelling Older Adults Using the Timed Up & Go Test. *Physical Therapy*, *80*(9), 896–903.

Shumway-Cook, A., & Woollacott, M. H. (1995). Motor Control: Theory and Practical Applications., 614.

Shumway-Cook, A., Woollacott, M., Kerns, K. A., & Baldwin, M. (1997). The Effects of Two Types of Cognitive Tasks on Postural Stability in Older Adults With and Without a History of Falls. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, *52A*(4), M232–M240. https://doi.org/10.1093/gerona/52A.4.M232

Sletvold, O., Tilvis, R., Jonsson, A., Schroll, M., Snaedal, J., Engedal, K., … Gustafson, Y. (1996). Geriatric work-up in the Nordic countries. The Nordic approach to comprehensive geriatric assessment. *The Nordic Approach to Comprehensive Geriatric Assessment.*, *43*(4), 350–359.

Smyth, R. P., & Davenport, M. P. (2012). The origin of genetic diversity in HIV-1. *Virus Research*, *169*(2), 415–429.

Somefun, A., Nwawolo, c c, & Okeowo, P. A. (2001). Otorhinolaryngological manifestations of HIV/AIDS in Lagos. *The Nigerian Postgraduate Medical Journal*, *8*(4), 170–174.

Strode, A., Slack, C., & Essack, Z. (2010). Child consent in south african law: Implications for researchers, service providers and policy-makers. *South African Medical Journal*, *100*(4), 247–249. https://doi.org/10.1080/01639625.2016.1197656

Su, H.-C., Huang, T.-W., Young, Y.-H., & Cheng, P.-W. (2004). Aging Effect on Vestibular Evoked Myogenic Potential. *Otology and Neurotology*, *25*(6), 977–980.

Sulyman, A., Alakija, S., Shuaib, A., Shola, A., Oluwayemisi, O., Leo, O., & Halima, A. (2012). Otologic and audiological evaluations among HIV patients in Ilorin, Nigeria: T003. *Clinical Otolaryngology*, *37*, 130. https://doi.org/10.1111/j.1749-4486.2012.02515.x

Swanepoel, D. W. (2017). Smartphone-based National Hearing, (January).

Swanepoel, D. W., & Louw, B. (2010). *HIV/AIDS related communication, hearing, and swallowing disorders*. San Diego, CA: Plural Pub.

Swanepoel, D. W., Maclennan-Smith, F., & Hall, J. W. (2013). Diagnostic Pure-Tone Audiometry in Schools: Mobile Testing without a Sound-Treated Environment. *Journal of the American Academy of Audiology*, *24*(10), 992–1000. https://doi.org/10.3766/jaaa.24.10.10

Swanepoel, D. W., & Stearn, N. (2010). Sensory and neural auditory disorders associated with HIV/AIDS. In *HIV/AIDS Related Communication, Hearing and Swallowing Disorders* (pp. 243–288). San Diego, CA: Plural Publishing.

Teggi R, Cesarani N, Lira Luce F, Lazzarin A, B. M. (2008). Otoneurological findings in human immunodeficiency virus positive patients. *The Journal of Laryngology & Otology*, *122*(February), 1289–1294. https://doi.org/10.1017/S0022215107001624

Teggi, R., Ceserani, N., Luce, F. L., Lazzarin, A., & Bussi, M. (2008). Otoneurological findings in human immunodeficiency virus positive patients, (November 2007), 1289–1294. https://doi.org/10.1017/S0022215107001624

Teggi, R., Giordano, L., Pistorio, V., & Bussi, M. (2006). Vestibular function in HIV patients: preliminary report. *Acta Otorhinolaryngologica Italica*, *26*(3), 140–146.

Terzian, A. S., Homan, S., Nathwani, N., Robison, E., Weber, K., Young, M., … Gange, S. J. (2010). Factors Associated with Preclinical Disability and Frailty among HIV-Infected and HIV-Uninfected Women in the Era of cART. *Journal of Women's Health*, *18*(12), 1965–1974.

Tianwu, H., Watanabe, Y., Asai, M., Shimizu, K., Takada, S., & Mizukoshi, K. (2009). Effects of Alcohol Ingestion on

Vestibular Function in Postural Control. *Acta-Oto Laryngologica*, *115*(1995), 127–131.

Tran, B. X., Ohinmaa, A., & Nguyen, L. T. (2012). Quality of life profile and psychometric properties of the EQ-5D-5L in HIV / AIDS patients Quality of life profile and psychometric properties of the EQ-5D-5L in HIV / AIDS patients. *Health and Quality of Life Outcomes*, *10*(1), 1. https://doi.org/10.1186/1477-7525-10-132

UNAIDS. (2013). *Getting to zero: HIV in Eastern and Southern Africa*.

UNAIDS. (2018). unaids-data-2018_en.pdf.crdownload.

UNAIDS (Joint United Nations Programme on HIV/AIDS). (2013). *UNAIDS report on the global AIDS epidemic*.

Van der Westhuizen, Y., Swanepoel, D. W., Heinze, B., & Hofmeyr, L. M. (2012). AUDITORY AND OTOLOGICAL MANIFESTATIONS IN ADULTS WITH HIV / AIDS Key words : Human Immune Deficiency Virus (HIV), Acquired Immunodeficiency. *International Journal of Audiology*, *52*, 37–43.

Van Der Westhuizen, Y., Swanepoel, D. W., Heinze, B., & Hofmeyr, L. M. (2013). Auditory and otological manifestations in adults with HIV / AIDS. *International Journal of Audiology*, *52*, 37–43. https://doi.org/10.3109/14992027.2012.721935

Vanspauwen, R., Wuyts, F., Krijger, S., & Maes, L. K. (2017). Comparison of different electrode configurations for the oVEMP with bone-conducted vibration. *Journals.Lww.Com*, *38*(2), 205–211.

Vincenti, V., Pasanisi, E., Bacciu, A., Giardano, D., Di Lella, F., Guida, M., & Bacciu, S. (2005). Cochlear Implantation in a Human Immunodeficiency Virus-Infected Patient. *The Laryngoscope*, *115*(6), 1079–1081. https://doi.org/10.1097/01.MLG.0000163099.01930.C2

Wang, M.-C., & Lee, G.-S. (2007). Vestibular evoked myogenic potentials in middle ear effusion. *Acta Oto-Laryngologica*, *127*(7), 700–704. https://doi.org/10.1080/00016480601002070

Whitney, S., Hudak, M., & Marchetti, G. (2000). The dynamic gait index relates to self-reported fall history in individuals with vestibular dysfunction. *Journal of Vestibular Research*, *10*(2), 99–105.

Whitney, S. L., Marchetti, G. F., Schade, A., & Wrisley, D. (2004). The sensitivity and specificity of the Timed " Up & Go " and the dynamic gait index for self-reported falls in persons with vestibular disorders. *Journal of Vestibular Research*, *14*, 397–409. https://doi.org/Article

Whitney, S., Wrisley, D., & Furman, J. (2003). Concurrent validity of the Berg Balance Scale and the Dynamic Gait Index in people with vestibular dysfunction. *Physiotherapy Research International : The Journal for Researchers and Clinicians in Physical Therapy*, *8*(4), 178–186. https://doi.org/10.1002/pri.288

WHO. (2013). Deafness and Hearing Loss. Retrieved from http://www.who.int/en/news-room/fact-sheets/detail/deafness-and-hearing-loss

WHO, UNICEF, & UNAIDS. (2013). *Global update on HIV treatment 2013: results, impact and opportunities*. Retrieved from http://apps.who.int/iris/handle/10665/85326%5Cnhttp://apps.who.int/iris/bitstream/10665/85326/1/9789241505734_eng.pdf?ua=1

Williamson, C., & Martin, D. P. (2005). HIV genetic diversity. In *In S.S Abdool Karim, & Q. Abdool Karim (Eds.), HIV/AIDS in South Africa* (pp. 109–118). Cambridge: Cambridge University Press.

Wilson, B. S., Tucci, D. L., Merson, M. H., & O'Donoghue, G. M. (2017). Global hearing health care: new findings and

perspectives. *The Lancet*, *390*(10111), 2503–2515. https://doi.org/10.1016/S0140-6736(17)31073-5

World Medical Association. (2013). World Medical Association Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects. *JAMA*, *310*(20), 2191.

Xu, X. Da, Ding, C. R., Yu, J., Han, Z., Gu, J., Gao, N., … Chi, F. L. (2016). The hidden dysfunction of otolithic organs in patients with profound sensorineural hearing loss. *Hearing Research*, *331*, 41–46. https://doi.org/10.1016/j.heares.2015.10.006

Yang, T.-L., & Young, Y.-H. (2007). Vestibular-Evoked Myogenic Potentials in Patients With Otosclerosis Using Air- and Bone-Conducted Tone-Burst Stimulation. *Otology & Neurotology*, *28*(1), 1–6.

Yin, R. K. (2003). *Case Study Research:Design and Methods* (3rd ed.). Thousand Oaks, CA: Sage.

Zapala, D. A., & Brey, R. H. (2004). Clinical Experience with the Vestibular Evoked Myogenic Potential. *Journal of American Academy of Audiology*, *15*(3), 198–215. Retrieved from https://www.ingentaconnect.com/content/aaa/jaaa/2004/00000015/00000003/art00003

Zelman, S. (1973). Correlation of Smoking History With Hearing Loss. *JAMA*, *223*(8), 920–920.

