

https://dspace.org/

Running head: vestibular function in adults with HIV

Millar, Alison

2018

https://hdl.handle.net/10539/26552

Millar, Alison (2018) Running head : vestibular function in adults with HIV, University of the Witwatersrand, Johannesburg, https://hdl.handle.net/10539/26552

Downloaded from a DSpace repository. https://dspace.org/

Vestibular function in adults with HIV

Alison Millar

Submitted in partial fulfilment of the requirements for the degree

Masters in Audiology

Discipline of Speech Pathology and Audiology

School of Human Community Development

Faculty of Humanities

University of the Witwatersrand

Johannesburg

March 2018

Declaration

I, Alison Millar, declare that this dissertation is my own work and has not been submitted, in whole or in part, for any other degree or qualification. All literature and research from other authors have been referenced accordingly, whilst the assistance received is summarized in the acknowledgements of this report.

Signature: _____ Date: _____

Acknowledgements

I am grateful to all those whom I have had the pleasure to work with during this research project.

Firstly, I would like to thank Dr Karin Joubert, my research supervisor. I am grateful for your encouragement throughout this project and reminding me that research is a process. Thank you for your editorial care and improvements to the layout of this report. All your input and academic expertise have enabled me to present my research in a comprehensive and systematic format.

My special gratitude goes to Dr Alida Naude, my second research supervisor, who worked actively to ensure that I was proficient in conducting the HIMP procedure. Thank you for sharing your passion and in-depth vestibular knowledge, for your valuable guidance and prompt feedback throughout this project. I am also grateful for the arrangements you made with Otometrics to use the vHIT system for this study.

To the Ndlovu Wits Audiology Clinic, thank you for covering the expenses related to the insurance and consumables of the test equipment and allowing me to use the audiology department. I also extend my thanks to the research assistants for their input during data collection. To the rest of the Ndlovu staff, thank you for considering me as part of the team.

I gratefully acknowledge the support of my family, especially my father and fiancé, for their mindful listening and unconditional love and support.

Finally to all the participants, thank you for your time and contribution to this study.

Abstract

Auditory disturbances in HIV-positive individuals have been reported in the literature. Although ample research is available regarding hearing impairment in HIV-positive individuals, there is a lack of research on the effects of this virus on the vestibular system. The aim of this study was therefore to describe the audiological and peripheral vestibular characteristics of a group of HIV-positive individuals and to compare these findings with those of a group of HIV-negative individuals.

A non-experimental, descriptive, cross-sectional research design was employed for the purpose of this study. Purposive sampling was used to recruit the two participant groups. The first participant group (n_1) included 60 HIV-positive individuals (mean age = 41.4 years; ± 5.3; range: 23-50) whilst the second participant group (n_2) included 32 HIV-negative individuals (mean age = 32.5 years; ± 9.1; range: 18-50). The clinical test protocol for both groups consisted of: case history, the Activities-specific Balance Confidence (ABC) scale, otoscopy, tympanometry, pure tone audiometry, and the head impulse test paradigm (HIMP). The findings indicate a significantly higher occurrence of tinnitus in the HIV-positive participant group compared to the control group. However, no significant differences were found between the two participant groups in respect of the remainder of the test battery.

In conclusion, results from this study suggest that HIV does not seem to affect higher frequencies of the vestibulo-ocular reflex (VOR) pathway. However, as comparable fall risk and audiological results were also found between the two groups, the similar results may be attributed to new ARV guidelines and effective management. A strong agreement was found between the ABC scores and the HIMP in both participant groups.

Keywords: Balance, inner ear, semi-circular canals, vestibular function, tinnitus, quality of life (QoL), human immunodeficiency virus (HIV), activities-specific balance

confidence (ABC) scale, video head impulse test (vHIT), head impulse test paradigm (HIMP).

Table of contents

Declaration ii

Acknowledgements iii

Abstract iv

Table of contents vi

List of tables xi

List of figures xii

List of appendices xiii

Chapter 1: Orientation 1

Introduction 1

Background 1

Rationale 4

List of abbreviations and acronyms 7

Chapter outlines 9

Chapter 2: Literature review 10

Introduction 10

The human immunodeficiency virus 10

Progressive stages of infection 11

HIV treatment 14

Prevalence of HIV globally 14

Prevalence of HIV in South Africa 16

Hearing and balance 20

Anatomical overview of the auditory and vestibular apparatus 20

Effects of HIV on hearing and balance 22

Vestibular impairment and QoL 30

Central and peripheral vestibular impairment 31

Balance function tests 35

Summary 43

Chapter 3: Methodology 45

Introduction 45

Research aims 45

Main aim 45

Sub-aims 45

Research design 46

Research context 47

Research phases 47

Pilot study 48

Main study 52

Data collection measures, material, and equipment 61

Data collection procedures 69

Participant recruitment 69

Research assistants 69

Test protocol 70

File review 70

Data capturing 70

Ethical considerations 71

Permission 71

Informed consent 71

Autonomy 71

Beneficence and non-maleficence 72

Confidentiality and anonymity 72

Reliability and validity 72

Reliability 72

Validity 74

Data analysis 76

Chapter 4: Results 77

Introduction 77

Audiological characteristics of the two participant groups 77

Self-reported auditory symptoms 77

Tinnitus 78

Otoscopy 81

Tympanometry 83

Pure tone audiometry 83

Prevalence of hearing loss 85

Hearing loss and tinnitus prevalence compared to previous studies 85

Balance characteristics of the two participant groups 91

Self-perceived balance confidence level (ABC scale) 91

HIMP 93

Prevalence of reduced semi-circular canal function (anterior, posterior and lateral SCCs) and its afferent neural pathways 97
Agreement between the ABC scores and the HIMP results 101
Chapter 5: Discussion 102
Introduction 102
Auditory symptoms and audiological characteristics 102
Prevalence of hearing loss 104
Balance characteristics 105
Subjective measure 105
Objective measure 106
Prevalence of reduced semi-circular canal function (anterior, posterior and lateral SCCs) and its afferent neural pathways 107
Agreement between the ABC scores and the HIMP results 109
Summary 109
Chapter 6: Conclusion 111
Introduction 111
Summary of the research findings 111
Critical evaluation of the study 111
Strengths 111
Limitations 112
Implications 112
Clinical implications 112
Policy implications 113
Recommendations for future research 114

References....117

Appendices....145

List of tables

Table 1: CDC clinical categories: Clinical categories based on co-morbid condition 11

Table 2: CDC classification system: CD4+ T-lymphocyte categories 13

Table 3: The pilot study objectives, procedures, results, and recommendations 49

Table 4: Participant selection criteria: Participant group 1 (n_1 = 60) 54

Table 5: Participant selection criteria: Participant group 2 (n_2 = 32) 56

Table 6: Hearing and balance measures, equipment/material, procedures, and norms 61

Table 7: Lateral and vertical HIMP procedure 66

Table 8: Statistical procedures 76

Table 9: Otoscopy and tympanometry results 82

Table 10: Pure tone audiometry 84

Table 11: Comparison of prevalence of hearing loss and tinnitus in the current study with previous studies 86

Table 12: Auditory results and associated history of HIV-positive participants presenting with hearing loss 88

Table 13: ABC scale results 92

Table 14: HIMP results 94

Table 15: Mean VOR gains and asymmetries of the HIMP 96

Table 16: Balance results and associated history of HIV-positive participants with balance impairment 99

List of figures

Figure 1: Acute unilateral vestibular lesion in the left lateral SCC 42

Figure 2: Gender distribution of HIV-positive and HIV-negative participants 57

Figure 3: Age distribution of HIV-positive and HIV-negative participants 58

Figure 4: Distribution of HIV-positive participants across various CDC categories 59

Figure 5: Various ARV protocols used by HIV-positive participants 59

Figure 6: Head movements to assess the lateral SCCs via horizontal head movements and movements in the vertical canals 68

Figure 7: Prevalence and type of auditory symptoms reported by HIV-positive and HIV-negative participants. 78

Figure 8: Visual illustration of auditory characteristics of HIV-positive participants ($n_1 = 60$) and HIV-negative participants ($n_2 = 32$). 80

List of appendices

Appendix A: Comparison of balance assessment scales and questionnaires 145

Appendix B: The Activities-specific Balance Confidence (ABC) Scale (Powell & Myers, 1995) 151

Appendix C: The Zulu translated ABC scale (Kamanji, 2016) 152

Appendix D: Ndlovu study advert 153

Appendix E: Data collection form 154

Appendix F: Participant informed consent form 159

Appendix G: Ndlovu Case history form 160

Appendix H: Human Research Ethics Committee (Medical) approval letter 163

Appendix I: Ndlovu Medical Centre approval letter 164

Appendix J: Limpopo Department of Health and Social Development approval letter 165

Appendix K: Participant information sheet 166

Appendix L: Booth calibration certificate 2016 169

Appendix M: Booth calibration certificate 2017 170

Appendix N: Interacoustics tympanometer and audiometer (Titan) calibration certificate (2016-2017) 171

Appendix O: Amtronix tympanometer (Madsen Otoflex) calibration certificate 2016 172

Appendix P: Amtronix tympanometer (Madsen Otoflex) calibration certificate 2017 173

Chapter 1: Orientation

Introduction

In this chapter the theoretical background and rationale for this study are explained. This is followed by a list of abbreviations and acronyms used throughout this dissertation. The chapter concludes with a short outline of each of the chapters in the study.

Background

The human immunodeficiency virus (HIV) is a world-wide pandemic (Swanepoel & Louw, 2010) and has been regarded as a serious public health threat for many decades (Sharp & Hahn, 2011). Improved access to antiretrovirals (ARVs) and effective treatment protocols have changed HIV from a life-threatening disease to a manageable illness for more people (Deeks, Lewin, & Havlir, 2013). As a result, the life expectancy of more HIV-positive individuals has increased and therefore more emphasis is placed on the general well-being and quality of life (QoL) of these individuals (Swanepoel & Louw, 2010).

HIV gradually compromises the body's immune response and predisposes it to opportunistic infections. The occurrence of various clinical manifestations surrounding the head and neck region is often the first indication of a suppressed immune response (Lacovou, Vlastarakos, Papacharalampous, Kampessis, & Nikolopoulos, 2012; Rzewnicki, Olszewska, & Rogowska-Szadkowska, 2012). As a result of enhanced awareness, reported cases of these manifestations are also increasing (Lasisi, 2005). Current estimates have suggested that 70% to 90% of HIV-positive individuals may develop a head and/or neck manifestation during the course of this infection (Lacovou et al., 2012; Lubbe, 2004). Such manifestations may appear in the head and neck itself, the nose and paranasal sinuses, the oral cavities, and in the form of otological, and neurological complications (Lacovou et al., 2012; Lubbe, 2004). When this disease process affects the auditory and/or vestibular system and its central connections to the brain, hearing and balance impairments may occur (Domenech, Fuste, & Traserra,

1996; Hofmeyr, 2015; Stearn & Swanepoel, 2010). The prevalence of auditory impairments has been reported to be 14% to 75% of HIV-positive individuals (Chandrasekhar et al., 2000; Khoza & Ross, 2002; Prasad, Bhojwani, Shenoy, & Prasad, 2006; Van der Westhuizen, Swanepoel, Heinze, & Hofmeyr, 2013; Zuniga, 1999). Similarly, vestibular involvement has been reported in 15% to 79% of HIV-positive individuals (Heinze, Vinck, Hofmeyr, & Swanepoel, 2014; Kohan, Hammerschlag, & Holliday, 1990).

There is growing evidence that HIV could either directly or indirectly, through opportunistic infections or ototoxic medication, have an adverse effect on the structures of the inner ear (Stearn & Swanepoel, 2010). The inner ear consists of the cochlea, semi-circular canals (SCCs), and vestibule, which are closely connected to each other within the osseous and membranous labyrinth (Bess & Humes, 2009; Hain & Helminski, 2014). Dysfunction in any of these structures may result in auditory symptoms including tinnitus, aural fullness, hearing loss, otalgia, otorrhea (Khoza-Shangase & Van Rie, 2016), and vestibular symptoms including vertigo, dizziness, gait instability, headaches, oscilliopsia, nausea, and disequilibrium (Zingler, Cnyrim, & Jahn, 2007). Any of these symptoms may be debilitating and therefore have a negative impact on QoL (Chandrasekhar et al., 2000).

Despite the shared anatomy and physiology of these two systems, the majority of research studies have focused on and investigated auditory dysfunction in HIV-positive individuals, despite the dearth of information on vestibular dysfunction related to HIV (Heinze, Swanepoel, & Hofmeyr, 2011). One explanation for this scarcity may include the lack of monitoring protocols. Unlike cochleotoxicity, no standardized test protocol has been accepted in order to monitor vestibulotoxicity (Schellack & Naude, 2012). Another possible explanation may be attributed to the lack of a single vestibular assessment that can accurately identify subtle vestibular impairments; resulting in researchers often wanting to use extended test batteries, which as a result of the impaired state of many patients, are not ideal (Rogers &

Petersen, 2011). Furthermore, the lack in research can also be explained by the perception that a hearing loss may be far more debilitating than an impairment associated with balance function (Harris & Heinze, 2013); therefore, the effects of vestibular impairment are underestimated as they may negatively influence an individuals' ability to work, lead to social isolation, and potentially contribute toward the development of depression (Khoza-Shangase & Van Rie, 2016; Monzani, Casolari, Guidetti, & Rigaletti, 2001; Whitney & Rossi, 2000).

Research has found that both central and peripheral vestibular impairments may occur throughout the HIV progressive stages of infection (Castello, Baroni, & Pallestrini, 1998; Hausler, Vibert, Koralnik, & Hirschel, 1991; Heinze et al., 2014; Teggi, Ceserani, Luce, Lazzarin, & Bussi, 2008; Teggi, Giordano, Pistorio, & Bussi, 2006). A higher prevalence of central vestibular involvement at more progressive stages of infection has been reported (Castello et al., 1998; Teggi et al., 2008; Teggi et al., 2006). However, controversy exists regarding peripheral vestibular function in HIV-positive individuals. Some studies have suggested no involvement of this system (Castello et al., 1998; Cohen et al., 2012), whilst a more recent study reported that peripheral vestibular impairment was the most prevalent finding in their HIV study sample (Heinze et al., 2014).

Various test procedures have been identified in order to evaluate peripheral labyrinthine function (Hain, 2012); however, the majority of studies conducted on HIV-positive individuals have utilized the caloric test procedure (Castello et al., 1998; Grimaldi et al., 1993; Hausler et al., 1991; Heinze et al., 2014; Mathews, Albert, & Job, 2012; Teggi et al., 2008; Teggi et al., 2006). The caloric test assesses lateral SCC and superior vestibular nerve function (Jacobson & Newman, 1997). Thus, a large portion of the labyrinth is not tested. Furthermore, this test does not provide information regarding physiologic head movements (Petrak, Bahner, & Beck, 2013) therefore, vestibular function used during everyday activities is not assessed.

Rationale

The epidemiology of HIV and its health outcomes may differ among various regions, populations, and globally (Johnson, Hu, & Dean, 2010; Mondal & Shitan, 2013). This may be attributed to socio-demographic and cultural differences, socio-economic status, and availability of education (Mondal & Shitan, 2013). In addition to these variables, different diagnostic criteria and data gathering techniques used during research may also lead to varying research results (Dickins & Graham, 1990).

As South Africa is largely affected by HIV (Joint United Nations Programme on HIV/AIDS [UNAIDS], 2016), conducting research on the effects of this virus specific to this region remains crucial.

Hearing abilities in HIV-positive individuals have been well documented, however, a scarcity regarding documentation of vestibular function persists (Heinze et al., 2011; Khoza-Shangase & Van Rie, 2016). Investigating vestibular function in HIV-positive individuals is vital, not only to establish these effects but to promote awareness, and strive toward establishing vestibular monitoring, and rehabilitation programmes; thereby, limiting effects of vestibulopathy on QoL.