Zuniga, J. (1999). Communication disorders and HIV disease. *Journal of the International Association of Physicians in AIDS Care*, *5*(4), 16–23.

Appendices

Appendix A: World Medical Association Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects

Special Communication

World Medical Association Declaration of Helsinki
Ethical Principles for Medical Research Involving Human Subjects

World Medical Association

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, and amended by the:
29th WMA General Assembly, Tokyo, Japan, October 1975
35th WMA General Assembly, Venice, Italy, October 1983
41st WMA General Assembly, Hong Kong, September 1989
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996
52nd WMA General Assembly, Edinburgh, Scotland, October 2000
53rd WMA General Assembly, Washington, DC, USA, October 2002 (Note of Clarification added)
55th WMA General Assembly, Tokyo, Japan, October 2004 (Note of Clarification added)
59th WMA General Assembly, Seoul, Republic of Korea, October 2008
64th WMA General Assembly, Fortaleza, Brazil, October 2013

Preamble

1. The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data.

   The Declaration is intended to be read as a whole and each of its constituent paragraphs should be applied with consideration of all other relevant paragraphs.

2. Consistent with the mandate of the WMA, the Declaration is addressed primarily to physicians. The WMA encourages others who are involved in medical research involving human subjects to adopt these principles.

General Principles

3. The Declaration of Geneva of the WMA binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act in the patient's best interest when providing medical care."

4. It is the duty of the physician to promote and safeguard the health, well-being and rights of patients, including those who are involved in medical research. The physician's knowledge and conscience are dedicated to the fulfilment of this duty.

5. Medical progress is based on research that ultimately must include studies involving human subjects.

6. The primary purpose of medical research involving human subjects is to understand the causes, development and effects of diseases and improve preventive, diagnostic and therapeutic interventions (methods, procedures and treatments). Even the best proven interventions must be evaluated continually through research for their safety, effectiveness, efficiency, accessibility and quality.

7. Medical research is subject to ethical standards that promote and ensure respect for all human subjects and protect their health and rights.

8. While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects.

9. It is the duty of physicians who are involved in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects. The responsibility for the protection of research subjects must always rest with the physician or other health care professionals and never with the research subjects, even though they have given consent.

10. Physicians must consider the ethical, legal and regulatory norms and standards for research involving human subjects in their own countries as well as applicable international norms and standards. No national or international ethical, legal or regulatory requirement should reduce or eliminate any of the protections for research subjects set forth in this Declaration.

11. Medical research should be conducted in a manner that minimises possible harm to the environment.

12. Medical research involving human subjects must be conducted only by individuals with the appropriate ethics and scientific education, training and qualifications. Research on patients or healthy volunteers requires the supervision of a competent and appropriately qualified physician or other health care professional.

Permission letters

Appendix B: Letter to the Deputy CEO of SBAH- Dr Mangwang

Permission to access Records / Files / Data base at the Steve Biko Academic Hospital

To: Deputy Chief Executive Officer
Steve Biko Academic Hospital
Dr M Mathebula

From: Waseema Mahomed
Department of Speech-Language Pathology and Audiology

Re: Permission to do research at the Infectious Disease Clinic at Steve Biko Academic Hospital

Professor Bart Vinck, Dr Barbara Heinze, Professor Anton Stoltz and I are researchers; I am requesting permission on behalf of us all to conduct a research study using the patients of the Infectious Disease Clinic at Steve Biko Academic Hospital. We will also require access to patient records/files, but we will additionally request their permission in the informed consent document.

The request is lodged with you in terms of the requirements of the Promotion of Access to Information Act. No. 2 of 2000.
The title of the study is: **Audiovestibular Function of HIV Positive Adults**

The researchers request access to the following information:

- Access to the clinical files, record book and the data base of HIV positive patients.
- Patients with HIV/AIDS.

We intend to publish the findings of the study in a professional journal and/ or at professional meeting like symposia, congresses, or other meetings of such a nature.

We intend to protect the personal identity of the patients by assigning each patient a random code number.

We undertake not to proceed with the study until we have received approval from the Faculty of Health Sciences Research Ethics Committee-University of Pretoria.

Yours sincerely,

Waseema Mahomed (Principal Investigator)

BA Audiology Student (University of Pretoria)

PERMISSION TO DO THE ABOVE RESEARCH STUDY AT THIS HOSPITAL AND TO ACCESS THE INFORMATION AS REQUESTED, IS HEREBY APPROVED.

Dr. ~~M Mathebula~~ Date

Deputy Chief Executive Officer
Steve Biko Academic Hospital

GAUTENG PROVINSIALE REGERING
DEPT VAN GESONDHEID
STEVE BIKO AKADEMIESE HOSPITAAL
STEVE BIKO ACADEMIC HOSPITAL
2018 -01- 09
PRIVAATSAK/PRIVATE BAG X160
PRETORIA 0001
GAUTENG PROVINCIAL GOVERNMENT
DEPT OF HEALTH

Hospital Official Stamp

Permission letters

Appendix C: Letter to the Head of the ID Clinic- Prof Anton Stoltz

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Humanities
Department of Speech-Language Pathology and Audiology

LETTER TO REQUEST PERMISSION FROM THE HOSPITAL
Steve Biko Academic Hospital

January 2018

The Infectious Disease Clinic
Steve Biko Academic Hospital
Pretoria

Dear Professor Anton Stoltz,

RE: PERMISSION TO CONDUCT A RESEARCH STUDY

I, Waseema Mahomed (Student number: 13007263; ID number: 9405110100080) will be a post-graduate master's student from the Speech-Language Pathology and Audiology Department, University of Pretoria, in 2018. As per the requirements of the MA (Audiology) degree, I am required to conduct a research project. I hereby request permission to approach patients from the Infectious Disease Clinic at Steve Biko Academic Hospital. If permission is granted, I plan to start with data collection from January 2018.

The title of my study is: **AUDIOVESTIBULAR PROFILE OF HIV POSITIVE ADULTS**

The aim of this study will be to describe the audiovestibular function as well as risk for falls in adults with HIV/AIDS and consequently the effect of the disease on their quality of life. Participants in the experimental group will undergo a single assessment, with an approximate duration of two hours per assessment, that will take place in the Infectious Disease clinic of Steve Biko Academic Hospital. Participants will be required to complete two self-administered questionnaires regarding their vestibular symptoms as well as their own percieved health status, i.e. the Dizziness Handicap Inventory and the EQ-5D-3L Questionnaire respectively. Participants will also undergo auditory assessments (otoscopy, acoustic immittance measurements and pure tone audiometry) and vestibular assessments (vestibular evoked myogenic potentials and video head impulse test) as well as functional balance assessments (dynamic gait index test, berg balance and the timed "Up and Go" test).

Room 3-28, Speech Language and Hearing Clinic,
University of Pretoria, Private Bag X20
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Fax +27 (0)12 420 5678
Email leigh.biagio@up.ac.za
www.up.ac.za

Fakulteit Geesteswetenskappe
Departement Spraak-Taalpatologie en Oudiologie
Lefapha la Bomotho
Kgoro ya Phatholotši ya Polelo-Maleme le Go kwa

I sincerely believe that this research will be of benefit to the field of audiology and HIV management and will allow for evidence based practice which will improve the quality of the services provided.

In order to conduct this study, clinical and outcome data of HIV positive adult patients of the ID clinic will be captured. If permission for this is granted from you as the coordinator of the Infectious Disease Clinic, you are requested to sign this letter of consent.

Please contact me should you require more information. Thank you in advance for your time and cooperation.
Yours sincerely,

Waseema Mahomed
Student Researcher
Tel: 0609718826
Email: *waseemamahomed@yahoo.com*

Prof Bart Vinck
Supervisor
Email: *bvinck.up@gmail.com*

Dr Barbara Heinze
Supervisor
Email: *barbara.heinze@up.ac.za*

PERMISSION FOR THE USE OF INFOMATION OF HIV POSITIVE ADULTS FROM THE INFECTIOUS DISEASE CLINIC (ID) IN STEVE BIKO ACADEMIC HOSPITAL (SBAH)

Herewith I, **Professor Anton Stoltz** give written permission that the researcher may approach patients of the ID clinic and use the information of HIV positive adults from the ID

clinic for the research project titled: *Audiovestibular Profile of HIV Positive Adults.*

Professor Anton Stoltz

Coordinator: Infectious Disease Clinic

Date: 4/12/2017

Faculty of Humanities
Department of Speech-Language Pathology and Audiology
Fakulteit Geesteswetenskappe
Departement Spraak-Taalpatologie en Oudiologie
Lefapha la Bomotho
Kgoro ya Phatholotši ya Polelo-Maleme le Go kwa

Permission letters

Appendix D: Letter to the CEO of TDH- Dr Sasha Nkusi

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Humanities
Department of Speech-Language Pathology and Audiology

LETTER TO REQUEST PERMISSION FROM THE HOSPITAL

Tshwane District Hospital

January 2018

Dr Sasha Nkusi
The Clinical Manager
Tshwane District Hospital
Pretoria

Dear Dr Sasha Nkusi,

RE: APPLICATION FOR PERMISSION TO CONDUCT A RESEARCH STUDY

I, Waseema Mahomed (Student number: 13007263; ID number: 9405110100080) will be a post-graduate master's student from the Speech-Language Pathology and Audiology Department, University of Pretoria, in 2018. As per the requirements of the MA (Audiology) degree, I am required to conduct a research project. I hereby request permission to approach patients from the Tshwane District Hospital. If permission is granted, I plan to start with data collection from January 2018.

The title of my study is: **AUDIOVESTIBULAR PROFILE OF HIV POSITIVE ADULTS ON TREATMENT**

The aim of this study will be to describe the audiovestibular function as well as risk for falls in adults with HIV/AIDS and consequently the effect of the disease on their quality of life. The results of this study can assist researchers in determining the nature and presentation of auditory and vestibular impairments presenting in individuals with HIV/AIDS in comparison to healthy (HIV negative) participants. If a hearing and/or vestibular impairment is identified in participants, a referral to the Department of Speech-Language Pathology and Audiology at the University of Pretoria will be made for further assessment and management.

Fakulteit Geesteswetenskappe
Departement Spraak-Taalpatologie en Oudiologie
Lefapha la Bomotho
Kgoro ya Phatholotši ya Polelo-Maleme le Go kwa

I sincerely believe that this research will be of benefit to the field of audiology and HIV management and will allow for evidence based practice which will improve the quality of the services provided.

In order to conduct this study, clinical and outcome data of HIV positive adult patients of the Tshwane District Hospital will be captured. Please find attached the Access to information form as I will need to obtain information from the patient's files.
If permission for this is granted from you as the CLINICAL MANAGER of Tshwane District Hospital, you are requested to sign this letter of consent.

Please contact me should you require further information. Thank you in advance for your time and cooperation.
Yours sincerely,

Waseema Mahomed
Student Researcher
Tel: 0609718826
Email: *waseemamahomed@yahoo.com*

FOR

Prof Bart Vinck
Supervisor
Email: *bvinck.up@gmail.com*

Prof Anton Stoltz
Supervisor
Email: *anton.stoltz@up.ac.za*

Dr Barbara Heinze
Supervisor
Email: *barbara.heinze@up.ac.za*

PERMISSION TO APPROACH HIV POSITIVE ADULT PATIENTS FROM THE TSHWANE DISTRICT HOSPITAL

Herewith I, **Dr. Sasha Nkusi,** give written permission that the researcher may approach HIV positive adult patients at the Tshwane District Hospital to conduct research for the research project titled: *Audiovestibular Profile of HIV Positive Adults on Treatment.*

Dr. Sasha Nkusi
CLINICAL MANAGER: Tshwane District Hospital

Date: 2018/1/11

Faculty of Humanities
Department of Speech-Language Pathology and Audiology
Fakulteit Geesteswetenskappe
Departement Spraak-Taalpatologie en Oudiologie
Lefapha la Bomotho
Kgoro ya Phatholotši ya Polelo-Maleme le Go kwa

Ethical Permission letters

Appendix E: Faculty of Health Sciences Ethical Approval Letter

The Research Ethics Committee, Faculty Health Sciences, University of Pretoria complies with ICH-GCP guidelines and has US Federal wide Assurance.
- FWA 00002567, Approved dd 22 May 2002 and Expires 03/20/2022.
- IRB 0000 2235 IORG0001762 Approved dd 22/04/2014 and Expires 03/14/2020.

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Health Sciences Research Ethics Committee

9/02/2018

Approval Certificate
New Application

Ethics Reference No: 38/2018

Title: Audiovestibular Profile of HIV positive Adults

Dear Miss Waseema Mahomed

The **New Application** as supported by documents specified in your cover letter dated 8/02/2018 for your research received on the 8/02/2018, was approved by the Faculty of Health Sciences Research Ethics Committee on its quorate meeting of 9/02/2018.

Please note the following about your ethics approval:
- Ethics Approval is valid for 1 year
- Please remember to use your protocol number (**38/2018**) on any documents or correspondence with the Research Ethics Committee regarding your research.
- Please note that the Research Ethics Committee may ask further questions, seek additional information, require further modification, or monitor the conduct of your research.

Ethics approval is subject to the following:
- The ethics approval is conditional on the receipt of **6 monthly written Progress Reports**, and
- The ethics approval is conditional on the research being conducted as stipulated by the details of all documents submitted to the Committee. In the event that a further need arises to change who the investigators are, the methods or any other aspect, such changes must be submitted as an Amendment for approval by the Committee.

We wish you the best with your research.

Yours sincerely

Dr R Sommers; MBChB; MMed (Int); MPharMed,PhD
Deputy Chairperson of the Faculty of Health Sciences Research Ethics Committee, University of Pretoria

The Faculty of Health Sciences Research Ethics Committee complies with the SA National Act 61 of 2003 as it pertains to health research and the United States Code of Federal Regulations Title 45 and 46. This committee abides by the ethical norms and principles for research, established by the Declaration of Helsinki, the South African Medical Research Council Guidelines as well as the Guidelines for Ethical Research: Principles Structures and Processes, Second Edition 2015 (Department of Health).

☎ 012 356 3084 deepeka.behari@up.ac.za / fhsethics@up.ac.za http://www.up.ac.za/healthethics
✉ Private Bag X323, Arcadia, 0007 - Tswelopele Building, Level 4, Room 60 / 61, 31 Bophelo Road, Gezina, Pretoria

Ethical approval letters

Appendix F: Faculty of Health Sciences Amended Ethical Approval Letter

The Research Ethics Committee, Faculty Health Sciences, University of Pretoria complies with ICH-GCP guidelines and has US Federal wide Assurance.
- FWA 00002567, Approved dd 22 May 2002 and Expires 03/20/2022.
- IRB 0000 2235 IORG0001762 Approved dd 22/04/2014 and Expires 03/14/2020.

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Health Sciences Research Ethics Committee

29/03/2018

Approval Certificate
Amendment
(to be read in conjunction with the main approval certificate)

Ethics Reference No: 38/2018

Title: Audiovestibular Profile of HIV positive Adults on treatment

Dear Miss Waseema Mahomed

The **Amendment** as described in your documents specified in your cover letter dated 6/03/2018 received on 7/03/2018 was approved by the Faculty of Health Sciences Research Ethics Committee on its quorate meeting of 28/03/2018.

Please note the following about your ethics amendment:
- Please remember to use your protocol number (**38/2018**) on any documents or correspondence with the Research Ethics Committee regarding your research.
- Please note that the Research Ethics Committe may ask further questions, seek additional information, require further modification, or monitor the conduct of your research.

Ethics amendment is subject to the following:
- The ethics approval is conditional on the receipt of **6 monthly written Progress Reports**, and
- The ethics approval is conditional on the research being conducted as stipulated by the details of all documents submitted to the Committee. In the event that a further need arises to change who the investigators are, the methods or any other aspect, such changes must be submitted as an Amendment for approval by the Committee.

We wish you the best with your research.

Yours sincerely

Dr R Sommers, MBChB; MMed (Int); MPharMed; PhD
Deputy Chairperson of the Faculty of Health Sciences Research Ethics Committee, University of Pretoria

The Faculty of Health Sciences Research Ethics Committee complies with the SA National Act 61 of 2003 as it pertains to health research and the United States Code of Federal Regulations Title 45 and 46. This committee abides by the ethical norms and principles for research, established by the Declaration of Helsinki, the South African Medical Research Council Guidelines as well as the Guidelines for Ethical Research: Principles Structures and Processes, Second Edition 2015 (Department of Health).

☎ 012 356 3084 deepeka.behari@up.ac.za / fhsethics@up.ac.za http://www.up.ac.za/healthethics
✉ Private Bag X323, Arcadia, 0007 - Tswelopele Building, Level 4, Room 60 / 61, 31 Bophelo Road, Gezina, Pretoria

Appendix G: Faculty of Humanities Amended Ethical Approval Letter

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Humanities
Research Ethics Committee

5 March 2018

Dear Ms Mahomed

Project:	**Audio vestibular profile of HIV positive adults**
Researcher:	**W Mahomed**
Supervisors:	**Prof B Vinck, Prof A Stoltz and Dr B Heinze**
Department:	**Speech-Language Pathology and Audiology**
Reference number:	**13007263 (GW20180206HS)**

Thank you for the application that was submitted for ethical consideration.

I am pleased to inform you that the above application was **approved** by the **Research Ethics Committee** at the meeting held on 1 March 2018. 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.

We wish you success with the project.

Sincerely

Prof Maxi Schoeman
Deputy Dean: Postgraduate Studies and Ethics
Faculty of Humanities
UNIVERSITY OF PRETORIA
e-mail:tracey.andrew@up.ac.za

cc: Prof J van der Linder (Acting-HoD)
Prof B Vinck (Supervisor)
Prof A Stoltz (Co-supervisor)
Dr B Heinze (Co-supervisor)

Appendix H: Informed Consent- HIV positive (experimental) group

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Humanities
Department of Speech-Language Pathology and Audiology

March 2018

Dear Participant,

INVITATION TO PARTCICPATE IN A RESEARCH STUDY

I (Waseema Mahomed) would like to invite you to participate in a research study entitled: "Audiovestibular Profile of HIV Positive Adults" from the Department of Speech-Language Pathology and Audiology at the University of Pretoria.

1. Information about the research study

The purpose of this study is to examine the auditory and vestibular (balance) function of HIV positive adults, in comparison to HIV negative individuals. Questionnaires will be used to assess general health as well as any functional, emotional and physical limitations experienced (quality of life). Diagnostic auditory assessments will be used to establish auditory thresholds (hearing ability). Thereafter, Risk for fall tests will be conducted and lastly vestibular evaluations and balance tasks will be conducted to assess balance in all planes of movement. Collectively these tests, evaluations and tasks will establish an audiovestibular profile.