The majority of studies have included the caloric test procedure to evaluate labyrinthine function in HIV-positive individuals (Castello et al., 1998; Grimaldi et al., 1993; Hausler et al., 1991; Heinze et al., 2014; Mathews et al., 2012; Teggi et al., 2008; Teggi et al., 2006). The selection of this test procedure may be attributed to research indicating that a peripheral impairment may affect lower frequencies of the vestibulo-ocular reflex (VOR) before higher frequencies (McCaslin, Dundas, & Jacobson, 2008). The VOR consists of low and high frequencies which represent different information regarding peripheral vestibular function. The purpose of these frequencies is better understood as detection or discrimination thresholds. Detection thresholds (low frequencies) provide information regarding stationary

head positions, whilst discrimination thresholds (high frequencies) are responsible for relaying information whilst the head is in motion. Therefore balance impairment, which may be associated with falls and in-motion tasks, is better represented by discrimination thresholds. Thus, these higher frequencies provide information regarding balance during real-life situations (Chang et al., 2014). In the light of this information, the limitation of the caloric test should not be overlooked, as this low-frequency test (0.003 Hz) does not resemble physiologic head movements (Eza-Nuñez, Fariñas-Alvarez, & Perez-Fernandez, 2014; Petrak et al., 2013). Therefore, these results do not accurately represent the effect of a peripheral vestibular impairment on an individual's everyday activities. For this reason, it is not surprising that information regarding lower VOR frequencies is also poorly correlated with symptoms of balance impairment (Baloh, Ying, & Jacobson, 2003). Furthermore, the caloric test is able to evaluate each labyrinth separately, however, the peripheral focus of this test is the lateral SCCs and superior vestibular nerve function (Jacobson & Newman, 1997). Thus, the function of the anterior and posterior SCCs, as well as the inferior vestibular nerve is not evaluated. Despite the limitations of the caloric test, this procedure, used in otologic practice since 1942 (Yetişer & Ince, 2017), was one of the first available tests to accurately assess peripheral vestibular function. Therefore, due to established protocols and ample available literature, this test is still widely used.

Some studies have utilized higher frequency test procedures which better represent head movements of everyday life, such as the head impulse test (5 Hz) (Heinze et al., 2014; Teggi et al., 2008). However, this measurement remains subjective to the clinicians' interpretation and covert, more subtle catch-up saccades may be missed (Curthoys et al., 2011).

A more recent study conducted by Heinze et al. (2014), reported a higher prevalence of peripheral vestibular involvement in HIV-positive subjects. The authors of the study

attributed this finding to the inclusion of the cervical vestibular evoked myogenic potential test (cVEMP), which is sensitive to peripheral vestibular function.

There is a dearth of information regarding the peripheral vestibular function in HIV-positive individuals as measured with the HIMP. This measure is sensitive to peripheral vestibular impairment and also evaluates all six SCCs and their afferent neural pathways (Barin, 2014a). As this procedure evaluates real-world frequencies (3–5 Hz) in an objective manner (Petrak et al., 2013; Redondo-Martínez et al., 2016), the effect of a peripheral impairment during everyday activities may be quantified with greater precision.

In the light of these facts, the purpose of the current study was to describe the audiological and peripheral vestibular characteristics of HIV-positive individuals, and to compare these findings with those of a group of HIV-negative individuals (control group).

This was achieved by answering the following research questions:

i) What are the audiological characteristics of HIV-positive individuals compared to those of HIV-negative individuals (control group)?

ii) What is the prevalence of hearing loss in HIV-positive individuals compared to that of HIV-negative individuals (control group)?

iii) What are the balance characteristics of HIV-positive individuals compared to those of HIV-negative individuals (control group), as determined via subjective (ABC scale) and objective (HIMP) measures?

iv) What is the prevalence of HIV-positive individuals and HIV-negative individuals (control group) who present with a dysfunction of the SCCs and their afferent neural pathways?

v) What is the agreement between the ABC scale and the HIMP?

List of abbreviations and acronyms

3TC	Lamivudine
ABC scale	Activities-specific balance confidence scale
ABC	Abacavir
ABR	Auditory brainstem response
AIDS	Acquired immune deficiency syndrome
ART	Antiretroviral treatment
ARV	Antiretroviral
AZT	Zidovudine
CD 4+	Cluster of differentiation 4+
CDC	Center for Disease Control and Prevention
CNS	Central nervous system
cVEMP	Cervical vestibular evoked myogenic potential
d4T	Stuvadine
dB HL	Decibels hearing level
DGI	Dynamic Gait Index
EFV	Efavirenz
FTC	Emtricitabine
HAART	Highly active antiretroviral therapy
HIMP	Head impulse test paradigm
HIV	Human immunodeficiency virus
Hz	Hertz
ICF	International Classification of Functioning, Disability and Health
kHz	Kilohertz

LARP	Left Anterior- Right Posterior
LL	Left lateral
LP	Left posterior
LPV/r	Lopinavir/low dose ritonavir
MDR TB	Multi-drug resistant tuberculosis
ms	Milliseconds
NMC	Ndlovu Medical Centre
NVP	Nevirapine
OAE	Oto-acoustic emission
oVEMP	Ocular vestibular evoked myogenic potential
PTA	Pure tone average
QoL	Quality of life
RALP	Right Anterior- Left Posterior
SCC	Semi-circular canal
SHIMP	Suppression Head Impulse test
SNHL	Sensory neural hearing loss
TB	Tuberculosis
TDF	Tenofovir
VCR	Vestibulocollic reflex
vHIT	video head impulse test
VOR	Vestibulo-ocular reflex
VSR	Vestibulospinal reflex
WHO	World Health Organization
XDR TB	Extensively drug-resistant tuberculosis

Chapter outlines

This research is presented in six chapters:

Chapter 1 provides an overview of the current literature and emphasizes the need for the current study. This chapter also includes a list of abbreviations used in this report as well as the chapter outlines.

Chapter 2 provides a discussion of HIV including the progressive stages of infection and prevalence of HIV. The anatomy of the auditory and vestibular mechanism is reviewed and studies investigating the effects of HIV on the auditory and vestibular system are critically discussed. Finally, a subjective as well as objective balance assessment is discussed.

Chapter 3 provides the aims of the current study, the research design, and research context. This chapter also contains a systematic description of the various research phases including the pilot study and the main study. The measures, material, and equipment used as well as the data collection procedures are also discussed. Furthermore, the ethical considerations as well as various types of reliability and validity relevant to the current study are reviewed. This chapter concludes with the data analysis employed.

Chapter 4 presents the results in accordance with the sub-aims of the current study. All results from the various tests are presented in tables and figures for ease of interpretation.

Chapter 5 provides a critical discussion regarding the results and relates these findings to previous studies.

In Chapter 6 the conclusion of the current study is presented, the critical reflection, as well as implications, and recommendations for future research.

Chapter 2: Literature review

"We live in a completely interdependent world,

which simply means we cannot escape each other.

How we respond to AIDS depends, in part,

on whether we understand this interdependence.

It is not someone else's problem.

This is everybody's problem."

– Bill Clinton

Introduction

In this chapter the reader is guided through literature relevant to this study. Specific aspects that are discussed include: HIV pathophysiology, progressive stages of infection, treatment, and HIV prevalence. This is followed by a description of the anatomical overview of the auditory and vestibular system; the effects of HIV on the hearing and balance system; as well as a subjective and objective test to assess vestibular function. Lastly, a brief summary of the rationale is provided.

The human immunodeficiency virus

HIV is well-known for its pervasive effects on the immune system and if not treated effectively, this virus may result in the development of acquired immune deficiency syndrome (AIDS). This virus targets and destroys the white blood cells of the immune system, known as cluster of differentiation 4 cells (CD4+) or T-lymphocytes (T-cells). Extensive destruction of CD4 + T-lymphocytes may result in impairment of cell-mediated immune responses. This impairment increases an individual's susceptibility toward certain opportunistic infections, atypical cancers, and other severe clinical manifestations (World Health Organization, [WHO], 2015). As the number of CD4+ T-lymphocytes decreases, the severity of these complications worsens (WHO, 2015). After confirming a positive HIV

diagnosis, various categories are used in order to determine the stage of infection, to select appropriate treatment, and to monitor the effectiveness of management (WHO, 2007a).

Progressive stages of infection

In the absence of effective treatment and management, an HIV-positive individual may transition through various progressive stages of infection (WHO, 2007a). Two classification systems are most commonly used in order to determine the HIV disease stage and appropriate medical management. These two systems are the staging suggested by the WHO and that suggested by the Center for Disease Control and Prevention (CDC). In the WHO classification system, staging is determined merely by the presence of specific clinical conditions or symptoms (WHO, 2007a). Similar to the WHO system, the CDC classification system, revised in 1993, additionally classifies HIV according to the presence of specific co-morbid conditions. These conditions are presented in Table 1.

Table 1

CDC clinical categories: Clinical categories based on co-morbid condition

CDC Classification System for HIV Infected Adults and Adolescents	
Clinical category	**Conditions**
A	• Asymptomatic: Acute HIV or persistent generalized lymphadenopathy (PGL)

B	• Conditions that are attributed to HIV infection or indicate a defect in cell-mediated immunity
	• Conditions that are considered to have a clinical course or management that is complicated by HIV infection. Examples include, but are not limited to, the following:
	  • Bacillary angiomatosis
	  • Oropharyngeal candidiasis (thrush)
	  • Vulvovaginal candidiasis, persistent or resistant
	  • Pelvic inflammatory disease (PID)
	  • Cervical dysplasia (moderate or severe)/cervical carcinoma in situ

CDC Classification System for HIV Infected Adults and Adolescents	
Clinical category	**Conditions**
C	• Bacterial pneumonia, recurrent (two or more episodes in 12 months) • Candidiasis of the bronchi, trachea, or lungs • Candidiasis, oesophageal • Cervical carcinoma, invasive, confirmed by biopsy • Coccidioidomycosis, disseminated or extrapulmonary • Cryptococcosis, extrapulmonary • Cryptosporidiosis, chronic intestinal (>1 month in duration) • Cytomegalovirus disease (other than liver, spleen, or nodes) • Encephalopathy, HIV-related • Herpes simplex: chronic ulcers (>1 month in duration), or bronchitis, pneumonitis, or esophagitis • Histoplasmosis, disseminated or extrapulmonary • Isosporiasis, chronic intestinal (>1-month in duration) • Kaposi sarcoma • Lymphoma, Burkitt, immunoblastic, or primary central nervous system • Mycobacterium avium complex (MAC) or Mycobacterium kansasii, disseminated or extrapulmonary • Mycobacterium tuberculosis, pulmonary or extrapulmonary • Mycobacterium, other species or unidentified species, disseminated or extrapulmonary • Pneumocystis jiroveci (formerly carinii) pneumonia (PCP) • Progressive multifocal leukoencephalopathy (PML) • Salmonella septicemia, recurrent (nontyphoid) • Toxoplasmosis of brain • Wasting syndrome caused by HIV (involuntary weight loss >10% of baseline body weight) associated with either chronic diarrhoea (two or more loose stools per day for ≥1 month) or chronic weakness and documented fever for ≥1 month

Note. Adapted from CDC (1992)

In addition to categories based on the individual's history of other co-morbidities, the CDC classification system also includes additional categories based on the CD4+ T-lymphocyte count (CDC, 1992). These categories are presented in Table 2. Individuals who had met the clinical criteria for category A3, B3 or C1 to C3, have progressed to the final progressive stage of infection, known as AIDS. Once individuals have met the specific criteria for one of these categories, they cannot transition back to another category at a later stage. Therefore, individuals who were diagnosed with mycobacterium tuberculosis (TB) will remain in category C even after full recovery from TB (CDC, 1992).

Table 2

CDC classification system: CD4+ T-lymphocyte categories

CDC Classification System for HIV-Infected Adults and Adolescents			
CD4* cell count	**Clinical categories**		
	A: Asymptomatic Acute HIV or PGL	**B: Symptomatic Conditions, not A or C**	**C: AIDS-Indicator Conditions**
(1) ≥500 cells/μL	A1	B1	C1
(2) 200-499 cells/μL	A2	B2	C2
(3) <200 cells/μL	A3	B3	C3

Note. Adapted from CDC (1992); CD 4* = cluster of differentiation 4+; μL = microliter

Similar to the categories based on co-morbid conditions, individuals will remain in the category which represents their lowest recorded CD4+ T-lymphocyte count (CDC, 1992). Although the WHO system had been revised in 2007, the majority of previous studies investigating vestibular function in HIV-positive individuals utilized the CDC classification system. Therefore this system was also used for the current study, in order to compare the results to previous studies which had utilized the same classification system.

Although no cure currently exists for HIV, this condition can be managed and progression thereof suppressed through the use of ARVs (WHO, 2007a).

HIV treatment

During 2002, the WHO published the initial antiretroviral treatment (ART) guidelines for HIV-positive adults and adolescents. Since 2013 however, various changes to these guidelines have been suggested including: i) earlier treatment initiation of HIV-positive individuals, ii) providing life-long treatment to all HIV-positive individuals irrespective of CD4 count; iii) the use of safer and more effective ARV drugs; and iv) the inclusion of more cost-effective treatment options for low- and middle-income countries (WHO, 2015; WHO, 2016).

HIV-positive individuals are generally treated with a protocol consisting of three or more ARV drugs which control viral replication within the body, permitting the immune system to regain function in order to combat infections (WHO, 2015). This combination of various ARVs is known as highly active antiretroviral therapy (HAART). With effective management and treatment, HIV-positive individuals can increase both their QoL and life expectancy. ARVs can also change the disease prognosis, limit the clinical progression, and alter this virus from a critical disease to a manageable condition (Deeks et al., 2013).

HIV research and treatment have received more global funds than any other single disease in history (Amico, Aran, & Avila, 2010; Institute for Health Metrics and Evaluation, [IHME], 2016). The large expenditure on this disease is not unexpected considering the prevalence estimates.

Prevalence of HIV globally

HIV has been regarded as a global pandemic since 1981 (Sharp & Hahn, 2011). This virus has infected 76.1 million people globally and 35 million mortalities have been attributed to complications associated with HIV (UNAIDS, 2017a).

Mortality associated with HIV has decreased to 1 million in 2016 compared to 1.9 million in 2005 (UNAIDS, 2017a). This decline may be attributed to ARV access, which has increased over the years. During 2010, 7.7 million HIV-positive individuals had access to treatment, compared to 17.1 million in 2015, reaching a peak of 20.9 million in 2017 (UNAIDS, 2017a). Although mortality figures suggest improved treatment outcomes, incidence rates remain suboptimal. As HIV can only be managed and not cured, these high incidence rates contribute to the increased prevalence.

In 2016, the global prevalence of HIV-positive individuals was reported as 36.7 million (UNAIDS, 2017a). Of this total, an average of 2.1 million adults (1.8 million – 2.4 million) were newly diagnosed cases. This incidence rate has not declined since 2010, as an estimated 1.9 million newly diagnosed cases have been reported annually (UNAIDS, 2017a). These unaltered incidence rates may be attributed to individuals being unaware of their HIV status and therefore, with no behavioural changes being implemented, transmission of the virus to HIV-negative individuals continues. This was confirmed by a Russian study conducted during 2010, which found that in a cohort of HIV-positive injection drug users, 64% (n = 123) were unaware of their HIV status (Niccolai et al., 2010). More recent global statistics, however, suggest that remarkable progress has been made toward increased awareness, as an estimated 70% (range: 51% - 84%) of all HIV-positive individuals were aware of their HIV status in 2016 (UNAIDS, 2017b).

Another explanation for the high incidence pertains to the difficulty of addressing social aspects and certain high-risk-behaviours associated with HIV transmission. These aspects include i) factors which deter individuals from disclosing their HIV status, such as stigma and discrimination, ii) cultural beliefs and misconceptions regarding HIV and ARV treatment, and iii) high-risk behaviours (e.g. HIV-positive individuals sleeping with multiple partners without the use of protection) (Cloete et al., 2010). These topics are more difficult to

confront compared to medical treatment and scientific intervention (Chin, 2007). Therefore, many HIV programmes and organizations place higher emphasis on the management of HIV as opposed to changing human behaviours, which may take decades or even generations to implement (Chin, 2007).

A region which has contributed significantly to the high HIV global prevalence, is sub-Saharan Africa (UNAIDS, 2017b). This region has the highest prevalence worldwide with an estimated 25.5 million HIV-positive individuals (UNAIDS, 2017b). Of this total, 19.4 million live in Eastern and Southern Africa.

Prevalence of HIV in South Africa

HIV prevalence in South Africa has gradually increased from 4.02 million in 2002 (Statistics South Africa [SSA], 2015a) to 7.1 million in 2016 (UNAIDS, 2016). Setswe (2016) argues that this increase represents progress rather than failure, indicating successful implementation and expansion of ARV programmes. South Africa has made significant progress regarding universal ARV access, with an estimated 56% accessing ARVs in 2016 (UNAIDS, 2016) compared to less than 30% in 2006 (WHO, 2007b). This increase in treatment coverage has also resulted in fewer HIV-related mortalities, which have been reduced by 29% since 2010 (UNAIDS, 2016).

Despite this progress, the HIV prevalence in South Africa (7.1 million) remains high (UNAIDS, 2016). This may be attributed to various factors, including poverty (Steinert, Cluver, Melendez-Torres, & Romero, 2016), geographical isolation, lack of education, and stigmatization (Food and Agriculture Organization of the United Nations [FAO], 2017; Michel & Matlakala, 2013; Michel, Matlakala, English, Lessells, & Newell, 2013; Mogotlane, Chauke, Van Rensburg, Human, & Kganakga, 2010).

The relationship between HIV and poverty has been described as bi-directional, as poverty may fuel HIV transmission, whilst the HIV diagnosis may exaggerate poverty (FAO,

2017). In adult-headed households, poverty may be intensified by HIV as a result of absenteeism from work (Sonnenberg et al., 2011). In addition, the income earned by these individuals may often be spent on medical expenses associated with HIV, as well as burial costs of family members, instead of livelihood necessities (Limpopo Provincial Treasury [LP Treasury], 2012). Many individuals affected by poverty may also reside in remote areas where access to services is limited. As a result of the remote location and vast distances to treatment facilities, transport may be unaffordable and therefore access and adherence to treatment protocols remain problematic (Cohen, 2006; FAO, 2017). These remote locations also complicate the ability to reach communities with regard to awareness programmes and thus prevention of transmission to HIV-negative individuals is compromised.

One of the poverty related characteristics in South Africa includes a low level of education (Tladi, 2006). When relating this statement to the prevalence of HIV, this may be attributed to child-headed households, where minors are forced to become the main family-provider as a result of adult mortalities associated with HIV. Therefore, school attendance may be sacrificed in order to provide a livelihood for their families, or to assist an adult member with household duties (Mogotlane et al., 2010). As these minors are not exposed to HIV awareness, knowledge regarding this virus and the transmission thereof may be limited.

Many communities may also habitually stigmatise HIV as the consequence of reprehensible behaviour (Azia, Mukumbang, & Van Wyk, 2016; Ganyaza-Twalo & Seager, 2005; Cloete et al., 2010). Such stigmas and discrimination may result in resistance to HIV testing, intervention, and disclosure of HIV status to partners (Cloete et al., 2010).

A study conducted by Cloete et al. (2010) investigated these stigmas via group discussions with community members in and around Cape Town townships. In one of these discussions, the following statements were made by HIV-positive women:

> My mother had AIDS and they said that she was sleeping around and she was drinking a lot… I think in the rural areas they still have that mentality that the person was sleeping around… She has AIDS, she has AIDS, she is a slut. (2010, p. 3).

It is clear that stigmatization and the poverty cycle remain central to the high HIV prevalence in this region. South Africa is still largely affected by income inequality among its population, with 55.5% (30.4 million people) affected by poverty in 2015 (SSA, 2015b). Therefore, HIV may be more prevalent in specific areas within this country. One such region is the Sekhukhune district in the Limpopo province. In this district, the majority of its residents live in rural areas and are affected by poverty (Greater Sekhukhune District Municipality Profile [GSDMP], 2011).

HIV prevalence in the Sekhukhune district (Limpopo)

The Sekhukhune district, one of five districts in the Limpopo province, consists of five local municipalities, namely Elias Motsoaledi, Ephraim Mogale, Fetakgomo, Greater Tubatse, and Makhuduthamaga (SSA, 2016). This district is home to an estimated 1, 169 762 people (SSA, 2016). The unemployment rate in this district (51.6%) (Census, 2011) is the highest in Limpopo (SSA, 2016) and subsequently poverty is high (67.99%) (GSDMP, 2011). There is also a lack of adequate infrastructure such as sanitation and water supply (Census, 2011; GSDMP, 2011; SSA, 2016).

Agriculture and mining are two of the main driving forces of income in the Sekhukhune district (Mafora & Anim, 2014). However, due to a lack of amenities (water supply), agriculture may not always be a sufficient means to cover living expenses (Integrated Development Plan [IDP], 2017). Although job opportunities in the mining sector exist, many of these positions require skilled workers, which exclude a majority of the local population (GSDMP, 2011; IDP, 2017).

Lack of education has been a major concern in this district. According to the census conducted in 2011, 20.9% (117 121) of residents received no formal education, 21.0% (117 725) finished high school, whilst only 5.2% (29 270) obtained a tertiary qualification (Census, 2011). Most recent figures only reported on the number of residents who had obtained a high school qualification, which was estimated at 16.6% (193 632) in 2016 (SSA, 2016).

In addition to unemployment and poverty, this district is also known for its constant inward migration from other provinces to fill mining positions. For this reason the majority of men residing in the Sekhukhune district have migrated outward seeking employment in urban areas (IDP, 2017). Therefore, the majority of this district consists of a female population (621 299) compared to males (548 463) (SSA, 2016).

The influx of male workers increases the risk of new HIV cases in this district, as separation from spouses, family members, and socio-cultural norms, may make these individuals more vulnerable to adopting high-risk sexual behaviours (Collinson, Wolff, Tollman, & Kahn, 2006; Gillespie, 2008; Lurie, 2000). Furthermore, reaching these individuals in terms of prevention strategies and treatment may also be more challenging, as many are employed on a contractual basis and therefore move to various sites or locations (Barnighausen, Hosegood, Timaeus, & Newell, 2007).

All these factors have attributed to high HIV prevalence in this district. However, efforts involving prevention campaigns and awareness have made a positive impact on HIV prevalence. In this district, HIV prevalence was estimated at 16.6% in 2009, 20.2% during 2010, and 18.9% in 2011 (LP Treasury, 2012); it should be noted however, that the majority of statistics regarding HIV prevalence are obtained from antenatal clinics and do not necessarily represent the entire population. Although there has been a decrease in HIV prevalence in this district, these numbers remain alarming.

Despite the high HIV prevalence, provision of health services in this district is still inadequate (SSA, 2016). It has been estimated that for every 17 000 people within this district, there is only one clinic. When considering all the possible secondary complications of HIV, including opportunistic infections or even hearing and balance impairments, the lack of medical facilities is concerning.

Hearing and balance

Anatomical overview of the auditory and vestibular apparatus

The ear is a remarkably complex sensory organ responsible for hearing and the maintenance of balance (Moller, 2013). The ear can be divided into three portions: the outer ear, middle ear, and inner ear. The outer ear consists of the pinna and ear canal. The pinna has two primary functions: i) collecting and guiding sound vibrations into the ear canal; and ii) establishing sound direction (localization). These vibrations are directed into the ear canal, where they are enhanced via natural resonance, and transmitted to the tympanic membrane. The tympanic membrane, a multi-layered structure, separates the outer ear from the middle ear. The middle ear is an air-filled cavity covered by mucous membrane which links the air-filled outer ear to the fluid-filled inner ear. This connection is achieved via three ossicles; the malleus, which is connected to the tympanic membrane, the incus, the intermediate link, and the stapes, which is last in this link and connects to the inner ear via the oval window. Sound vibrations are transmitted through this chain and cause a rocking movement of the stapes against the oval window (Bess & Humes, 2009). This movement results in a pressure build-up of cochlear fluids within the inner ear. Another opening on the inner ear, the round window, is responsible for relieving this pressure. This membranous opening is displaced in an opposite direction of vibrations being directed into the inner ear, ultimately relieving pressure and enabling movement of cochlear fluid. This process is responsible for the creation of sound waves. The inner ear, also known as the labyrinth,

consists of an osseous outer casing, which encloses a membranous labyrinth. The osseous labyrinth consists of the cochlea and vestibular apparatus, responsible for balance. The organ of Corti located in the cochlea, receives, analyses, and separates the sound vibration according to frequency, and utilizes delicate hair cells to transduce this signal into a neural code, which is then transferred to the brain via the auditory nerve (Bess & Humes, 2009; Moller, 2013).

In addition to housing the cochlea, or the primary organ of hearing, the inner ear also controls the body's sense of balance (Bess & Humes, 2009; Moller, 2013). The four osseous landmarks responsible for balance include the three superior, lateral and posterior semi-circular canals (SCCs), and the vestibule (Bess & Humes, 2009), whilst the membranous labyrinth consists of the cochlear ducts, ampullary tissue of the SCCs, as well as the otolith organs (utricle and saccule). The vestibular apparatus, along with the central vestibular system, is responsible for maintaining postural equilibrium (Hain & Helminski, 2014).

The three SCCs and otoliths form the basis of the peripheral vestibular apparatus. The SCCs are linked to the vestibule by a widened bulb at one end, known as the ampulla. Each SCC is named according to its anatomical position (superior, lateral and posterior), and is located in such a way to detect head movements in various planes. These structures are responsible for detecting information regarding angular head movements via hair cells within the ampulla, which are displaced by cochlear fluid (endolymphatic fluid) in response to head movements. In addition, two otolith organs, namely the utricle and saccule, are located within the vestibule. Similar to the SCCs, these structures detect movement consistent with their orientation in space. The utricle is responsible for detecting horizontal head accelerations, whilst the saccule, is responsible for detecting vertical accelerations. Both the SCCs and otoliths relay this information regarding head position to the brain, via central processes (Hain & Helminski, 2014).

The central vestibular pathways, including the cerebellum and vestibular nuclei within the brainstem, combine this input along with other sensory information (such as vision and proprioception) (Harsha, Philips, & Backous, 2008) to determine head and body orientation (Hain & Helminski, 2014). After this information has been processed, the output in the form of motor commands (Goebel, 2008), is received by three important reflexes, the vestibulo-ocular reflex (VOR), the vestibulocollic reflex (VCR), and the vestibulospinal reflex (VSR). The VOR is responsible for generating eye movements, in order to maintain clear vision during head movements, while the VCR controls the neck musculature in order to stabilize the head. Compensatory body movements are generated by the VSR in order to maintain head and postural stability, ultimately preventing an individual from falling. The activities of these three reflexes are continuously monitored by the central nervous system (CNS). This monitoring process enables the cerebellum and other cortical mechanisms to implement changes that are required in order to maintain postural stability (Hain & Helminski, 2014).

As with any other organ systems of the human body, the hearing and balance system may be vulnerable to viral infections, resulting in auditory and vestibular dysfunction (Agrup, Gleeson, & Rudge, 2007; Cohen, Durstenfeld, & Roehm, 2014).

Effects of HIV on hearing and balance

Effects of HIV on the auditory mechanism

Hearing impairment may be unilateral or bilateral and may vary in nature based on the portion of the auditory pathway affected (Stearn & Swanepoel, 2010). Therefore, hearing loss may be conductive, sensory neural, or mixed in nature. For this reason, auditory symptoms may also vary. These symptoms may include: tinnitus, aural fullness, otalgia, otorrhea, and hearing loss (Khoza-Shangase & Van Rie, 2016).

Prevalence of hearing loss in HIV-positive individuals is reported to be between 14% and 29% (Chandrasekhar et al., 2000; Khoza & Ross, 2002; Van der Westhuizen et al.,

2013). Differences in prevalence may be attributed to methodological differences in these studies (Dickins & Graham, 1990; Khoza & Ross, 2002) including sample characteristics and the test battery used. Most studies investigating the negative effects of HIV on the auditory system agree that sensory neural hearing loss (SNHL) may be a predominant finding (Khoza & Ross, 2002; Lalwani & Sooy, 1992; Prasad et al., 2006; Van der Westhuizen et al., 2013; Zuniga, 1999). These studies also agree that the prevalence and severity of this type of hearing loss may be directly related to more progressive stages of infection or reduced immunological status.

Auditory manifestations may be caused by direct infection of various portions of the auditory pathway, and/or indirect damage caused by opportunistic infections and the use of ototoxic medications (Stearn & Swanepoel, 2010).

Direct effects

The inner ear may be affected by direct damage to the cochlea, the eighth cranial nerve, as well as neural pathways, and centres within the brain (Lalwani & Sooy, 1992; Larsen, 1998; Reyes-Contreras et al., 2002). These abnormalities may be caused by infection of glial and neurological cells (Petito, 1988). Damage to auditory structures has been demonstrated with the use of auditory evoked potentials, such as the auditory brainstem response (ABR) (Matas, Silva, Marcon Bde, & Gonçalves, 2010). Electrophysiological abnormalities shown on this test procedure have suggested that HIV may cause alterations along both the peripheral and central auditory nervous system (Birchall, Wight, French, Cockbain, & Smith, 1992; Matas et al., 2010; Reyes-Contreras et al., 2002). Although opportunistic infections and the use of ototoxic medication may contribute to these abnormalities (Matas et al., 2010; Stearn & Swanepoel, 2010), these findings may be present even amongst asymptomatic HIV-positive subjects (Reyes-Contreras et al., 2002).

Indirect effects

Opportunistic infections. HIV-positive individuals are susceptible to opportunistic infections such as upper respiratory tract infections, cytomegalovirus, toxoplasmosis, meningitis, and the herpes zoster virus (CDC, 2015; Hofmeyr & Baker, 2010; Lalwani & Sooy, 1992; Stearn & Swanepoel, 2010). Opportunistic infections associated with the external ear and middle ear include Kaposi's sarcoma (Marcusen & Sooy, 1985), acute otitis externa, otitis media, and pneumocystis carinii otitis media (Beers & Abramo, 2004; Lalwani & Sooy, 1992; Larsen 1998). These abnormalities may result in a conductive or mixed hearing loss (Lalwani & Sooy, 1992; Stearn & Swanepoel, 2010).

In addition to the effects of opportunistic infections, ototoxic properties of drugs used to treat associated conditions and HIV may worsen auditory symptoms experienced (Kallail, Downs, & Scherz, 2008; Simdon, Watters, Bartlett, & Connick, 2001; Tseng, Dolovich, & Salit, 1997).

Ototoxicity. Ototoxicity refers to the nature of a therapeutic agent and other chemical substances, to cause structural damage to the inner ear, resulting in hearing loss and/or balance disturbances (Roland & Cohen, 1998; Theunissen et al., 2014). The occurrence of alterations to hearing abilities as a result of ARV agents has been suggested by numerous studies (Khoza & Ross, 2002; Marra et al., 1997; Matas et al., 2010; Simdon et al., 2001).