2. Participant candidacy

For this study, participants are required to be HIV positive adults between the ages of 18-45 years. If you consent, I will need to collect all necessary information from your hospital file, for e.g. your HIV status, ARV usage and CD4 cell counts.

3. Requirements from Participants

In this study participants will be required to complete the following tests and actions:

	Test Name	Requirements
PROCEDURES	EQ-5D-5L Questionnaire	Answer and complete the questionnaire regarding the 5 different levels of problems.
	Dizziness Handicap Inventory	Answer and complete the questionnaire in all 3 content domains.
	Otoscopy	You will need to sit still for the duration of the test.
	Acoustic Immitance	You will need to sit still, whilst a soft probe will be placed into your ear. You will feel a slight pressure build up in your ear, please do not talk or swallow whilst the probe is in your ear.
	Pure Tone Audiometry	There will be a series of "beeps" played to you, please press the button every single time you hear the "beep".
	cVEMPs	Your head will be turned to one side while you are lying down/sitting on a chair and you will be required to lift your head towards the side being tested whilst three electrodes will be attached to the skin of your neck.

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	oVEMPs	You will need to look up while lying down/sitting on a chair, whilst three electrodes will be placed on your face around your eyes.
	(v)HIT	You will need to sit on a chair in front of a computer screen and focus on a fixed point, whilst wearing a pair of goggles, during which your head will be rapidly turned in different directions.
	Dynamic Gait Balance	You will be required to walk normally and thereafter walk whilst given certain tasks, such as turning your head to one side.
	Berg Balance	You will be required to balance on one foot whilst performing certain tasks.
	Timed "Up & Go" test	You will be required to be seated, thereafter stand up and walk to a certain point, turn around and walk back to the starting point and be seated once more.

4. Test duration and venue

You will only need to come for testing once and testing will take approximately 90 minutes. All testing will be conducted at the Infectious Disease Clinic (ID) in Steve Biko Academic Hospital and at Tshwane District Hospital, where patients will be invited to participate when visiting the ID clinic.

5. Possible risks and benefits of this study

Participants will not be exposed to any risk or experience any discomfort during this research study. There are no direct benefits for participation in this study. However, the data collected from this study will aid in advancing audiovestibular data in HIV positive individuals.

6. Confidentiality and anonymity

You will be identified by and allocated a random alpha numeric research code, therefore none of your personal identifying information will be known and will be kept strictly confidential during data collection and the reporting of results. If permission is granted by you as the participant, only the researcher and the supervisors will have access to your information. The results of the research study will be stored at the Department of Speech-Language Pathology and Audiology for 15 years.

7. Sharing of Results

The results obtained from this research study will be reported in the form of a scientific article and dissertation, which will be available to professionals in the field of audiology. The results from this research may be used by future researchers. If you would like a summary of the findings of this research study, a copy can be made available to you when the project is complete.

8. Refusal or withdrawal from the research

Participation in this research is entirely voluntary, therefore you may withdraw from the study at any point, should you wish to do so.

9. Has this study received ethical approval?

This study has received written approval from the Research Ethics Committee of the Faculty of Humanities and the Research Ethics Committee of the Faculty of Health Sciences at the University of Pretoria. The contact person of the Ethics Committee for the study is Mrs Manda Smith – 012 356 3085

10. Contact

Should you have any questions or concerns regarding any aspect of this study, please feel free to contact Ms. Mahomed at: Tel: +27 60 971 8826 or via Email at: waseemamahomed@yahoo.com. Alternatively you may

contact my supervisors: Prof. Bart Vinck @: bvinck.up@gmail.com; Dr Barbara Heinze @: barbara.heinze@up.ac.za; Prof. Anton Stoltz @: anton.stoltz@up.ac.za.

11. Consent to participate in this study

I hereby give consent to participate in the research study entitled 'Audiovestibular Profile of HIV Positive Adults' undertaken by Waseema Mahomed. I have also given my consent to the researcher, Waseema Mahomed, to access my hospital file in order for her to acquire all information necessary for the study's testing purposes. I have read and understood the information sheet explaining the purpose of the research study. I have been given the opportunity to ask the researcher questions about the study and I am satisfied that they have been answered satisfactorily. I am aware that data from this study may be used in current and future research. I am aware that participation in this study is entirely voluntary and that I may withdraw from this project, at any time, and this will not alter my medical treatment in any way. I am aware that the results of the study, including personal details, will be anonymously processed in research reports. I am participating willingly.

I have received a signed copy of this agreement.

Participant's Name: _____

(Please print)

Participant's Signature: _____ **Date:** _____

Investigator's name: _____

(Please print)

Investigator's Signature: _____ **Date:** _____

Witness's Name: _____

(Please print)

Witness's Signature: _____ **Date:** _____

Verbal informed consent

I, the undersigned, have read and have fully explained the participant information leaflet, which explains the nature, process, risks, discomforts and benefits of the study, to the participant whom I have asked to participate in the study.

The participant indicates that s/he understands that the results of the study, and that his/her personal details will be anonymously processed into a research report. The participant indicates that s/he has had an

opportunity to ask questions and has no objection to participate in the research study. S/he understands that there is no penalty should s/he wish to discontinue with the study. This withdrawal will have no effect on his/her medical treatment in any way. I hereby certify that the participant has agreed to participate in this study.

Participant's Name _____

(Please print)

Person seeking consent _____

(Please print)

Signature_____ **Date** _____

Witness's name_____

(Please print)

Signature _____ **Date**_____

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Humanities
Department of Speech-Language Pathology and Audiology

March 2018

Dear Participant,

INVITATION TO PARTCICPATE IN A RESEARCH STUDY

I (Waseema Mahomed) would like to invite you to participate in a research study entitled: "Audiovestibular Profile of HIV Positive Adults" from the Department of Speech-Language Pathology and Audiology at the University of Pretoria.

1. Information about the research study

The purpose of this study is to examine the auditory and vestibular (balance) function of HIV positive adults, in comparison to HIV negative individuals. Diagnostic auditory assessments will be used to establish auditory thresholds (hearing ability). Thereafter, Risk for fall tests will be conducted and lastly vestibular evaluations and balance tasks will be conducted to assess balance in all planes of movement. Collectively these tests, evaluations and tasks will establish an audiovestibular profile.

2. Participant candidacy

For this study, HIV negative adults are required to be between the ages of 18-45 years and in overall good general health as well have normal hearing. If you consent, as a participant with an HIV^- status, you are required have underwent/ be willing to undergo an HIV screening. Staff members and students of the University of Pretoria may have the screening done at the University clinic should they wish to do so or use their own medical aids/financial means at their preferred physician or at an alternate clinic of their choice. Friends & family members of the researcher will be required to use their own financial means/medical aids and may be screened at their local clinic, e.g. the local Dischem or Clicks, their preferred physician or at an alternate clinic of their choice. Proof of the aforementioned screening will then be needed to be presented to the researcher before testing can commence. In the event where the screen indicates a positive result, the staff at the clinic/health facility that administered the test will provide counselling to you. Thereafter, if you do still wish to participate in this study, you will be assigned to the experimental (HIV^+) group.

3. Requirements from Participants

In this study participants will be required to complete the following tests and actions:

	Test Name	Requirements
PROCEDURES	EQ-5D-5L Questionnaire	Answer and complete the questionnaire regarding the 5 different levels of problems.
	Dizziness Handicap Inventory	Answer and complete the questionnaire in all 3 content domains.
	Otoscopy	You will need to sit still for the duration of the test.

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	Pure Tone Audiometry	There will be a series of "beeps" played to you, please press the button every single time you hear the "beep".
	cVEMPs	Your head will be turned to one side while you are lying down/sitting on a chair and you will be required to lift your head towards the side being tested whilst three electrodes will be attached to the skin of your neck.
	oVEMPs	You will need to look up while lying down/sitting on a chair, whilst three electrodes will be placed on your face around your eyes.
	(v)HIT	You will need to sit on a chair in front of a computer screen and focus on a fixed point, whilst wearing a pair of goggles, during which your head will be rapidly turned in different directions.
	Dynamic Gait Balance	You will be required to walk normally and thereafter walk whilst given certain tasks, such as turning your head to one side.
	Berg Balance	You will be required to balance on one foot whilst performing certain tasks.
	Timed "Up & Go" test	You will be required to be seated, thereafter stand up and walk to a certain point, turn around and walk back to the starting point and be seated once more.

4. Test duration and venue

You will only need to come for testing once and testing will take approximately 90 minutes. All testing will be conducted at the University of Pretoria, Department of Speech-Language Pathology and Audiology.

5. Possible risks and benefits of this study

Participants will not be exposed to any risk or experience any discomfort during this research study. There are no direct benefits for participation in this study and no reimbursements will be given to participants. However, the data collected from this study will aid in advancing audiovestibular data in HIV positive individuals.

6. Confidentiality and anonymity

You will be identified by and allocated a random alpha numeric research code, therefore none of your personal identifying information will be known and will be kept strictly confidential during data collection and the reporting of results. If permission is granted by you as the participant, only the researcher and the supervisors will have access to your information. The results of the research study will be stored at the Department of Speech-Language Pathology and Audiology for 15 years.