Marra and colleagues (1997) reported that hearing loss was more prevalent in HIV-positive patients with a history of ear infection and older patients, whilst the association between ARV drugs and hearing loss was only relevant in older patients (≥ 35 years). These findings were supported by Simdon et al. (2001), who reported hearing changes in three HIV-positive patients using ARVs. However, similar to the study conducted by Marra and colleagues (1997), some confounding variables may have contributed to the worsening of hearing abilities in their study. These variables included the following: a long-standing

history of hearing loss, increased age (> 45 years), and possible auditory deprivation (Arlinger, 2003) as two of these patients were had only been fitted with hearing aids at a much later stage, whilst it was not clear whether the last patient had been fitted with hearing aids at all.

Factors that increase susceptibility toward ototoxic damage are complex and difficult to establish (Khoza-Shangase, 2011). Such factors may include: age (very young or >60 years); genetic influences that increase susceptibility; treatment duration; dosage; simultaneous diuretic therapy; or co-treatment with other ototoxic drugs; history of receiving ototoxic regimens or history of sensitivity to these agents; impaired renal or hepatic function; pre-existing hearing problems; and history of noise exposure (Bauman, 2003). Thus, with all these confounding variables, isolating and establishing the effect of ARVs on the hearing mechanism remains a challenge.

Contrary to the findings reported by Marra et al. (1997) and Simdon et al. (2001), a study conducted on HIV-positive individuals with no pre-existing hearing loss, suggested that ARVs had little to no impact on hearing abilities (Schouten, Lockhart, Rees, Collier, & Marra, 2006). A strength of the study conducted by Schouten et al. (2006), pertains to the use of a longitudinal research design, allowing changes which may have occurred at later stages to be evaluated. In addition, some confounding variables which may have influenced the test results were also considered, including age, CD4+ T cell count, and history of noise exposure. The findings suggested that baseline hearing thresholds (before initiating ART), may be affected by HIV itself; however, these thresholds may improve after initiating ART, which may be attributed to enhanced immune function. A significant limitation in this study however, pertains to the exclusion of oto-acoustic emission (OAE) testing, an essential component of the ototoxic test battery (American Academy of Audiology, [AAA], 2009; Campbell, 2007; Ranjan & Bhat, 2008). Therefore, more subtle damage to the hearing

mechanism, not yet detectable by audiometric thresholds, may have been overlooked. Furthermore, although acknowledged by the authors, generalization of the results was limited by a small sample size (n = 33).

As a result of the intricate relationship that exists between HIV and its effects on hearing abilities (Assuiti, Lanzoni, Dos Santos, Erdmann, & Meirelles, 2013), the aetiology of hearing loss in HIV-positive individuals should be interpreted holistically. As the entire auditory apparatus may be vulnerable to HIV, vestibular impairments may also be more prevalent in HIV-positive individuals (Teggi et al., 2008; Teggi et al., 2006; Heinze et al., 2011). Although various research studies have reported on the auditory manifestations, much controversy exists regarding the exact vestibular mechanisms affected by HIV (Heinze, et al., 2011).

Mechanisms of HIV associated with vestibular function

The vestibular system, similarly to the hearing mechanism, may be vulnerable to both direct and indirect infection caused by HIV (Khoza-Shangase & Van Rie 2016). The prevalence of vestibular involvement has been reported in 15% to 79% of HIV-positive individuals (Heinze, Vinck, Hofmeyr, & Swanepoel, 2014; Kohan, Hammerschlag, & Holliday, 1990). Differences in prevalence reported may be attributed to many factors, including, amongst others, the test battery employed as well as criteria used to distinguish normal versus abnormal results (Dickins & Graham, 1990; Heinze et al., 2011). These factors may also influence the nature and degree of vestibular impairment reported, however, both the central and peripheral vestibular system may be vulnerable to direct and indirect damage from HIV (Chandrasekhar, Siverls, & Sekhar, 1992; Heinze et al., 2011; Pappas, Roland, Lim, Lai, & Hillman, 1995).

Direct effects

The direct effects of HIV on the vestibular apparatus have been described by earlier post-mortem studies (Chandrasekhar et al., 1992; Hart, Cokely, Schupbach, Dal Canto, & Coppleson, 1989; Pappas et al., 1995) which revealed alterations and structural changes in the vestibular system (Chandrasekhar et al., 1992; Pappas et al., 1995; Hart et al., 1989; Pappas et al., 1995). These changes may have been attributed to the use of ototoxic agents, as both Chandrasekhar et al. (1992) and Pappas et al. (1995) revealed that all cases were receiving potentially ototoxic treatment at their time of death. However, viral-like particles consistent with HIV were found within the vestibular end-organs, including the vestibular hair cells, SCCs, utricle, and saccule (Pappas et al., 1995); suggesting direct involvement of the virus.

Indirect effects

Similar to the indirect mechanisms acting on the auditory system, opportunistic infections and agents used to treat these infections may damage the vestibular apparatus.

Opportunistic infections. The most common opportunistic infections associated with the onset of vestibular symptoms in HIV-positive individuals include syphilis (Weder, Senn, Caversaccio, & Vibert, 2013), otosyphilis (Smith & Canalis 1989; Song, Lee, Chae, & Hwang, 2005), and TB (Khoza-Shangase & Van Rie 2016).

Cochleo-vestibular impairments have been reported as the first manifestation of syphilis in HIV-positive individuals (Weder et al., 2013). In a case study conducted by Weder et al. (2013), auditory and vestibular symptoms were attributed to syphilis rather than HIV as both auditory and vestibular function were restored after vigorous treatment of the syphilis infection. Damage to vestibular structures associated with syphilis was supported by a histopathology study (Hizli et al., 2016). Hizli and colleagues (2016) found structural changes in the vestibular hair cells, saccule, utricle, and SCCs.

Another case study reported fluctuating hearing abilities and total vestibular loss in a 35-year-old male diagnosed with HIV (Song et al., 2005). This clinical presentation was attributed to secondary syphilis affecting the inner ear (otosyphilis). Findings from their study suggested that HIV co-occurring with otosyphilis, may compromise sensitivity to the otosyphilis treatment protocol. As otosyphilis treatment is ineffective, the destructive effects of this infection (otosyphilis) on the auditory system may be accelerated (Smith & Canalis 1989; Song et al., 2005).

All these studies suggest that syphilis may cause damage to auditory and vestibular structures. However, these studies have focussed more on the effects of the opportunistic infection rather than HIV itself. Therefore, in addition to damage caused by syphilis, the direct effects of HIV may have contributed to these findings.

Another opportunistic process associated with vestibular impairment includes the secondary effects from TB (Khoza-Shangase & Van Rie 2016). Post-mortem studies conducted in Sub-Saharan Africa have revealed that 32% to 45% of HIV-related deaths may be attributed to TB (Ansari et al., 2002; Cox et al., 2010; Murray et al., 2007; Rana et al., 2000). In addition to the high TB mortality rate (Ansari et al., 2002; Cox et al., 2010; Murray et al., 2007; Rana et al., 2000; Wong et al., 2012), this condition may also be most prevalent in relation to poor treatment adherence (Den Boon et al., 2007). Reduced patient compliance with TB regimens may necessitate retreatment or result in the development of multi-drug resistant TB (MDR TB) or extensively drug resistant TB (XDR TB) (Den Boon et al., 2007; Harris & Heinze, 2013). All the aforementioned circumstances necessitate the use of aminoglycosides (Harris & Heinze, 2013), which have been associated with damage to vestibular structures (vestibulotoxicity) (Selimoglu, 2007).

Ototoxicity. Various studies have stressed the importance of monitoring hearing abilities in individuals receiving potential ototoxic treatment (Bardien et al., 2009; Duggal &

Sarkar, 2007; Harris, 2012; Hotz, Harris, & Probst, 1994); however, monitoring vestibular function has been neglected for various reasons. These may include, lack of one specific test procedure able to accurately detect subtle changes resulting from vestibulotoxicity; the impaired state of many patients to endure an extended test battery (Rogers & Petersen, 2011); as well as the notion that hearing impairment is a more permanent disability, whilst a patient can still compensate for a balance impairment (Harris & Heinze, 2013).

Although limited, many studies investigating vestibular function in HIV-positive individuals (Castello et al., 1998; Grimaldi et al., 1993; Hart et al., 1989; Hausler et al., 1991; Teggi et al., 2008; Teggi et al., 2006; Song et al., 2005) have not indicated whether ARVs were being used. Therefore, findings regarding the vestibulotoxicity of these agents remain scarce.

A study conducted by Heinze et al. (2014), revealed that HIV-positive subjects had a higher occurrence of vestibular dysfunction (79.2%) compared to HIV-negative subjects (18.4%). These authors reported no significant difference in vestibular function among subjects using ARVs and those not using ARVs. These findings supported an earlier study (Cohen et al., 2012), which reported that HAART had no harmful effects on the vestibular system. However, the latter study also suggested no difference in vestibular function between HIV-positive subjects on HAART and HIV-negative subjects (Cohen et al., 2012). Cohen et al. (2012) attributed their findings to the therapeutic nature of these agents, which may preserve function of vestibular structures.

The dissimilar findings between these two studies may be attributed to various factors. Firstly, the inclusion criteria were different for the two studies, Cohen et al. (2012) only included asymptomatic subjects, whilst Heinze et al. (2014) included both symptomatic and asymptomatic subjects. Secondly, the test procedures employed may have influenced the findings, Cohen et al. (2012) utilized screening procedures whilst Heinze et al. (2014)

included objective vestibular tests, which may have been more sensitive. Finally, the nature of different therapeutic agents may have attributed to the findings, as the South African ARV protocol may vary from that used by other countries, the manifestations may also differ (Khoza, 2007).

It is evident that more research is required regarding the possible relationship between ARVs and vestibular impairment. Although a hearing impairment may have devastating effects on an individual's QoL, the impact of a vestibular impairment resulting from ototoxicity should not be underestimated (Rogers & Petersen, 2011).

Vestibular impairment and QoL

Symptoms indicating possible vestibular damage may include vertigo, dizziness, gait instability, headaches, oscillopsia, nausea, and disequilibrium (Zingler et al., 2007). However, as a result of these symptoms often being difficult for patients to describe (Rogers & Petersen, 2011; Smith & Darlington, 2013), and more emphasis being placed on the management of the virus, these indicators of possible vestibular impairment are often overlooked (Teggi et al., 2008).

Many patients who experience vestibulotoxic symptoms are advised to avoid heights, operating machinery, or driving until they are able to do these tasks safely (Whitney & Rossi, 2000). Therefore, these symptoms may disrupt vocational abilities, resulting in financial strain. In addition to physical restrictions, vestibulotoxic symptoms may also lead to withdrawal from social activities, anxiety, lack of confidence, and ultimately depression (Monzani et al., 2001). The World Health Organization (WHO) recognises that a vestibular impairment may have far-reaching effects on QoL, by stating that subjective well-being and mental health may be influenced by the realization of an individual's own abilities, including the ability to function and be productive as part of a community (WHO, 2001a).

A study by Black, Pesznecker and Stallings (2004), revealed that symptoms consistent with vestibulotoxicity were reported by all participants in their study (n = 33) after starting gentamicin treatment. As a result of these symptoms, which included disequilibrium and oscillopsia, none of the participants were able to return to their previous occupations, and the overwhelming majority became reliant on social and disability grants. Of utmost concern, is the finding that vestibulotoxicity remained unrecognized, even after these patients had been discharged. Therefore, a need for improved awareness regarding vestibular impairments, even amongst medical teams, remains crucial.

Although literature remains limited regarding the exact structures of the vestibular system affected by HIV and ototoxic treatments (Heinze et al., 2011), research has suggested that the entire vestibular system may be vulnerable to damage (Hausler et al., 1991; Heinze et al., 2011; Heinze et al., 2014; Mathews, et al., 2012; Stearn & Swanepoel, 2010; Teggi et al., 2006).

Central and peripheral vestibular impairment

A few authors have stressed that central vestibular involvement may be a more prevalent finding compared to peripheral impairments, and that the severity thereof may increase at more progressive stages of infection (Castello et al., 1998; Hausler et al., 1991; Teggi et al., 2008; Teggi et al., 2006).

These specific findings were reported by Hausler et al. (1991) and Castello et al. (1998). In both these studies, central vestibular impairment occurred in asymptomatic patients and across all progressive stages of infection. Only two patients (14%) presented with peripheral vestibular impairment in the study by Hausler et al. (1991) however, this impairment was prevalent only in symptomatic patients at later progressive stages of infection. These two patients also presented with central vestibular involvement. Although the test battery used by Haulser et al. (1991) evaluated both central and peripheral vestibular

function (spontaneous and positional nystagmus, pursuit and rotary tests, as well as pendular and bi-thermal caloric tests), the criteria used to classify an abnormal caloric response were unreasonably high (Heinze et al., 2011). In their study, a unilateral weakness of ≥ 40% was considered significant, whilst other studies have utilized more conservative criteria of ≥ 15% or ≥ 25% (Heinze et al., 2014; Teggi et al., 2008; Teggi et al., 2006). Thus, prevalence of peripheral vestibular impairment may have been underreported. Castello et al. (1998) used oculomotor tests (smooth pursuit and saccades), ABR, and bi-thermal caloric irrigation in their study. Results from the oculomotor tests and ABR suggested CNS involvement of the acoustic pathways within the brainstem, pontocerebellar paths, and supratentorial areas. However, the caloric test results were within normal quantitative limits; therefore, this study concluded that HIV had no effect on labyrinthine function. Heinze et al. (2011) argue that the peripheral test battery used by Castello and colleagues was not comprehensive and thus, similar to the study conducted by Hausler et al. (1991), peripheral impairment may have been overlooked.

A later study also included oculomotor and bi-thermal caloric testing to evaluate vestibular function in HIV-positive patients (Teggi et al., 2006). Teggi and colleagues (2006) agreed that prevalence of central vestibular involvement increased at more progressive stages of infection. However, this study also reported peripheral vestibular impairment in all patients irrespective of progressive stage, whilst central vestibular impairments only occurred at more progressive stages of infection and were not prevalent in any asymptomatic patients. These findings were supported by a later study which utilized a similar test battery with the addition of the head shake and head impulse test (Teggi et al., 2008). The more prevalent peripheral vestibular findings reported by these two studies may be attributed to the inclusion of patients with a positive history of vestibular complaints and chronic dizziness, whilst Castello et al. (1998) did not include any patients reporting these symptoms, and Haulser et

al. (1991) only included 14 patients with these symptoms, which were all in the final progressive stage of infection.

Two other studies also conducted the caloric test and reported reduced peripheral labyrinthine function in HIV-positive individuals (Grimaldi et al., 1993; Mathews et al., 2012). However, the generalization of the results reported by Grimaldi and colleagues (1993) is limited, as findings had been based on a case study. Mathews et al. (2012) found that labyrinthine function was significantly affected (unilaterally and bilaterally) in the HIV-positive group compared to the HIV-negative group; and agreed with Teggi et al. (2006) that the difference in peripheral vestibular function between HIV-positive individuals at initial stages of infection compared to those at later stages was not significant. This insignificant difference of peripheral vestibular impairments between individuals at various stages of infection was also reported by another study (Heinze et al., 2014). The limitation of the study by Mathews et al. (2012), however, involves the use of a mono-thermal test protocol during the caloric test, which has been associated with reduced diagnostic accuracy (Farid, El-Abd, & Abou-Elew, 2003).

On the other hand, Cohen et al. (2012) reported comparable peripheral vestibular function between HIV-positive and HIV-negative participants, whilst presence of non-classical nystagmus and gaze evoked nystagmus were attributed to possible central vestibular impairments. However, the occurrence of these central impairments was not significant. It should be noted, however, that the test battery consisted only of screening tests (head thrust, test Dix-Hallpike manoeuvres, and the Romberg balance test) and therefore, sub-clinical peripheral vestibular impairments may have been missed (Heinze et al., 2011). Furthermore, although the study did not specify the distribution of participants across various progressive stages of infection, more than half of the participants (n = 159; 64.4%) were virologically controlled with a mean current CD4 count of 556.4 (SD = 284) and had not been diagnosed

with AIDS. These sample characteristics may explain the insignificant difference between the HIV-positive and HIV-negative group. It was also reported that HIV-positive participants on HAART showed a significantly lower likelihood of central vestibular impairments and therefore, a therapeutic effect of ARVs on vestibular function was suggested. These authors concluded that previous studies which reported higher vestibular impairments had been conducted in the pre-ARV era and therefore vestibular impairments were more prevalent (Hasuler et al., 1991).