7. Sharing of Results

The results obtained from this research study will be reported in the form of a scientific article and dissertation, which will be available to professionals in the field of audiology. The results from this research may be used by future researchers. If you would like a summary of the findings of this research study, a copy can be made available to you when the project is complete.

8. Refusal or withdrawal from the research

Participation in this research is entirely voluntary, therefore you may withdraw from the study at any point, should you wish to do so.

9. Has this study received ethical approval?

This study has received written approval from the Research Ethics Committee of the Faculty of Humanities and the Research Ethics Committee of the Faculty of Health Sciences at the University of Pretoria. The contact person of the Ethics Committee for the study is Mrs Manda Smith – 012 356 3085

10. Contact

Should you have any questions or concerns regarding any aspect of this study, please feel free to contact Ms. Mahomed at: Tel: +27 60 971 8826 or via Email at: waseemamahomed@yahoo.com. Alternatively you may contact my supervisors: Prof. Bart Vinck @: bvinck.up@gmail.com; Dr Barbara Heinze @: barbara.heinze@up.ac.za; Prof. Anton Stoltz @: anton.stoltz@up.ac.za.

11. Consent to participate in this study

I hereby give consent to participate in the research study entitled 'Audiovestibular Profile of HIV Positive Adults' undertaken by Waseema Mahomed. I have read and understood the information sheet explaining the purpose of the research study. I have been given the opportunity to ask the researcher questions about the study and I am satisfied that they have been answered satisfactorily. I am aware that data from this study may be used in current and future research. I am aware that participation in this study is entirely voluntary and that I may withdraw from this project, at any time. I am aware that the results of the study, including personal details, will be anonymously processed in research reports. I am participating willingly.

I have received a signed copy of this agreement.

Participant's Name: _____

(Please print)

Participant's Signature: _____ **Date:** _____

Investigator's name: _____

(Please print)

Investigator's Signature: _____ **Date:** _____

Witness's Name: _____

(Please print)

Witness's Signature: _____ **Date:** _____

Verbal informed consent

I, the undersigned, have read and have fully explained the participant information leaflet, which explains the nature, process, risks, discomforts and benefits of the study, to the participant whom I have asked to participate in the study.

The participant indicates that s/he understands that the results of the study, and that his/her personal details will be anonymously processed into a research report. The participant indicates that s/he has had an opportunity to ask questions and has no objection to participate in the research study. S/he understands that

there is no penalty should s/he wish to discontinue with the study. This withdrawal will have no effect on his/her medical treatment in any way. I hereby certify that the participant has agreed to participate in this study.

Participant's Name

(Please print)

Person seeking consent

(Please print)

Signature **Date**

Witness's name

(Please print)

Signature **Date**

Appendix J: Dynamic Gait Index (DGI) Score sheet

DYNAMIC GAIT INDEX SCORE SHEET

Randomized participant number: _____
Date of visit: _____

1. Gait level surface _____

Instructions: Walk at your normal speed from here to the next mark (6m)
Grading: Mark the lowest category that applies.

(3) Normal: Walks 6m, no assistive devices, good speed, no evidence for imbalance, normal gait pattern
(2) Mild Impairment: Walks 6m, uses assistive devices, slower speed, mild gait deviations.
(1) Moderate Impairment: Walks 6m, slow speed, abnormal gait pattern, evidence for imbalance.
(0) Severe Impairment: Cannot walk 6m without assistance, severe gait deviations or imbalance.

2. Change in gait speed _____

Instructions: Begin walking at your normal pace (for 2m), when I tell you "go," walk as fast as you can (for 2m). When I tell you "slow," walk as slowly as you can (for 2m).
Grading: Mark the lowest category that applies.

(3) Normal: Able to smoothly change walking speed without loss of balance or gait deviation. Shows a significant difference in walking speeds between normal, fast and slow speeds.
(2) Mild Impairment: Is able to change speed but demonstrates mild gait deviations, or not gait deviations but unable to achieve a significant change in velocity, or uses an assistive device.
(1) Moderate Impairment: Makes only minor adjustments to walking speed, or accomplishes a change in speed with significant gait deviations, or changes speed but has significant gait deviations, or changes speed but loses balance but is able to recover and continue walking.
(0) Severe Impairment: Cannot change speeds, or loses balance and has to reach for wall or be caught.

3. Gait with horizontal head turns _____

Instructions: Begin walking at your normal pace. When I tell you to "look right," keep walking straight, but turn your head to the right. Keep looking to the right until I tell you, "look left," then keep walking straight and turn your head to the left. Keep your head to the left until I tell you "look straight," then keep walking straight, but return your head to the center.

Grading: Mark the lowest category that applies.

(3) Normal: Performs head turns smoothly with no change in gait.

(2) Mild Impairment: Performs head turns smoothly with slight change in gait velocity, i.e., minor disruption to smooth gait path or uses walking aid.

(1) Moderate Impairment: Performs head turns with moderate change in gait velocity, slows down, staggers but recovers, can continue to walk.

(0) Severe Impairment: Performs task with severe disruption of gait, i.e., staggers outside 0.4m path, loses balance, stops, reaches for wall.

4. Gait with vertical head turns _____

Instructions: Begin walking at your normal pace. When I tell you to "look up," keep walking straight, but tip your head up. Keep looking up until I tell you, "look down," then keep walking straight and tip your head down. Keep your head down until I tell you "look straight," then keep walking straight, but return your head to the centre.

Grading: Mark the lowest category that applies.

(3) Normal: Performs head turns smoothly with no change in gait.

(2) Mild Impairment: Performs head turns smoothly with slight change in gait velocity, i.e., minor disruption to smooth gait path or uses walking aid.

1) Moderate Impairment: Performs head turns with moderate change in gait velocity, slows down, staggers but recovers, can continue to walk.

(0) Severe Impairment: Performs task with severe disruption of gait, i.e., staggers outside 0.4m path, loses balance, stops, reaches for wall.

5. Gait and pivot turn _____

Instructions: Begin walking at your normal pace. When I tell you, "turn and stop," turn as quickly as you can to face the opposite direction and stop.

Grading: Mark the lowest category that applies.

(3) Normal: Pivot turns safely within 3 seconds and stops quickly with no loss of balance.

(2) Mild Impairment: Pivot turns safely in > 3 seconds and stops with no loss of balance.

(1) Moderate Impairment: Turns slowly, requires verbal cueing, requires several small steps to catch balance following turn and stop.

(0) Severe Impairment: Cannot turn safely, requires assistance to turn and stop.

6. Step over obstacle ____

Instructions: Begin walking at your normal speed. When you come to the shoebox, step over it, not around it, and keep walking.

Grading: Mark the lowest category that applies.

(3) Normal: Is able to step over the box without changing gait speed, no evidence of imbalance.

(2) Mild Impairment: Is able to step over box, but must slow down and adjust steps to clear box safely.

(1) Moderate Impairment: Is able to step over box but must stop, then step over. May require verbal cueing.

(0) Severe Impairment: Cannot perform without assistance.

7. Step around obstacles _____

Instructions: Begin walking at normal speed. When you come to the first cone (about 2m away), walk around the right side of it. When you come to the second cone (2m past first cone), walk around it to the left.

Grading: Mark the lowest category that applies.

(3) Normal: Is able to walk around cones safely without changing gait speed; no evidence of imbalance.

Berg Balance Scale

The Berg Balance Scale (BBS) was developed to measure balance among older people with impairment in balance function by assessing the performance of functional tasks. It is a valid instrument used for evaluation of the effectiveness of interventions and for quantitative descriptions of function in clinical practice and research. The BBS has been evaluated in several reliability studies. *A recent study of the BBS, which was completed in Finland, indicates that a change of eight (8) BBS points is required to reveal a genuine change in function between two assessments among older people who are dependent in ADL and living in residential care facilities.*

Description:
14-item scale designed to measure balance of the older adult in a clinical setting.

Equipment needed: Ruler, two standard chairs (one with arm rests, one without), footstool or step, stopwatch or wristwatch, 15 ft walkway

Completion:

Time: 15-20 minutes

Scoring: A five-point scale, ranging from 0-4. "0" indicates the lowest level of function and "4" the highest level of function. Total Score = 56

Interpretation:
41-56 = low fall risk
21-40 = medium fall risk
0 –20 = high fall risk

A change of 8 points is required to reveal a genuine change in function between 2 assessments.

Berg Balance Scale

Name: _____ Date: _____

Location: _____ Rater: _____

ITEM DESCRIPTION	SCORE (0-4)
Sitting to standing	_____
Standing unsupported	_____
Sitting unsupported	_____
Standing to sitting	_____
Transfers	_____
Standing with eyes closed	_____
Standing with feet together	_____
Reaching forward with outstretched arm	_____
Retrieving object from floor	_____
Turning to look behind	_____
Turning 360 degrees	_____
Placing alternate foot on stool	_____
Standing with one foot in front	_____
Standing on one foot	_____

Total _____

GENERAL INSTRUCTIONS

Please document each task and/or give instructions as written. When scoring, please record the lowest response category that applies for each item.

In most items, the subject is asked to maintain a given position for a specific time. Progressively more points are deducted if:

- the time or distance requirements are not met
- the subject's performance warrants supervision
- the subject touches an external support or receives assistance from the examiner

Subject should understand that they must maintain their balance while attempting the tasks. The choices of which leg to stand on or how far to reach are left to the subject. Poor judgment will adversely influence the performance and the scoring.