A more recent study did not agree with these conclusions (Heinze et al., 2014). Heinze and colleagues (2014) reported insignificant differences in vestibular function between HIV-positive subjects on HAART and treatment naïve HIV-positive subjects. Their study did, however, agree with previous reports (Castello et al., 1998; Hausler et al., 1991; Mathews et al., 2012) that HIV-positive subjects presented with significantly more vestibular impairments compared to HIV-negative subjects. Central vestibular impairments did increase at more progressive stages of infection, however, this increase was not significant. These authors concluded that there was a significantly higher occurrence of peripheral vestibular impairments in the HIV-positive group. A comprehensive test battery was conducted, consisting of bedside assessments, the cVEMP, ocular motor tests, positional tests, and bi-thermal caloric irrigation. The authors attributed the increased peripheral prevalence (45.3%; $n = 24$) to the inclusion of two peripheral sensitive objective measures (cVEMP and bi-thermal calorics). In addition, information regarding history of opportunistic infections was not available to the researcher. Thus, secondary effects may have contributed to the increased peripheral vestibular prevalence. Of interest however, was the finding that peripheral impairments decreased at more advanced stages of infection. Although this decrease was not significant, this finding was attributed to two possible mechanisms - the possible occurrence of central compensation at later stages of infection; or as Cohen et al.

(2012) suggested, a protective effect of ARVs, as more subjects were using HAART at more progressive stages of infection.

In summary, differences among these studies may be attributed to criteria which were used to distinguish normal versus abnormal results, characteristics and symptoms of individuals included in the study, the effect of ARVs on vestibular function, and the test procedures employed. A wide variety of vestibular tests are available today which provide essential information regarding specific vestibular structures and systems. Once these impairments have been identified, aspects such as fall risk can be established, a management or rehabilitation approach can be followed, and ultimately the effects on QoL may be reduced (Majumi, Aparajit, & Mohammed, 2014).

Balance function tests

Subjective and objective measures of balance

The International Classification of Functioning, Disability, and Health (ICF) framework describes health and disability based on various domains of function (WHO, 2001b). These domains do not only include physical body function and structures but also the effects thereof on overall function. Thereby, this framework provides a more holistic understanding of health and disability (Vargus-Adams & Majnemer, 2014). The ICF also classifies the effects of vertigo according to these various domains, enabling a better understanding of the impact vertigo may have on an individual's everyday life, irrespective of the physiological severity (Arya, Thawani, & Rangasayee, 2016). The ICF core sets for vertigo include physical body functions and structures, environmental factors, activity, and participation (Grill, Bronstein, Furman, Zee, & Müller, 2012). As vestibular impairment may have far-reaching effects on activity and participation and ultimately on QoL (Marchetti, Whitney, Redfern, & Furman, 2011; Rogers & Petersen, 2011), the current study employed a similar approach as suggested by the ICF framework. For this reason an objective measure,

which is able to quantify the biological effect of specific impairments on the balance system (Cameron & Huisinga, 2013), was combined with a subjective measure, which provides information regarding subjective physical function during participation in everyday activities. By employing this test battery more insight may be gained regarding the effect of a balance impairment on functional status.

Subjective measure: The Activities-specific Balance Confidence (ABC) scale

A number of scales have been developed in order to assess an individual's risk of falling. Some of these scales have been compared based on their purpose, reliability, validity and their applicability to the current study (Appendix A). Based on this comparison, the ABC scale was selected owing to its good test-retest reliability and high sensitivity to identify subjects with a balance impairment (Powell & Myers, 1995; Whitney et al., 2005). In addition, this scale was also selected based on the availability of a Zulu translation (Kamanji, 2016), which may be more relevant to a rural area such as the Sekhukhune district.

The purpose of the ABC scale (Appendix B) is to evaluate an individual's self-perceived confidence level whilst performing everyday indoor and outdoor activities (Powell & Myers, 1995). This scale consists of 16 items, which are rated by the individual on a percentage scale (using whole numbers), with 0% indicating no confidence in performing the specific activity and 100% indicating complete confidence (Powell & Myers, 1995). The ABC scale was selected for the current study in order to determine whether HIV-positive participants perceived that their functional ability had been affected as a result of their HIV diagnosis. This scale may also provide insight regarding the effect of HIV on balance self-efficacy, which has been associated with perceived health status and overall physical function (Salbach et al., 2006; Schmid et al., 2012). Thereby ultimately providing information regarding QoL.

A study conducted by Teggi et al. (2006) utilized the dynamic gait index (DGI) tool to evaluate the risk of falls in HIV-positive subjects. This study reported that subjects at more progressive stages of infection showed a higher risk for future falls (A = 0%; B = 17.8%; C = 40%). However, two other studies found no correlation between HIV and fall risk (Erlandson et al., 2012; Erlandson et al., 2016). These studies rather attributed increased fall risk in HIV-positive participants to subjective reports of imbalance and presence of other chronic conditions, such as hypertension and diabetes. A study utilizing the ABC scale also suggested that HIV-positive individuals do not show a higher risk for future falls when compared with HIV-negative individuals (Conference on Retroviruses and Opportunistic Infections [CROI], 2015). Although the DGI and ABC scales measure balance in different ways (functional test versus subjective scoring), it may be argued that the DGI was a more sensitive tool. However, a study comparing various balance scales (Five-Times-Sit-to-Stand Test, ABC, and DGI) reported that the ABC scale was most sensitive in identifying subjects with a balance impairment (Whitney et al., 2005).

This Canadian-developed scale (Powell & Myers, 1995) has been translated into various languages, including French-Canadian, Brazilian-Portuguese, and Chinese. The reason for these translations was to ensure applicability of the scale to specific populations being assessed, as well as the validity of the scale to these individuals' environments and cultural values (Mak, Lau, Law, & Cheung, 2007; Marques, Mendes, Taddei, Pereira, & Assumpcao, 2013). This scale has also recently been translated into one of South Africa's eleven official languages, namely isiZulu. The Zulu ABC version (Appendix C), ABC-Z scale, has been translated in such a way to bridge the cross-cultural gap between the original scale and the South African context (Kamanji, 2016). These alterations were made in order to compensate for variances such as access to infrastructure, socioeconomic, linguistic, and climate differences (Kamanji, 2016).

Furthermore, screening HIV-positive individuals in primary healthcare settings may be valuable in order to determine whether further referral for diagnostic testing may be required (Heinze et al., 2014). Therefore, the use of the ABC scale may be useful in such settings where availability of balance equipment may be limited. However, subjective measures should ideally be combined with an objective assessment in order to quantify the degree of perceived disability in relation with physiological changes (Cameron & Huisinga, 2013).

Objective measures: The video Head Impulse Test/Head Impulse Test Paradigm

Various vestibular procedures are currently available in order to assess peripheral labyrinthine function. The caloric and rotary chair test are used to assess lateral (horizontal) SCC function. Otolith function has been assessed using the vestibular evoked myogenic potential test (VEMP), ocular counter roll test (OCR), and the subjective vertical test (Hain, 2012). VEMPs have become an essential component of the vestibular test battery (Rosengren, Welgampola, & Colebatch, 2010) and even more so after receiving approval from the Food and Drug Administration (FDA) in 2015. These measurements are recorded from averaged electromyography in response to high-intensity auditory stimuli (Macambiraa, Carnaúba, Fernandes, Bueno, & Menezes, 2017). VEMPs have been recorded from contracted cervical muscles (cVEMPs) providing information regarding the saccule, as well as extraocular muscles (oVEMPs) which provide information related to utricle function (Craig, 2016; Hain, 2017). Utricular function can also be assessed with the use of the OCR and the subjective vertical test (Hain, 2012).

More recently another test, the HIMP, was added to the vestibular test battery. This test was chosen for the current study as more comprehensive information regarding peripheral vestibular function can be obtained, including lateral, anterior, and posterior SCC

function. The HIMP is also able to provide this information in a shorter and less invasive manner (MacDougall, McGarvie, Halmagyi, Curthoys, & Weber, 2013).

The head impulse test (HIT), also known as the Halmagyi head thrust test, was first described by Halmagyi and Curthoys in 1988. This procedure has been used ever since in clinical practice, as a useful bedside evaluation tool to detect deficient function of the lateral SCCs as a result of inadequate VOR function (Halmagyi & Curthoys, 1988). During this procedure the clinician thrusts the head rapidly and unpredictably to the left or right side. Individuals are instructed to maintain fixation on the clinician's nose during this head movement (Curthoys et al., 2011). The HIT evaluates the VOR after the stimulation of each receptor within the ampulla of the lateral SCC (Hendelman, Humphreys, & Skinner, 2017). The function of this reflex is to stabilize images on the retina during head movement by producing eye movements in the direction opposite to head movement. A normal HIT response would mean that the individual will be able to fixate on the target (clinician's nose); however, a dysfunction in the VOR will cause the eyes to move with the head, requiring the individual to make a corrective eye movement back to the clinician's nose after the head rotation. This corrective eye movement, or catch-up saccade, is better known as an overt saccade (Weber et al., 2008). The side which the head is rotated to represents canal function on that side. Therefore, the presence of an overt saccade whilst the head is turned to the right may indicate SCC dysfunction on the right side.

The disadvantage of this procedure, however, pertains to the subjective interpretation of the clinician regarding the presence of an overt catch-up saccade (Curthoys et al., 2011). Furthermore, the absence of an overt catch-up saccade does not exclude abnormal SCC function (Curthoys et al., 2011). Individuals with SCC dysfunction may also adapt smaller corrective saccades during the head movement (Weber et al., 2008). Thus an overt catch-up saccade will not be required to bring the eyes back to the target at the end of the head

rotation. These smaller, quick corrective movements, occurring during the head movement, can mask an inadequate VOR. These saccades, known as covert catch-up saccades, are not obvious to the naked-eye and were discovered through the use of scleral search coils (Weber et al., 2008). Although scleral search coils have been recommended as the gold standard to detect these eye movements, this procedure may not always be feasible due to excessive costs, invasiveness (a contact lens placed on the eye), as well as the complexity of interpreting test data (Curthoys et al., 2011).

This led to the development of a more refined measurement system, namely the vHIT. The protocol used during this measurement is referred to as the head impulse test paradigm (HIMP) (Halmagyi et al., 2017). These two terms, vHIT and HIMP, are used interchangeably in current literature, as the HIMP has only recently been introduced as the term referring to the test protocol, whilst vHIT refers to the system being used (Halmagyi et al., 2017). For the remainder of this report, the protocol term HIMP will be used.

During the HIMP, the function of each SCC on both sides is evaluated via the VOR pathway (MacDougall, Weber, McGarvie, Halmagyi, & Curthoys, 2009) whilst both overt and covert catch-up saccades, when present, can be detected objectively (Curthoys et al., 2011). The function of the lateral SCCs is evaluated via horizontal head movements, whilst the anterior and posterior SCCs are examined by head rotations delivered in the planes of the vertical canals – left anterior-right posterior (LARP) and right anterior-left posterior (RALP) (MacDougall et al., 2013). As the superior vestibular nerve innervates the utricle, anterior SCC, and lateral SCC, and the inferior vestibular nerve innervates the posterior SCC and saccule, the test results may also provide evidence regarding vestibular nerve function (Barin, 2014a).

The accuracy of the scleral search coil method and the ICS vHIT system were compared and found to be identical when used to detect peripheral vestibulopathy

(MacDougall et al., 2009). It was also confirmed that the ICS Impulse, which had received approval from the FDA in February 2013, is the only device which has been validated against scleral search coils to accurately identify dysfunction in each SCC. Furthermore, the ICS Impulse has also been recommended as a more practical test for use in clinical practice, compared to scleral search coils (Crumley-Welsh, 2013, Curthoys et al., 2009).

A healthy individual may also present with catch-up saccades during the HIMP, especially during high velocity head impulses, however, these catch-up saccades are infrequent and random in direction (Barin, 2014b). Once the presence of catch-up saccades which meet all the criteria for abnormality has been established (Table 6), the VOR gain should also be evaluated to identify possible peripheral vestibular lesions. The VOR gain quantifies the relationship between the head and eye movements. In healthy individuals, the VOR gain is estimated to be ~1 for both tested canals, and starts declining with increased head velocity. Therefore, the interpretation of the VOR gain should be conducted only when optimal head velocities were obtained. The presence of abnormal VOR gain in the absence of any catch-up saccades could indicate possible artefacts or saccadic palsy; therefore the gain should be interpreted with the presence of catch-up saccades. As the VOR gain is influenced by both canals in the plane in which the head is being moved, independent canal function cannot be estimated from this parameter (Barin, 2014b).

Results from the HIMP are depicted as plots on a graph, displaying the velocity (º/s) on the y-axis and time (ms) on the x-axis. This graph, generated by the software program (OtosuiteV), enables the direct comparison of head and eye velocity after the head movement (Crumley-Welsh, 2013).

Spontaneous nystagmus, usually associated with acute peripheral vestibular lesions, may also present as saccades. These saccades, which represent the fast phase of spontaneous nystagmus, have a smaller velocity than typical catch-up saccades and can occur before,

during, or after the head impulses. Head impulses conducted toward the side of lesion result in saccades in the same direction as catch-up saccades, resulting in difficulty to identify these saccades. However, when the head impulses are conducted toward the intact side, these saccades will occur on the normal side in the opposite direction of the VOR eye-movement (Barin, 2014b) (Figure 1).

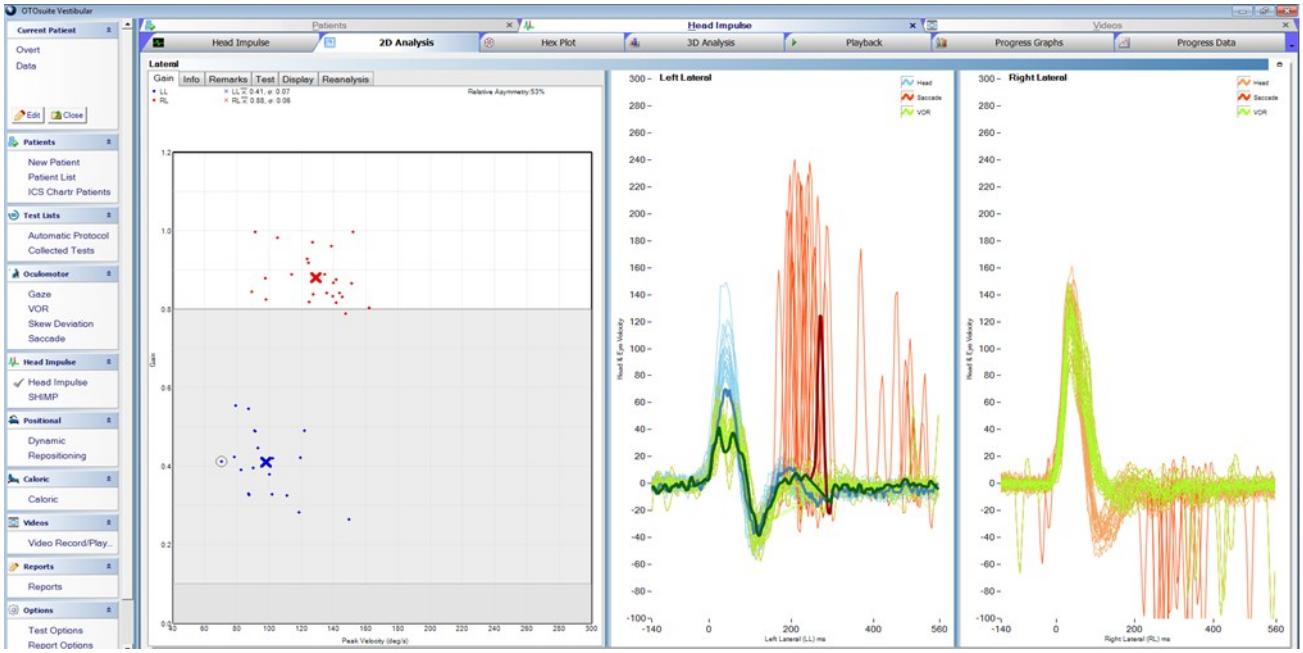


Figure 1. Acute unilateral vestibular lesion in the left lateral SCC

The 2-D representation in Figure 1 depicts the presence of overt catch-up saccades in the left lateral SCC. The gain on the left side is also within the abnormal range (grey shaded area). The result obtained on the right side represents a normal HIMP response with no catch-up saccades and normal VOR gain. The presence of saccades on the right, in the opposite direction of the VOR eye-movement, represents the fast phase of right beating spontaneous nystagmus. These saccades are also present on the left side but not as visible, as they occur in the same direction as the catch-up saccades (Source: Barin, 2014b).

Summary

The entire auditory and vestibular system may be vulnerable to the effects of HIV, however, research investigating these effects on the vestibular system remains limited (Heinze et al., 2011). In addition to the scarcity of this research, greater emphasis has been placed on the occurrence of central vestibular impairments and its increased prevalence at more progressive stages of infection (Castello et al., 1998; Teggi et al., 2008; Teggi et al., 2006). However, a more recent study utilizing a peripheral sensitive test battery, which included the caloric test and the cVEMP test, suggested that the peripheral vestibular system may be more affected than previously reported (Heinze et al., 2014). Other studies have also included the caloric test but reported normal peripheral vestibular function (Castello et al., 1998; Hausler et al., 1991). Heinze et al. (2011) argue that certain limitations may have affected the reduced peripheral prevalence reported. Firstly Castello et al. (1998) should have included a more comprehensive test battery to evaluate peripheral vestibular function, whilst Hausler et al. (1991) used unreasonable criteria during the caloric test to classify an impairment. Therefore, peripheral vestibular impairments may have been underreported. Furthermore, although the caloric test is valuable in order to assess peripheral vestibular function, this test only evaluates the lateral SCCs, the superior vestibular nerve (Jacobson & Newman, 1997), and frequencies representing non-physiologic head movements (Petrak, Bahner, & Beck, 2013). Thus, various portions of the labyrinth are not assessed and as lower frequencies of the VOR are evaluated, this test does not accurately represent physiologic head movements. The rationale of the current study was therefore to describe the auditory and peripheral vestibular characteristics of HIV-positive individuals and to determine the prevalence of impairments. The HIMP was used, which is able to evaluate a larger portion of the vestibular labyrinth and also evaluates vestibular function used during physiologic head

movements. By including the HIMP and a subjective scale, the current test battery could evaluate functional balance used during realistic situations.

Chapter 3: Methodology

Introduction

This chapter includes the research aims, research design, research context, various phases of the current study, measures, material and equipment used, data collection procedures, and ethical considerations. The specific types of reliability and validity relevant to the current study are also reviewed, which is followed by the data analysis methods.

Research aims

Main aim

The main aim of the study was to describe the audiological and peripheral vestibular characteristics of HIV-positive individuals, and to compare these findings with those of a group of HIV-negative individuals (control group).

Sub-aims

The main aim was realised with the following sub-aims:

i) To describe the audiological characteristics of HIV-positive individuals (participant group 1) and those of an HIV-negative control group (participant group 2)

ii) To determine the prevalence of HIV-positive individuals who present with hearing loss and compare this prevalence with hearing loss to those of an HIV-negative control group.

iii) To compare the prevalence of hearing loss and tinnitus in the current study with previous studies.

iv) To describe the balance characteristics of HIV-positive individuals and to compare these findings to those of an HIV-negative control group as determined with subjective (ABC scale/ABC-Z scale) and objective (HIMP) measures.

v) To determine the prevalence of HIV-positive individuals and an HIV-negative control group who present with reduced semi-circular canal function (anterior, posterior and lateral SCCs), and its afferent neural pathways.

vi) To determine the agreement between the ABC scores and HIMP results.

Research design

The research employed a non-experimental, descriptive, cross-sectional research design to achieve the aims of the study.

In a non-experimental research design, no external variables are controlled or introduced. In this design various participants are included with different attribute variables, therefore it is difficult to establish whether outcome differences are solely attributed to the independent variable being investigated (Belli, 2008). For the current study this design allowed auditory and vestibular function to be measured in participants with different variables, such as gender, age, HIV status, and treatment protocols.

A descriptive research design involves organizing collected data via graphs, tables, or figures, in order to describe various characteristics in relation to the results (CDC, 2013; McNabb, 2009). This design is, however, limited in terms of establishing cause and effect relationships (Baha, 2016). A descriptive design was used to describe the specific characteristics of the sample population as well as the various test results and prevalence estimates.

A cross-sectional research design involves collecting data at a particular point in time from a subset of individuals which are representative of the whole population (Sedgwick, 2014). A cross-sectional design was chosen after considering two important strengths of this design, namely the suitability for estimating prevalence and the ability to generalize test results to a specific population (CDC, 2013; Sedgwick, 2014). As a limitation, this study

design also lacks the ability to establish causality (Sedgwick, 2014). Owing to the measurements (audiological test battery, ABC scale, and HIMP) being taken at a specific point in time, the effect that HIV and its treatment regimen may have had on the auditory and vestibular system could not be established.

Research context

This study was conducted at the Ndlovu Medical Centre (NMC), situated in the Elandsdoorn Township in the Elias Motsoaledi local municipality of the Sekhukhune district, in the Limpopo Province of South Africa. The NMC provides free integrated Primary Health Care (PHC) services to patients with TB and HIV. These services include, amongst others, two clinics (12-hour and 24-hour) with a dedicated on-site HIV monitoring laboratory, digitalized radiology, and two research centres (NCG, 2015). This centre has since its establishment in 1994 provided an estimated 15 000 HIV-positive patients with ARV treatment (NCG, 2015). As established, comprehensive audiological services are also available at the NMC, therefore this site was ideal as equipment could be utilized for the audiological test procedures. In addition, participants who required audiological management could be referred on-site for further management (e.g. amplification or management of middle ear dysfunction) if required.

Research phases

The current study comprised three phases, namely the development phase, the pilot study, and the main study. The first phase, the development phase, was used to develop the research protocol, identify potential participants for inclusion in the main study, and obtain permission and ethical clearance to conduct the study. The second phase, the pilot study, was essential in refining the data collection procedures.

Pilot study

The pilot study was used as a small-scale feasibility trial to determine the efficiency and quality of the sampling strategy, research design, suitability of the equipment, and test procedures. This enabled the researcher to make necessary adaptations before conducting the study on a large scale (Clark-Carter, 2009). The pilot study also served to improve the methodological quality of the procedures and material related to the implementation of the test battery.

Participants

The pilot study participants met the same inclusion criteria as for the main study. Two female participants were included in the pilot study, aged 35 and 37 years respectively, and in CDC category 1A. These participants were not included in the main study.

Procedures

Purposive sampling was used to recruit the pilot study participants. Only participants that provided written informed consent were included in the pilot study. In addition to the data collection procedures outlined in the main study, VEMPS (oVEMPs and cVEMPs) were also conducted in order to evaluate the entire peripheral vestibular system. The objectives, procedures, results, and recommendations of the pilot study are outlined in Table 3.

Table 3

The pilot study objectives, procedures, results, and recommendations

Objectives	Procedures	Results	Recommendations
To improve the enrolment of participants.	Staff were verbally informed of the purpose and procedures of the study.	Additional awareness was required regarding the study, the location where the study was being conducted, and eligibility criteria, as many staff members and patients were still unaware of the study.	An advert was designed (Appendix D) and placed around the clinic waiting areas, as well as the Ndlovu Wits Audiology Clinic. This advertisement briefly explained the testing procedures as well as inclusion criteria for the study. Furthermore, a presentation was conducted by the researcher to all Ndlovu Wits Audiology Clinic staff in order to promote referrals of potential participants.
	Initially exclusion criteria included participants with a history of TB or those in the final progressive stage of infection (AIDS).	Reviewing files prior to enrolment proved time consuming, which resulted in hesitance of participation.	Files were reviewed at the end of data collection, therefore the exclusion criteria of TB and AIDS were omitted. Thus, vestibular function at various progressive stages of infection was evaluated.

Objectives	Procedures	Results	Recommendations
To refine the data collection procedures prior to the main study.	Potential participants were phoned and appointments scheduled.	Participant recruitment was ineffective, as individuals did not arrive for their appointments as they had not been scheduled on the same day as their clinic visits.	Participant recruitment was changed for the pilot study. Instead, the researcher approached individuals after their clinic appointments.
	Individuals were approached after their appointments (before leaving the clinic).	Many individuals had already been at the clinic for an extended duration and therefore were not interested in participating.	Finally, individuals were rather approached at the pharmacy and clinic waiting areas. In this way, participants could be tested whilst waiting to collect their medication or to see the doctor.
	The English ABC scale was applied.	Participants experienced difficulties in answering all questions on the ABC scale as a result of inadequate language proficiency.	The ABC-Z scale was included and administered with the help of a first-language isiZulu interpreter.
	The cVEMP and oVEMP were conducted.	Electric interference from the test rooms resulted in faulty readings during the VEMP procedures.	The VEMP procedures were excluded from the main study as no suitable test room was available to obtain accurate results at the time of data collection. After the VEMP procedures were excluded, the duration of the test session was one hour.
	The HIMP was conducted.	Results from the HIMP revealed abnormal gain values in the absence of any catch-up saccades. These results were attributed to excessive artefacts.	The researcher received additional training in conducting the HIMP technique in order to eliminate the excessive artefacts. These techniques were practised on various healthy individuals until the researcher felt comfortable with conducting the HIMP and normal results were obtained in these individuals.

Objectives	Procedures	Results	Recommendations
To evaluate the efficiency of logistical and practical factors related to data collection.	New files were opened by the researcher for each participant at the Ndlovu Wits Audiology Clinic.	Opening files, which required extensive administrative details (address, contact details, etc.) proved time-consuming.	The Ndlovu Wits Audiology Clinic staff assisted with administration, allowing the researcher to focus on testing more participants.
	All the results from the test battery were recorded on the data collection form (Appendix E) after testing each participant.	The completion of this form after each test proved time-consuming.	The completed ABC-Z scale, along with the audiological results, were scanned and saved electronically in a password protected file on the researcher's computer. This enabled the researcher to summarize all the results on the data collection form at the end of each day.

In conclusion, the pilot study proved valuable in order to refine the data collection procedures and finalise the test battery. The major adaptations that were implemented prior to the main study included enrolling participants with TB and those in the final progressive stage of HIV, recruiting participants from the pharmacy and clinic waiting areas, exclusion of VEMPS, and refining the technique for the HIMP.

Main study

Participant selection

Sampling strategy

A purposive sampling, a non-probability technique, was utilised to recruit participants for this study. This form of sampling refers to a strategy where participants are selected based on the presence of certain characteristics that would provide knowledge regarding the specific topic of interest (Hajimia, 2014). By using this sampling technique, participants could be categorised according to their HIV status. The researcher had no knowledge of the participants' disease process and history prior to enrolment, therefore selection bias was minimized.

Sample size

The number of participants were based on the available time frame for data collection. A total of 120 participants were tested (81 HIV-positive individuals and 39 HIV- negative controls). However, 21 test results from the HIV-positive group, and 7 test results from the control group were excluded after data analysis, based on the presence of excessive artefacts during the HIMP.

After this exclusion, the final sample size consisted of 92 participants in two participant groups. The first participant group (n_1) included 60 HIV-positive individuals whilst the second participant group (n_2) included 32 HIV-negative individuals. The HIV-negative group served as a basis for comparison of test results (control group).

Participant selection criteria

The inclusion and exclusion criteria were similar for both groups with the exception of HIV diagnosis. These criteria are summarized for the two groups in Table 4 and Table 5 respectively.

Table 4

Participant selection criteria: Participant group 1 ($n_1 = 60$)

Inclusion criteria		
Criteria	*Rationale*	*Procedure*
Confirmed HIV diagnosis and receiving HIV treatment at the NMC.	HIV-positive participants were included to evaluate the effects of the HIV disease process on auditory and vestibular function. All HIV participants had to be receiving treatment at NMC in order for the researcher to have access to their medical records.	Participants were recruited from the pharmacy and clinic waiting areas and were thus current NMC patients. The HIV diagnosis was confirmed by the participants' medical records.
Between 18 and 50 years of age.	The maximum age was 50 years in order to limit the occurrence of vestibular impairment as a result of the natural aging process, which may occur in individuals >55 years old (Maes et al., 2010).	Date of birth was confirmed during the case history and review of medical records.
No pre-existing vestibular dysfunction prior to the HIV diagnosis.	HIV-positive participants who reported balance problems prior to their HIV diagnosis were excluded. In doing so, vestibular impairment could more likely be attributed to HIV.	History of pre-existing vestibular dysfunction was determined during the case history.
Written informed consent to participate in the study.	Written informed consent was obtained in order to adhere to ethical guidelines.	Written informed consent (Appendix F) was obtained from all participants prior to enrolment.

Exclusion criteria		
Criteria	*Rationale*	*Procedure*
Individuals with neck injuries that severely restrict their range of head movement.	Individuals with restricted neck movement were excluded in order to optimize the test output (Halmagyi et al., 2017) and minimize the risk of different results between the two participant groups being attributed to external factors.	Participants were informed how the head movements would be conducted (small quick movements) in order to ensure that they were comfortable with the procedure and giving the participant the opportunity to mention any neck problems or concerns.
Individuals with poor eye-sight.	Clear visual input contributes to balance (Harsha et al., 2008). Therefore, individuals with poor eye-sight which influenced their ability to see the target on the wall were excluded, as impairments in the HIMP may have been attributed to visual rather than vestibular disturbances.	The examiner placed a target (the blue Otometrics symbol) on the wall 1 metre away from the participants and asked them if they were still able to see the image on the wall in front of them. Individuals who were unable to focus on the target without using their spectacles were excluded.

Table 5

Participant selection criteria: Participant group 2 ($n_2 = 32$)

Inclusion criteria		
Criteria	*Rationale*	*Procedure*
Negative HIV diagnosis.	Participants in the HIV-negative group served as a control to compare test results with HIV-positive participants.	HIV-negative status was self-reported by participants.
Between 18 and 50 years of age.	Participants older than 50 years were excluded to limit the occurrence of vestibular impairment as a result of the natural aging process, which may occur in individuals >55 years old (Maes et al., 2010).	Date of birth was confirmed during the case history and review of medical records.
Written informed consent to participate in the study.	Written informed consent was obtained in order to adhere to ethical guidelines.	Written informed consent was obtained (Appendix F) from each participant prior to enrolment.
Exclusion criteria		
Criteria	*Rationale*	*Procedure*
Any neck injuries which severely restrict individuals' range of head movement.	Individuals with restricted neck movement were excluded in order to enhance the test output (Halmagyi et al., 2017) and minimize the risk of different results between the two participant groups being attributed to external variables.	Participants were informed regarding the procedure used during the HIMP (small quick head movements). This was explained in order to ensure that the participant did not have any concerns or problems regarding this head movement.
Poor eye-sight.	As visual abilities contribute to balance (Harsha et al., 2008) individuals with poor eye-sight which influenced their ability to see the target on the wall, were excluded as HIMP abnormalities may have been attributed to their sight rather than vestibular impairment.	A target (the blue Otometrics symbol) was placed on the wall 1 metre away from the participants and they were asked if they were still able to see the image on the wall in front of them. Individuals who were unable to focus on the target without using their spectacles were excluded.