Equipment required for testing is a stopwatch or watch with a second hand, and a ruler or other indicator of 2, 5, and 10 inches. Chairs used during testing should be a reasonable height. Either a step or a stool of average step height may be used for item # 12.

Berg Balance Scale

SITTING TO STANDING
INSTRUCTIONS: Please stand up. Try not to use your hand for support.
( ) 4 able to stand without using hands and stabilize independently
( ) 3 able to stand independently using hands
( ) 2 able to stand using hands after several tries
( ) 1 needs minimal aid to stand or stabilize
( ) 0 needs moderate or maximal assist to stand

STANDING UNSUPPORTED
INSTRUCTIONS: Please stand for two minutes without holding on.
( ) 4 able to stand safely for 2 minutes
( ) 3 able to stand 2 minutes with supervision
( ) 2 able to stand 30 seconds unsupported
( ) 1 needs several tries to stand 30 seconds unsupported
( ) 0 unable to stand 30 seconds unsupported

If a subject is able to stand 2 minutes unsupported, score full points for sitting unsupported. Proceed to item #4.

SITTING WITH BACK UNSUPPORTED BUT FEET SUPPORTED ON FLOOR OR ON A STOOL
INSTRUCTIONS: Please sit with arms folded for 2 minutes.
( ) 4 able to sit safely and securely for 2 minutes
( ) 3 able to sit 2 minutes under supervision
( ) 2 able to able to sit 30 seconds
( ) 1 able to sit 10 seconds
( ) 0 unable to sit without support 10 seconds

STANDING TO SITTING
INSTRUCTIONS: Please sit down.
( ) 4 sits safely with minimal use of hands
( ) 3 controls descent by using hands
( ) 2 uses back of legs against chair to control descent
( ) 1 sits independently but has uncontrolled descent
( ) 0 needs assist to sit

TRANSFERS
INSTRUCTIONS: Arrange chair(s) for pivot transfer. Ask subject to transfer one way toward a seat with armrests and one way toward a seat without armrests. You may use two chairs (one with and one without armrests) or a bed and a chair.
( ) 4 able to transfer safely with minor use of hands
( ) 3 able to transfer safely definite need of hands
( ) 2 able to transfer with verbal cuing and/or supervision
( ) 1 needs one person to assist
( ) 0 needs two people to assist or supervise to be safe

STANDING UNSUPPORTED WITH EYES CLOSED
INSTRUCTIONS: Please close your eyes and stand still for 10 seconds.
( ) 4 able to stand 10 seconds safely
( ) 3 able to stand 10 seconds with supervision
( ) 2 able to stand 3 seconds
( ) 1 unable to keep eyes closed 3 seconds but stays safely
( ) 0 needs help to keep from falling

STANDING UNSUPPORTED WITH FEET TOGETHER
INSTRUCTIONS: Place your feet together and stand without holding on.
( ) 4 able to place feet together independently and stand 1 minute safely
( ) 3 able to place feet together independently and stand 1 minute with supervision
( ) 2 able to place feet together independently but unable to hold for 30 seconds
( ) 1 needs help to attain position but able to stand 15 seconds feet together
( ) 0 needs help to attain position and unable to hold for 15 seconds

Berg Balance Scale continued…

REACHING FORWARD WITH OUTSTRETCHED ARM WHILE STANDING
INSTRUCTIONS: Lift arm to 90 degrees. Stretch out your fingers and reach forward as far as you can. (Examiner places a ruler at the end of fingertips when arm is at 90 degrees. Fingers should not touch the ruler while reaching forward. The recorded measure is the distance forward that the fingers reach while the subject is in the most forward lean position. When possible, ask subject to use both arms when reaching to avoid rotation of the trunk.)
( ) 4 can reach forward confidently 25 cm (10 inches)
( ) 3 can reach forward 12 cm (5 inches)
( ) 2 can reach forward 5 cm (2 inches)
( ) 1 reaches forward but needs supervision
( ) 0 loses balance while trying/requires external support

PICK UP OBJECT FROM THE FLOOR FROM A STANDING POSITION
INSTRUCTIONS: Pick up the shoe/slipper, which is in front of your feet.
( ) 4 able to pick up slipper safely and easily
( ) 3 able to pick up slipper but needs supervision
( ) 2 unable to pick up but reaches 2-5 cm(1-2 inches) from slipper and keeps balance independently
( ) 1 unable to pick up and needs supervision while trying
( ) 0 unable to try/needs assist to keep from losing balance or falling

TURNING TO LOOK BEHIND OVER LEFT AND RIGHT SHOULDERS WHILE STANDING
INSTRUCTIONS: Turn to look directly behind you over toward the left shoulder. Repeat to the right. (Examiner may pick an object to look at directly behind the subject to encourage a better twist turn.)
( ) 4 looks behind from both sides and weight shifts well
( ) 3 looks behind one side only other side shows less weight shift
( ) 2 turns sideways only but maintains balance
( ) 1 needs supervision when turning
( ) 0 needs assist to keep from losing balance or falling

TURN 360 DEGREES
INSTRUCTIONS: Turn completely around in a full circle. Pause. Then turn a full circle in the other direction.
( ) 4 able to turn 360 degrees safely in 4 seconds or less
( ) 3 able to turn 360 degrees safely one side only 4 seconds or less
( ) 2 able to turn 360 degrees safely but slowly
( ) 1 needs close supervision or verbal cuing
( ) 0 needs assistance while turning

PLACE ALTERNATE FOOT ON STEP OR STOOL WHILE STANDING UNSUPPORTED
INSTRUCTIONS: Place each foot alternately on the step/stool. Continue until each foot has touched the step/stool four times.
( ) 4 able to stand independently and safely and complete 8 steps in 20 seconds
( ) 3 able to stand independently and complete 8 steps in > 20 seconds
( ) 2 able to complete 4 steps without aid with supervision
( ) 1 able to complete > 2 steps needs minimal assist
( ) 0 needs assistance to keep from falling/unable to try

STANDING UNSUPPORTED ONE FOOT IN FRONT
INSTRUCTIONS: (DEMONSTRATE TO SUBJECT) Place one foot directly in front of the other. If you feel that you cannot place your foot directly in front, try to step far enough ahead that the heel of your forward foot is ahead of the toes of the other foot. (To score 3 points, the length of the step should exceed the length of the other foot and the width of the stance should approximate the subject's normal stride width.)
( ) 4 able to place foot tandem independently and hold 30 seconds
( ) 3 able to place foot ahead independently and hold 30 seconds
( ) 2 able to take small step independently and hold 30 seconds
( ) 1 needs help to step but can hold 15 seconds
( ) 0 loses balance while stepping or standing

STANDING ON ONE LEG
INSTRUCTIONS: Stand on one leg as long as you can without holding on.
( ) 4 able to lift leg independently and hold > 10 seconds
( ) 3 able to lift leg independently and hold 5-10 seconds
( ) 2 able to lift leg independently and hold ≥ 3 seconds
( ) 1 tries to lift leg unable to hold 3 seconds but remains standing independently.
( ) 0 unable to try of needs assist to prevent fall

( ) TOTAL SCORE (Maximum = 56)

The Timed "Up & Go" Test

Directions

The timed "Up and Go" test measures, in seconds, the time taken by an individual to stand up from a standard arm chair (approximate seat height of 46 cm [18in], arm height 65 cm [25.6 in]), walk a distance of 3 meters (118 inches, approximately 10 feet), turn, walk back to the chair, and sit down. The subject wears their regular footwear and uses their customary walking aid (none, cane, walker). No physical assistance is given. They start with their back against the chair, their arms resting on the armrests, and their walking aid at hand. They are instructed that, on the word "go" they are to get up and walk at a comfortable and safe pace to a line on the floor 3 meters away, turn, return to the chair and sit down again. The subject walks through the test once before being timed in order to become familiar with the test. Either a stopwatch or a wristwatch with a second hand can be used to time the trial.

Instructions to the patient

"When I say 'go' I want you to stand up and walk to the line, turn and then walk back to the chair and sit down again. Walk at your normal pace."

Variations

You may have the patient walk at a fast pace to see how quickly they can ambulate. Also you could have them turn to the left and to the right to test any differences.

*Podsiadlo D, Richardson S. The timed "up and go": a test of basic functional mobility for frail elderly persons. *JAGS* 1991; 39: 142-148.

Scoring

Time for 'Up and Go' test _____sec.
Unstable on turning?
Walking aid used? Type of aid: _____

Appendix M: Feedback Letter-Referral letter for participants

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Humanities
Department of Speech-Language Pathology and Audiology

PARTICIPANT FEEDBACK LETTER

AUDIOVESTIBULAR PROFILE OF HIV POSITIVE ADULTS

Participant: _____

Date of assessment: _____

Clinic: _____

Dear Participant,

Thank you for participating in the above mentioned research study.