Participant description

Two participant groups were included in the study. Participant group 1 comprised HIV-positive individuals ($n_1 = 60$) whilst participant group 2 comprised HIV-negative individuals ($n_2 = 32$). The gender distribution of the two groups is presented in Figure

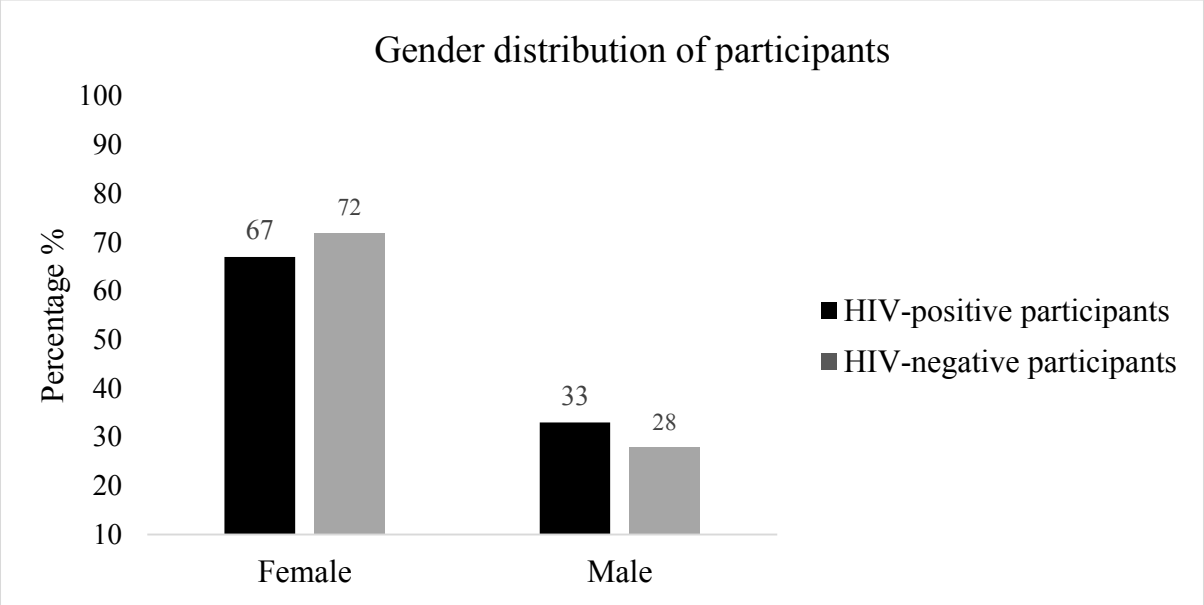


Figure 2. Gender distribution of HIV-positive and HIV-negative participants

The majority of participants in both participant groups were female (Figure 2). This gender distribution is representative of the population distribution in the Sekhukhune district, with a majority female population (SSA, 2016).

The mean age of participants in group 1 was 41.4 years (±5.3) and 32.5 years (±9.1) for participants in group 2 (Figure 3).

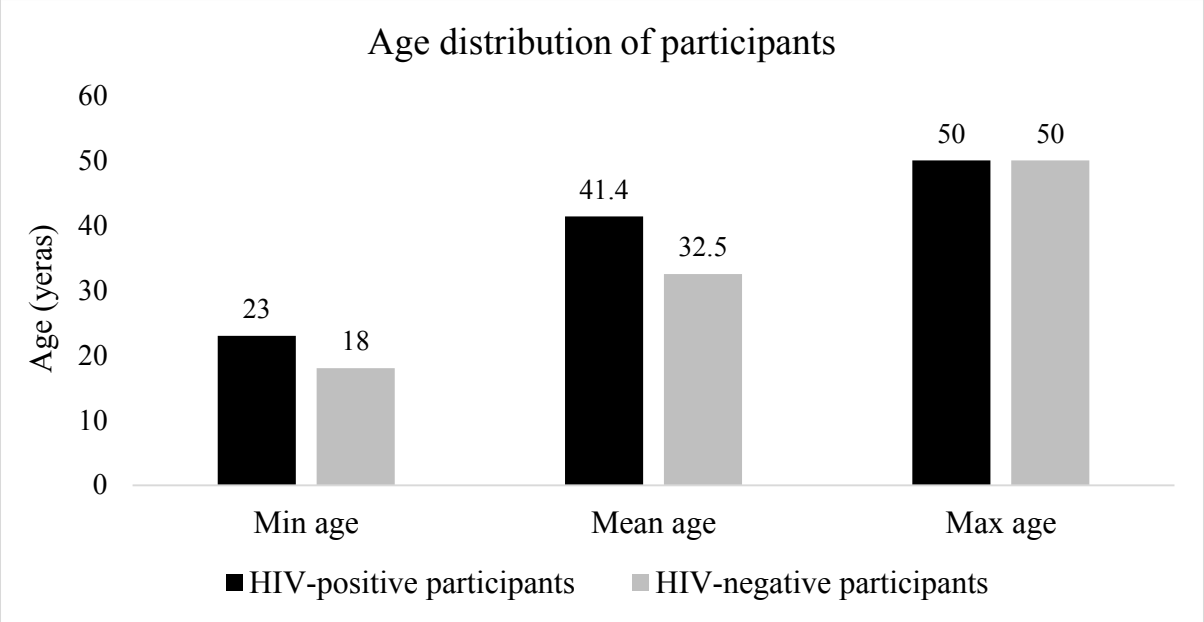


Figure 3. Age distribution of HIV-positive and HIV-negative participants

Increased age was an important consideration for the current study as it may affect both the auditory and vestibular results (Bess & Humes, 2008; Maes et al., 2010).

The majority of HIV-positive participants (58%; $n_1 = 35$) were in category A (A1 - A3) suggesting that they were asymptomatic according to the CDC progressive stages of infection (CDC, 1992) (Figure 4). The remainder of participants (42%; $n_1 = 25$) were distributed among the symptomatic CDC stages (B and C) presenting with various conditions ranging from TB, different types of candidiasis, oral thrush, herpes, shingles, signs of neuropathy, hepatitis B, and bacterial pneumonia.

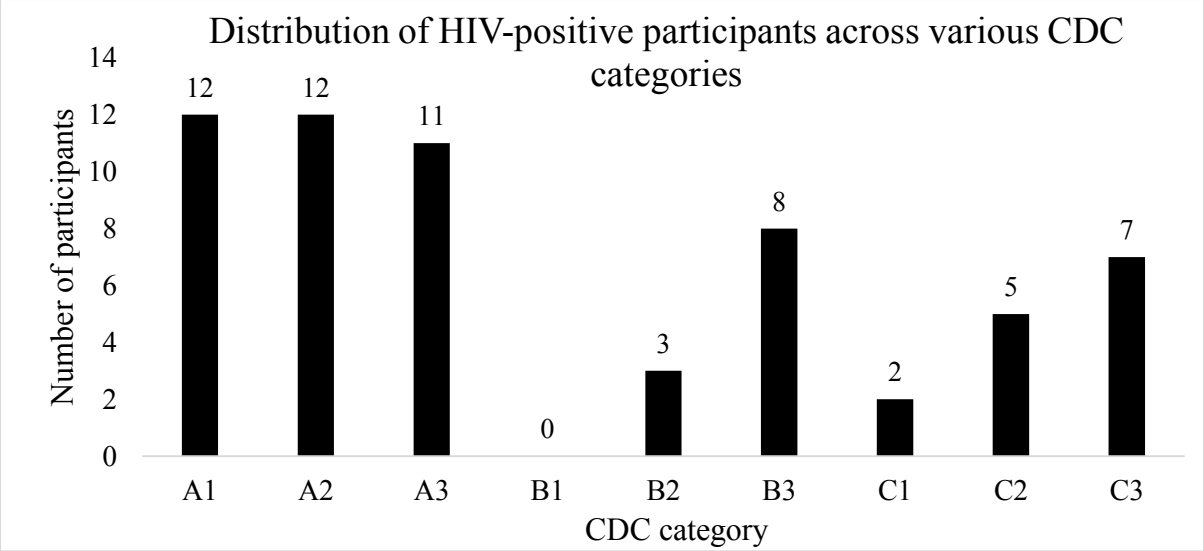


Figure 4. Distribution of HIV-positive participants across various CDC categories

Furthermore, 4 participants also had hypertension and one experienced chronic pain. All these participants were using medication on a regular basis, in conjunction with their ARVs, to manage these conditions as well.

A wide variety of ARV protocols (12) were used in the current study sample (Figure 5), as opposed to six different ARV combinations used in a recent study conducted by Heinze and colleagues (2014).

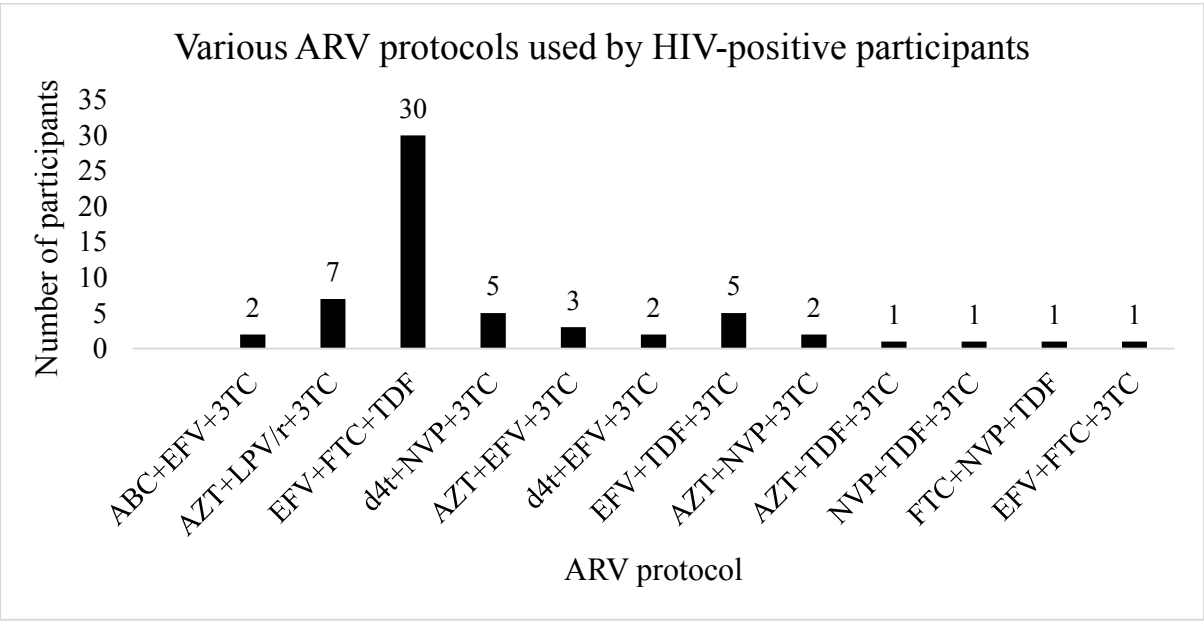


Figure 5. Various ARV protocols used by HIV-positive participants

Half of the participants (50%; $n_1 = 30$) in the current study sample were using the ARV combination consisting of Efavirenz (EFV), Emtricitabine (FTC), and Tenofovir disoproxil fumarate (TDF). This ARV regimen is prescribed as a first-line fixed-dose combination, and has been linked with improved adherence due to its once-daily dosing (WHO, 2016). Furthermore, this regimen has also been associated with less-toxic effects (WHO, 2013). The majority of HIV-positive participants (62%; $n_1 = 37$) had been using ARVs between one to five years, whilst the mean length of ARV use was 5.2 years (±3.6; range: 1 - 13).

Data collection measures, material, and equipment

The various measures, equipment/material, procedures, and norms used during the hearing and balance assessment are summarized in Table 6.

Table 6

Hearing and balance measures, equipment/material, procedures, and norms

Measures	Equipment/Material	Procedure	Norms
Infection control	Webcol Alcohol Preps and sterilant (Steritech).	Probe tips used during otoscopy and tympanometry were disinfected according to the guidelines recommended by the Health Professions Council of South Africa (HPCSA) (HPCSA, 2002). All probe tips were washed and soaked in a Steritech solution after use.	Steritech products are GHS and SANS11014 compliant.
Case history form	Ndlovu Wits Audiology Clinic case history form (Appendix G).	During the conduction of the case history pertaining to demographic information (surname, date of birth, etc.), auditory and vestibular history, and medical history was obtained.	N/A

Measures	Equipment/Material	Procedure	Norms
ABC scale	ABC scale (English version) and ABC-Z scale	For isiZulu first-language speakers, the ABC-Z scale was used and for participants who were proficient in English, the ABC scale was used. Standard scoring procedures were used (Powell & Myers, 1995).	***Criteria for high level of physical function:*** >80% ***Criteria for moderate level of physical function:*** 50-80% ***Criteria for low level of physical function:*** <50% Overall ABC scores of ≤ 67% were considered a strong indicator for a higher risk of future falls (Lajoie & Gallagher, 2004).
Otoscopy	Heine Mini3000 otoscope with reusable specula (Heine Optotechnik, Germany).	The otoscopic examination was conducted by gently pulling the auricle up and backward in order to view the auditory meatus and tympanic membrane. Excessive or occluding cerumen was removed via water irrigation by the researcher or Ndlovu Wits audiologists, allowing accurate measures of the remaining test battery (tympanometry and pure tone audiometry). Participants who presented with any abnormalities were referred to the NMC for medical management.	***Criteria for normal otoscopy:*** No ear canal abnormalities or obstructions. A clear view of the intact tympanic membrane which should have a pale grey semi-transparent colour, presence of a light reflection on the pars tensa, and visibility of the handle and short process of the malleus (Martin & Clark, 2009; Sanna, 2002). ***Criteria for abnormal otoscopy:*** The presence of any infection, inflammation, or abnormalities of the tympanic membrane, including a dull colour, retracted, protruding, or perforated tympanic membrane.