The following tests were performed:

Auditory evaluation

Otoscopic Examination
Tympanometry
Acoustic Reflex Measurements
Pure tone audiometry

Vestibular evaluation

Cervical Vestibular Evoked Myogenic Potentials (cVEMPs)
Ocular Vestibular Evoked Myogenic Potentials (oVEMPs)
Video Head Impulse Test

Fall risk tests

Dynamic Gait Index
The Berg Balance Scale

The timed up and go test

Considering the test results obtained, it is recommended that you visit an:

- ☐ Audiologist at Steve Biko Academic Hospital/University of Pretoria for a diagnostic hearing evaluation
- ☐ Audiologist at University of Pretoria for further vestibular testing
- ☐ Ear Nose and Throat Specialist/General Practitioner
- ☐ Psychologist/ Psychiatrist
- ☐ Other

Reasons for referral

_____

_____

_____

Kind Regards,

_____

Waseema Mahomed
(Student Researcher)

Appendix N: Feedback Letter- Pass letter for participants

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Humanities
Department of Speech-Language Pathology and Audiology

PARTICIPANT FEEDBACK LETTER

AUDIOVESTIBULAR PROFILE OF HIV POSITIVE ADULTS

Participant: _____

Date of assessment: _____

Clinic: _____

Dear Participant,

Thank you for participating in the above mentioned research study.

The following tests were performed:

Auditory evaluation

Otoscopic Examination
Tympanometry
Acoustic Reflex Measurements
Pure tone audiometry

Vestibular evaluation

Cervical Vestibular Evoked Myogenic Potentials (cVEMPs)
Ocular Vestibular Evoked Myogenic Potentials (oVEMPs)
Video Head Impulse Test

Fakulteit Geesteswetenskappe
Departement Spraak-Taalpatologie en Oudiologie
Lefapha la Bomotho
Kgoro ya Phatholotši ya Polelo-Maleme le Go kwa

Fall risk tests

Dynamic Gait Index
The Berg Balance Scale
The timed up and go test

Based on the test results obtained, we are pleased to inform you that you have passed the auditory and vestibular tests and will not need any further assessment. We would however recommend an annual diagnostic hearing evaluation to ensure that your hearing and balance remains in optimal condition.

Kind Regards,

_____

Waseema Mahomed
(Student Researcher)

Appendix O: Principal Investigator(s) Declaration for the storage of research data and/or documents

Protocol No. 38/2018

Principal Investigator's Declaration for the storage of research data and/or documents

I, the Principal Investigator, Waseema Mahomed, of the following study titled **AUDIOVESTIBULAR PROFILE OF HUMAN IMMUNODEFICIENCY VIRUS POSITIVE ADULTS**

---

will be storing all the research data and/or documents referring to the above mentioned study at the following non-residential address:

Department of Speech-Language Pathology and Audiology
University of Pretoria
Corner of Lynwood Road and Roper Street
Hatfield
Pretoria
South Africa

I understand that the storage for the abovementioned data and/or documents must be maintained for a minimum of 15 years from the end of this study.

START DTATE OF TRIAL/SUDY: January 2018

END DATE OF TRIAL/STUDY: September 2018

UNTIL WHICH YEAR WILL DATA BE STORED: 2033

Name: Dr Barbara Heinze

Signature: 

Date: 04 December 2017

Appendix P: Calculation of Power Analysis

6 February 2018

To whom it may concern

This is to confirm that a power analysis was performed by me. This was done in order to determine the minimum sample size required for the study. More details regarding the analysis is given below.

Details relating statistical analysis:

In order to determine the minimum sample size required for the study, the following information is needed:

- Anticipated effect size (Cohen's d) = 0.8
- Desired statistical power level = 0.8
- Probability level = 0.05

The motivation for the setting Cohen's d equal to 0.8, the desired statistical power equal to 0.8 and the probability level equal to 0.05 is given below.

Cohen (1988) reasoned that studies should be designed to have a minimum of 80% power. Here is how he got to the value of 80%.

A Type I error is the incorrect rejection of a true null hypothesis. Thus, this is when the researcher rejects the null hypothesis, but the null hypothesis was true.

A Type II error is incorrectly retaining a false null hypothesis. Thus, this is when the researcher does not reject the hull hypothesis, but the null hypothesis is false.

Obviously, the researcher would like the probability of a Type I error and the probability of Type II error to be small, respectively.

α = P(Type I error) = 0.05
β = P(Type II error) = 0.2

How were the values for α and β chosen?

The value of α should be decided by the researcher beforehand and, typically, α = 0.05 is used in literature, meaning that the researcher allows for a probability of 0.05 that a true null hypothesis is incorrectly rejected.

Cohen (1988) argued that most researchers view the Type I error as being four times more serious

the Type II error. Thus, if α is set at 0.05, then β should be set at 0.2.

Then, by definition statistical power is calculated by subtracting β from 1 (power = 1 - β), so the minimum power of test should be 1 – 0.2 = 0.8.

This only leaves the choice for Cohen's *d*. This is motivated next.

Cohen's d / Cohen's effect size	Classification	Meaning
0.2	Small effect size	There is a small change, but one can only see it through careful study
0.5	Medium effect size	A medium change – in between small and large.
0.8	Large effect size	A big change that is really substantial. A large effect size is an effect that is big enough and/or consistent enough that you can see it 'with the naked eye'

Since the researcher expects there to be a large difference between her controlled and experimental groups (as the controlled is supposed to exhibit normal test results and the experimental abnormal and to worsen as the virus progresses), a Cohen's d value of 0.8 was selected.

Finally, the pre-selected values (Cohen's d equal to 0.8, the desired statistical power equal to 0.8 and the probability level equal to 0.05) can be entered into any statistical package that is equipped to handle a power analysis (SPSS being one of these), and the output read as follows:
A minimum total sample size of 52 is needed for a two-tailed hypothesis. This means that the researcher will need a minimum of 26 in each group.

References: Cohen, J. (1988). Statistical power analysis for the behavioral sciences 2nd edn.

Dr MA Graham
PhD (Mathematical Statistics), University of Pretoria
Phone: +27 (0) 12 420 6637
e-mail: marien.graham@up.ac.za

Faculty of Education
Fakulteit Opvoedkunde
Lefapha la Thuto

Appendix Q: Data Collection Sheet- HIV positive Group

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Humanities
Department of Speech-Language Pathology and Audiology

AUDIOVESTIBULAR FUNCTION IN ADULTS WITH HIV/AIDS

Data Capturing sheet for HIV positive participants

Date of visit:
Randomized participant no.:
Cell phone number 1:
Cell phone number 2:
Age:
Gender:
Male □ Female □
Duration of ART usage:

CD4⁺ cell count:

Any other Co-morbid diseases/disorders:

List of any medications being taken:
_____
_____
_____
_____
_____

Smoking: _____
Alcohol Abuse: _____
History/ current continuous noise exposure (occupational or recreational):

RESULTS

1. *OTOSCOPY*

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Departement Spraak-Taalpatologie en Oudiologie
Lefapha la Bomotho
Kgoro ya Phatholotši ya Polelo-Maleme le Go kwa

RESULTS

1. *OTOSCOPY*

Left ear:
Right ear:

2. *ACCOUSTIC IMMITANCE MEASUREMENTS*

Tympanometry:

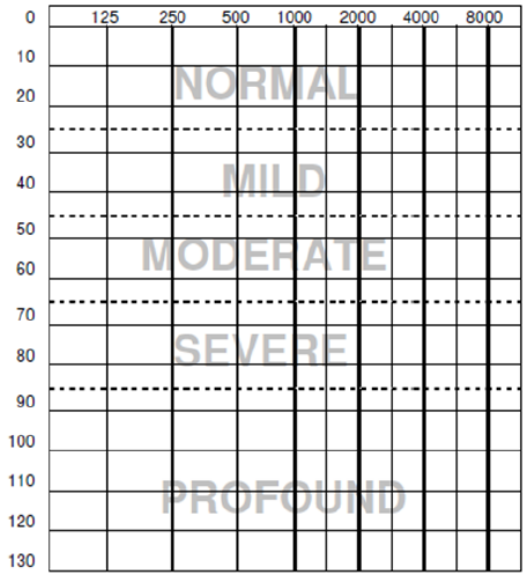
LEFT EAR:	RIGHT EAR:
Tympanogram type:	Tympanogram type:
Ear canal pressure:	Ear canal pressure:
Static compliance:	Static compliance:
Ear canal volume:	Ear canal volume:

Acoustic reflex measurements

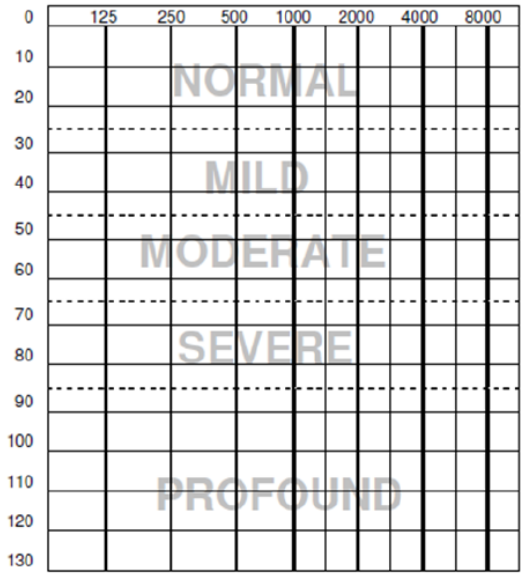
LEFT EAR:	RIGHT EAR:
Reflex present at 500Hz:	Reflex present at 500Hz:
Reflex present at 1000Hz:	Reflex present at 1000Hz:
Reflex present at 2000Hz:	Reflex present at 2000Hz:
Reflex present at 4000Hz:	Reflex present at 4000Hz:

3. *PURE TONE AUDIOMETRY*

Regteroor / Right Ear



Linkeroor / Left Ear



4. *DYNAMIC GAIT INDEX*

Total score: _____/24

5. *THE BERG BALANCE SCALE*

Total Score: _____/56

6. *THE TIMED "UP & GO" TEST*

Time for "Up & Go" test _____sec
Unstable on turning?
Walking aid used? Type of aid: _____

7. VESTIBULAR EVOKED MYOGENIC POTENTIALS

Cervical Vestibular Evoked Myogenic Potentials (cVEMPs):

Ear	P1 latency (ms)	N1 latency (ms)	Inter-peak amplitude (μV)	Asymmetry ratio (%)	Normal (N) Abnormal (A)
Left					
Right					

Ocular Vestibular Evoked Myogenic Potentials (oVEMPs):

Ear	N1 latency (ms)	P1 latency (ms)	Inter-peak amplitude (μV)	Asymmetry ratio (%)	Normal (N) Abnormal (A)
Left					
Right					

8. *VIDEO HEAD IMPULSE TEST (vHIT):*

Canal	Gain	Covert saccades	Overt saccades	Normal (N) Abnormal (A)
Left lateral				
Right lateral				
Left anterior				
Right posterior				
Right anterior				
Left posterior				

Appendix R: Data Collection Sheet- HIV negative Group

AUDIOVESTIBULAR FUNCTION IN ADULTS WITHOUT HIV/AIDS

Data Capturing sheet for HIV negative participants

Date of visit:
Randomized participant no.:
Cell phone number 1:
Cell phone number 2:
Age:
Gender:
Male □ Female □
Medications:
Alcohol Abuse:
Smoking:
History/current continuous noise exposure (occupational/recreational):

RESULTS

1. *OTOSCOPY*

Left ear:
Right ear:

2. *ACCOUSTIC IMMITANCE MEASUREMENTS*

Tympanometry:

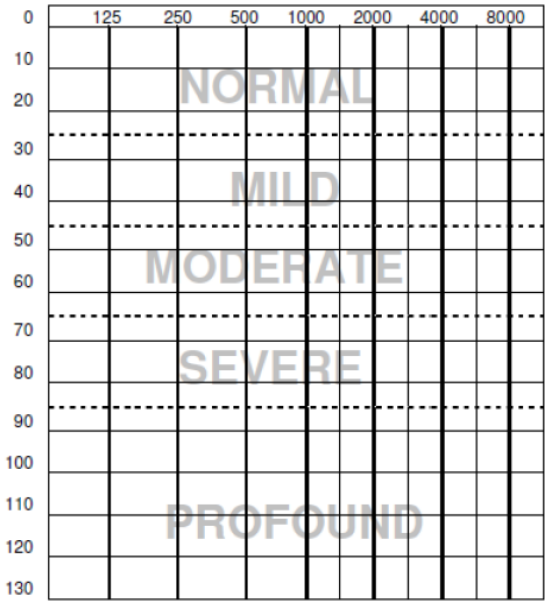
LEFT EAR:	RIGHT EAR:
Tympanogram type:	Tympanogram type:
Ear canal pressure:	Ear canal pressure:
Static compliance:	Static compliance:
Ear canal volume:	Ear canal volume:

Acoustic Reflex Measurements:

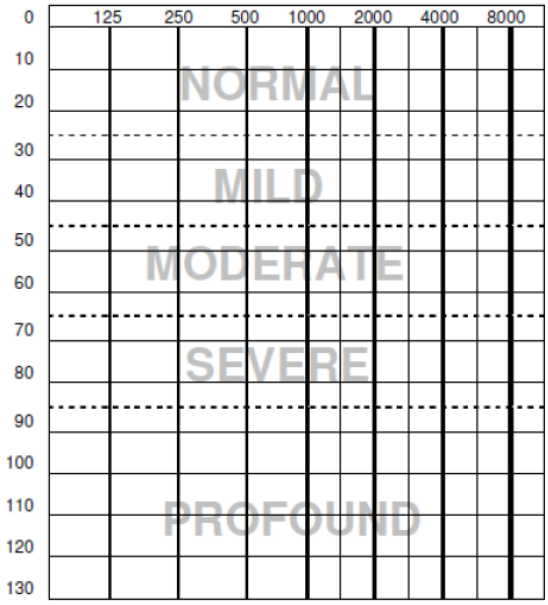
LEFT EAR:	RIGHT EAR:
Reflex present at 500Hz:	Reflex present at 500Hz:
Reflex present at 1000Hz:	Reflex present at 1000Hz:
Reflex present at 2000Hz:	Reflex present at 2000Hz:
Reflex present at 4000Hz:	Reflex present at 4000Hz:

3. *PURE TONE AUDIOMETRY*

Regteroor / Right Ear



Linkeroor / Left Ear



4. *DYNAMIC GAIT INDEX*

Total score: _____/24

5. *THE BERG BALANCE SCALE*

Total Score: _____/56

6. *THE TIMED "UP & GO" TEST*

Time for "Up & Go" test _____sec
Unstable on turning?
Walking aid used? Type of aid: _____

7. *VESTIBULAR EVOKED MYOGENIC POTENTIALS:*

Cervical Vestibular Evoked Myogenic Potentials (cVEMPs):

Ear	P1 latency (ms)	N1 latency (ms)	Inter-peak amplitude (μV)	Asymmetry ratio (%)	Normal (N) Abnormal (A)
Left					
Right					

Ocular Vestibular Evoked Myogenic Potentials (oVEMPs):

Ear	N1 latency (ms)	P1 latency (ms)	Inter-peak amplitude (µV)	Asymmetry ratio (%)	Normal (N) Abnormal (A)
Left					
Right					

8. VIDEO HEAD IMPULSE TEST (vHIT):

Canal	Gain	Covert saccades	Overt saccades	Normal (N) Abnormal (A)
Left lateral				
Right lateral				
Left anterior				
Right posterior				
Right anterior				
Left posterior				

Appendix S: Health Related Quality of Life (EQ-5D-5L) Questionnaire

Health Questionnaire

English version for the UK

Under each heading, please tick the ONE box that best describes your health TODAY.

MOBILITY

I have no problems in walking about ❑
I have slight problems in walking about ❑
I have moderate problems in walking about ❑
I have severe problems in walking about ❑
I am unable to walk about ❑

SELF-CARE

I have no problems washing or dressing myself ❑
I have slight problems washing or dressing myself ❑
I have moderate problems washing or dressing myself ❑
I have severe problems washing or dressing myself ❑
I am unable to wash or dress myself ❑

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*

I have no problems doing my usual activities ❑
I have slight problems doing my usual activities ❑
I have moderate problems doing my usual activities ❑
I have severe problems doing my usual activities ❑
I am unable to do my usual activities ❑

PAIN / DISCOMFORT

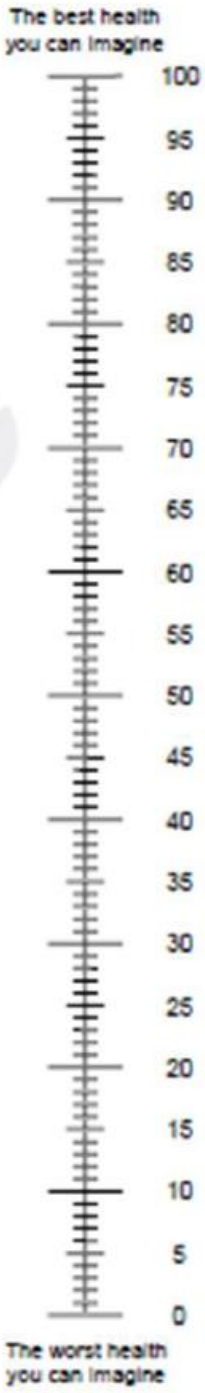
I have no pain or discomfort ❑
I have slight pain or discomfort ❑
I have moderate pain or discomfort ❑
I have severe pain or discomfort ❑
I have extreme pain or discomfort ❑

ANXIETY / DEPRESSION

I am not anxious or depressed ❑
I am slightly anxious or depressed ❑
I am moderately anxious or depressed ❑
I am severely anxious or depressed ❑
I am extremely anxious or depressed ❑

- We would like to know how good or bad your health is TODAY.
- This scale is numbered from 0 to 100.
- 100 means the best health you can imagine.
  0 means the worst health you can imagine.
- Mark an X on the scale to indicate how your health is TODAY.
- Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY = ☐



Appendix T: Letter of Clearance from the Biostatistician- Dr MA Graham

Date: 23/01/2018

LETTER OF CLEARANCE FROM THE BIOSTATISTICIAN

This letter is to confirm that the student(s), with the Name(s): ***Waseema Mahomed***

Studying at the ***University of Pretoria***

discussed the Project with the title:

"Audiovestibular Profile of HIV positive Adults" *with me.*

I hereby confirm that I am aware of the project and also undertake to assist with the Statistical analysis of the data generated from the project.

The analytical tool that will be used will be: **a power analysis by making use of SPSS**

to achieve the objective(s) of the study.

Name: **Dr MA Graham** Date: **23/01/2018**

Signature: Graham Tel: **012 420 6637**

Department or Unit: **Previously employed at the Department of Statistics, University of Pretoria, 2004 – 2013; holds a PhD in Mathematical Statistics. Currently employed at the Faculty of Education, University of Pretoria.**

Official Stamp of Biostatistician