Measures	Equipment/Material	Procedure	Norms
Tympanometry	Titan tympanometer, 226 Hz frequency probe tone (Interacoustics, Denmark) Madsen Otoflex 100 tympanometer, 226 Hz frequency probe tone (Otometrics, Denmark).	A 226 Hz probe tone was utilized. Participants who presented with abnormal middle ear function were referred to the NMC for medical management.	***Criteria for normal middle ear function:*** A Type A tympanogram suggested normal middle ear function. This was classified according to the following norms: - Ear canal volume: 0.8 to 2.0 ml - Static compliance: 0.3 to 1.8 ml - Middle ear pressure: - 100 daPa to + 50 daPa (Jerger, 1970). ***Criteria for abnormal middle ear function:*** Any measurement other than a Type A tympanogram.
Pure tone audiometry	Interacoustics Diagnostic Audiometer (AD629) Double-walled sound treated room, in accordance with ISO R389 and/or ANSI S3.6 and/or SANS 10154:2006 standards.	An audiological assessment was conducted, which adhered to the Standard Operating Procedures at the study site, which requires all individuals with HIV to undergo a hearing test. Participants were provided with instructions regarding the test procedure. Air-conduction (AC) thresholds were obtained via headphones across the 250 Hz to 8 kHz frequency range for both ears. The AC results were used to determine whether bone conduction (BC) testing was required. Bone conduction testing was conducted when AC thresholds exceeded 25 dB at any frequency between, and including 250 Hz to 4 kHz. Bone conduction	***Criteria for hearing within normal limits:*** Hearing within normal limits was classified as a pure tone average (calculated from the average AC thresholds obtained at 500 Hz, 1 kHz, and 2 kHz) of ≤ 25 dB HL (Bess & Humes, 2008). ***Criteria for hearing loss:*** Thresholds exceeding 25 dBs HL were considered significant. The degree of hearing impairment was defined as follows: - Mild: 26-40 dB HL - Moderate: 41-55 dB HL - Moderately severe: 56-70 dB HL

		thresholds were obtained systematically by placing the bone vibrator on the mastoid bilaterally, or only on the specific ear in the case of a unilateral impairment. After this procedure, all hearing test results were explained to participants. Participants who presented with a hearing loss were counselled by the audiologist regarding possible hearing aid options and details regarding the hearing aid fitting.	- Severe: 71-90 dB HL - Profound: >91 dB HL (Clark, 1981).
Measures	**Equipment/Material**	**Procedure**	**Norms**
HIMP	*Measurement system:* ICS Impulse vHIT (Otometrics, Denmark), consisting of a video Frenzel lightweight goggle, with USB camera and disposable face cushion *Software used on the vHIT:* OtosuiteV (Version 2.00); Database version 2.0.14 *Specifications of laptop for vHIT data collection:* - i5 processor	The procedures for this test are summarized in Table 7. During HIMP the head movement stimulus as well as the responsive eye movement is measured objectively. This is achieved by lightweight video frenzel goggles, secured on the individual's eyes, which consists of a high-speed USB camera. The camera records eye movements, whilst motion sensors track head position (Crumley-Welsh, 2013). After this procedure all participants were verbally informed that HIV may be associated with balance impairment. Participants were encouraged, should they experience constant spells of dizziness, to bring this to their doctor's attention. This may enable the medical team to review patients' treatment regimens and implement possible changes.	***Criteria for normal HIMP:*** *Presence of catch-up saccades:* None or minimal (inconsistent) catch-up saccades should be present. Furthermore, in the presence of abnormal catch-up saccades which meet all the criteria for abnormality (consistency, direction, latency/timing and velocity/amplitude), HIMP should be considered abnormal regardless of the VOR gain, whilst abnormal VOR gain, in the absence of any catch-up saccades, may be attributed to artefacts or saccadic palsy. However, the finding of saccadic palsy is extremely rare (Barin, 2014b). *Normative VOR gain and asymmetry ratio:* - Lateral impulse: 0,8 to 1,2 - Vertical impulse (LARP and RALP): 0,7 to 1,2

	- 8 GB RAM - 500 GB Hard drive - Screen resolution 1920 x 1080		(Barin, 2014b). - Asymmetry ratio: <13.3% (Curthoys et al., 2014). ***Criteria for abnormal HIMP:*** *Consistency*: Abnormal catch-up saccades occur consistently and can be seen for most head impulses, to at least one side. *Direction*: The direction of abnormal catch-up saccades occurs in the same direction as the VOR eye movement. This occurs due to the inadequacy of the eye to follow the head movement, therefore catch-up saccades occur in the same direction, in order to refocus the eyes on the target. *Latency/timing*: True catch-up saccades generally occur within ~100 ms during the first head impulse, or ~100 ms after the head has come to a stop. *Velocity/amplitude profile*: These catch-up saccades have amplitudes which are comparable to or larger than head amplitudes (Barin, 2014b).

The test procedures for the lateral and vertical HIMP are presented in Table 7.

Table 7

Lateral and vertical HIMP procedure

Procedure description	Lateral HIMP	Vertical HIMP
Participant set-up	Participants were seated on a static chair one metre in front of a blank wall in a dimly lit room. The researcher placed the lightweight video frenzel goggles over the participants' eyes. It was ensured that the goggles fit snugly over the eyes, which not only improves patient comfort, but also limits the goggles from shifting during the abrupt head movements, causing artefacts. Participants were instructed to stare straight ahead, enabling the researcher to focus an earth-fixed target at eye-level on the wall in front.	Participants were not moved again for the vertical HIMP.
Calibration	After the HIMP goggles were secured, a quick calibration was conducted. The goggles were adjusted over the eyes so that the cross-hair (displayed on the software) was in the centre of the pupil and any light reflection on the image was eliminated. *Eye calibration*: participants were instructed to stare at a laser dot, which moved around horizontally on the wall in front of them (without head movements).	Calibration was already conducted during the lateral procedure and was therefore not repeated for the vertical plane. Vertical head calibration was done via the on-screen 45 degree guide – the chair was moved 45 degrees to the right for LARP and 45 degrees to the left for RALP. Thereafter, the head was centred at a 45 degree angle according to the software.

Procedure description	Lateral HIMP	Vertical HIMP
Canal impulses	*Lateral canal impulses*: participants were instructed to fixate on the earth-fixed target on the wall in front of them, keeping the head straight, while the researcher held the top of the participant's head. The head was moved rapidly and unpredictably in the horizontal plane (right and left) using a small amplitude. This movement is illustrated in Figure 6.	*Left Anterior-Right Posterior (LARP):* the participant and the chair were positioned at a 45 degree angle to the right. Participants were instructed to fixate on the target projected on the wall for the duration of the procedure. The researcher placed one hand on the head, whilst the other hand was placed beneath the chin. The head was moved rapidly and unpredictably in the vertical plane using a pitch movement toward the SCC tested (anterior or posterior). *Right Anterior-Left Posterior (RALP):* this procedure was similar to that followed during LARP with the exception of the participant and the chair being positioned at a 45 degree angle to the left. These impulses are illustrated in Figure 6.

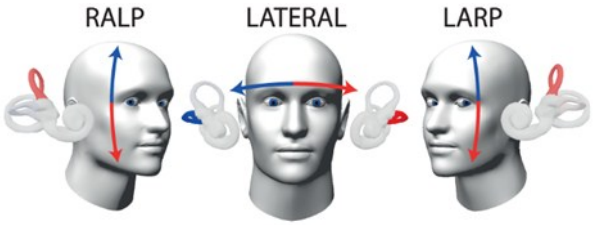


Figure 6. Head movements to assess the lateral SCCs via horizontal head movements and movements in the vertical canals, in order to assess the right anterior-left posterior (RALP), and left anterior-right posterior (LARP) SCCs (source: MacDougall et al., 2013, p. 2).

Procedure description	Lateral HIMP	Vertical HIMP
Movement	Rapid and unpredictable both in time and direction	Rapid and unpredictable both in time and direction
Amplitude	10 to 15 degrees	10 degrees
Peak head velocity	150 deg/s - 250 deg/s	100 deg/s - 200 deg/s
Impulses in each direction	20	20
Frame rate	250 Hz	250 Hz

Note. Lateral HIMP (Barin, 2014b; McGarvie et al., 2015); Vertical HIMP (Barin, 2014b; Crumley-Welsh, 2016; MacDougall et al., 2013).

Data collection procedures

Once ethical clearance (Appendix H) and permission from the relevant bodies (Appendices I – J) had been obtained, data collection commenced and included the following:

Participant recruitment

Potential participants were approached at the pharmacy and clinic waiting areas of the NMC Clinic. The researcher verbally informed potential participants of the nature of the study and that the study was being done through the University of Witwatersrand and not conducted by the NMC so that individuals would not feel obliged to partake. The researcher also stressed that participation was voluntary. All the information of the study was also provided in written format to each potential participant (Appendix K) therefore, the criteria of HIV diagnosis was not verbally discussed with the individual in order to ensure confidentiality in the waiting area. After written informed consent was obtained, participants were taken to the Ndlovu Wits Audiology Clinic where the test battery was conducted. The research assistant explained the nature of the study to each participant again at the Ndlovu Wits Audiology Clinic if participants were not proficient in English. Furthermore, the researcher informed the administrative personnel responsible for calling patients from the waiting area, which individuals were participating in the study. This was done in order for the administration staff to keep these patient files separate, and once the patients returned they could be assisted immediately without having to wait in the queue again.

Participant group 2, the HIV-negative control group, comprised family members and friends of HIV-positive patients attending the clinic, as well as staff members at the NMC.

Research assistants

The research team included the researcher and four research assistants. The audiologist employed by the Ndlovu Wits Audiology Clinic acted as the first research assistant. This assistant, along with the researcher, are both qualified audiologists, with two

years' clinical experience. The second research assistant was an audiologist with eight years' clinical experience and employed by the University of the Witwatersrand. The role of these two assistants was to conduct some of the case histories and audiological assessments (otoscopy, tympanometry and pure tone audiometry) when more than one participant was waiting to be assessed. The researcher completed the ABC scale (English version) and HIMP with all the participants. The other two research assistants were both first-language isiZulu speakers with experience as research assistants and trained in the data collection protocol. They assisted with the ABC-Z scale and translation during data collection, when necessary.

Test protocol

The data collection measures as outlined in Table 6 were applied.

File review

The medical files of the HIV-positive participants included in the study were retrieved by the NMC file coordinator and reviewed by the researcher. This enabled the researcher to group participants into specific CDC categories based on their CD4 count and presence of co-morbid conditions. Files were also reviewed in order to capture the ARV protocol and duration of ARV treatment, as well as any use of potential ototoxic drugs (MDR/XDR TB). The researcher reviewed these files at a private desk and ensured not to leave any information unattended during this process. All necessary information was captured in electronic format on an Excel spreadsheet.

Data capturing

The results were recorded on the relevant forms, scanned, saved electronically, and later summarized on the data collection form (Appendix E) which was used for data analysis. The hard copies of the case history and hearing test were filed in the participants' audiology files at the Ndlovu Wits Audiology Clinic for future follow-up. These files are kept in a locked cabinet in the audiology clinic according to standard operating procedures. All raw

data, including data analysis, were stored in a password-protected electronic database and will be destroyed after five years.

Ethical considerations

Negligence of ethical considerations prior to the twentieth century, which were governed by conscience and professional codes of conduct, has introduced a new era of ethical scrutiny involving human research (Schneider, 2005). These ethical guidelines ensure that research is conducted in such a way to safeguard the well-being of all research participants (World Medical Association's [WMA], 2013).

The current study adhered to the World Medical Association's (WMA) Declaration of Helsinki Principles (WMA, 2013). The ethical principles specific to this study include permission, informed consent, autonomy, beneficence and non-maleficence, confidentiality and anonymity. The relevance of these principles in the current study is discussed below.

Permission

Approval was obtained prior to the commencement of this study from the Human Research Ethics Committee (Medical) (Appendix H), the NMC (Appendix I), as well as the Limpopo Department of Health and Social Development (DHSD) (Appendix J).

Informed consent

The nature of the research, test procedures and aims of the research were presented in written (Appendix K) and verbal format to each individual. Only individuals who provided written informed consent were included in the study (Appendix F).

Autonomy

The researcher informed individuals that participation was voluntary, and that they had the right to withdraw from the study at any stage, with no negative consequences.

Beneficence and non-maleficence

As the study population is considered vulnerable due to their medical condition (WMA, 2014), the researcher was skilled in conducting the HIMP. No risks were involved with participating in this study. Individuals who presented with any auditory symptoms or hearing impairment were referred to the Ndlovu Wits Audiology Clinic for further management, or to the Ndlovu Medical Centre for free medical care if they presented with any infections or abnormalities which required medical treatment.

Confidentiality and anonymity

The participants' right to privacy was respected at all times, as research participant numbers were used instead of any personal information. The confidentiality of HIV diagnosis was ensured by presenting this criteria in written format only (Appendix K) when approaching potential participants in the waiting areas. Furthermore, participants were selected randomly therefore, other people in the waiting area would not have known if the individual was assigned to the HIV positive or HIV negative participant group. The findings are also presented anonymously in the research report. Raw data were captured in an electronic database, which was password protected. These results were accessible only to the researcher and research supervisors.

Reliability and validity

Reliability

Reliability is defined as the consistency and accuracy of measures (Shively, 2017). For the purposes of this study, test-retest reliability and inter-rater reliability were applicable.

Test retest reliability

Test retest reliability is determined by conducting the same test procedure twice, on the same group of people over a period of time and obtaining the same test results (Phelan & Wren, 2005). The researcher conducted the HIMP on four HIV-negative participants and

retested the same four participants one week later. HIV-negative participants were selected, as test-retest reliability should be established in individuals not affected by an impairment or disease process which could influence the measured construct (Paiva et al., 2014). These test results were compared and classified as normal or abnormal. All four participants presented with normal HIMP results (in terms of gain and absence of any catch-up saccades) at similar velocities (lateral: 150 deg/sec to 250 deg/sec; vertical: 100 deg/sec to 200 deg/sec) on both test dates; thereby indicating excellent test retest reliability.

Inter-rater reliability

Inter-rater reliability refers to the extent to which two raters agree when evaluating assessment results (Phelan & Wren, 2005). All HIMP results were analysed and interpreted by both the researcher and an experienced inter-rater.

The inter-rater, a qualified audiologist holding a PhD, has 17 years practical experience in vestibular assessment and management, and four years teaching experience in vestibular audiology, and is currently responsible for the vestibular clinic at a tertiary institution. She is a certified Otometrics vHIT trainer and has also obtained additional training certificates in sensory integration, balance, and vestibular assessment and rehabilitation.

The percentage of agreement was calculated by the observed agreement divided by the possible agreement (McHugh, 2012). The initial inter-rater agreement was high (93%) (Bajpai, Bajpai, & Chaturvedi, 2015). However, after the rater with more vestibular experience showed the second rater how to analyse the raw data of the test results, 100% inter-rater agreement was established.

Validity

If a direct relationship is evident between the outcome of a measure and its intended concept, the measure shows good validity (Shively, 2017). In this study, face validity, content validity, internal validity, and external validity were applicable.

Face validity

Face validity refers to the subjective judgement of an instrument to portray results according to its specified interest (Patel & Joseph, 2016; Shively, 2017). This form of validity was applied by utilizing a validated balance assessment scale (ABC scale and ABC-Z scale). As the ABC scale comprises various items involving indoor and outdoor activities which are scored by the individual (Powell & Myers, 1995), this scale showed good face validity for subjective balance confidence during daily tasks.

Content validity

Content validity pertains to the inclusion of appropriate test procedures (hearing test and HIMP), in order to measure the construct (hearing and peripheral vestibular function) (McLeod, 2013).

Internal validity

Internal validity refers to the exclusion of confounding variables which could contribute to differences in the dependent variable (Taylor & Asmundson, 2008). Internal validity may also be achieved by reducing observer and assessment bias (Godwin et al., 2003). All equipment, including the soundproof booth, were calibrated (Appendices L - P) in order to strengthen internal validity. By ensuring that all equipment was calibrated, different results between participants were not attributed to faulty equipment. Risk of bias was also reduced during the hearing test procedure and the ABC scale. The audiological assessment was conducted by either the researcher or qualified audiologists, therefore reducing the possible risk of researcher bias toward certain results. In addition, the ABC scale was also

conducted in an African language, which more participants may have been comfortable with. Although isiZulu is not the most prominent spoken language in the Sekhukhune district, this questionnaire was still chosen as the questions on the ABC-Z scale were more relevant to the South African context compared to the original version. Due to the questions being more relevant, the research assistant was able to explain the questions to specific participants in another African language if they were not proficient in either isiZulu or English. The language which participants were most comfortable with was determined by the research assistant, whilst confirming details needed to open their files (name, surname, home language etc.). Therefore, differences in scores being attributed to language or contextual barriers were minimized. This scale was also conducted with the help of an interpreter, further reducing the risk of researcher bias.

External validity

External validity refers to the generalizability of test results and conclusions to different measures, persons, contexts, and times (Steckler & McLeroy, 2008). This form of validity was achieved by using a cross-sectional research design, which included participants that were representative of the general population. In addition, the inclusion and exclusion criteria allowed different participants from both groups, which would represent the general population in terms of gender, background, and co-morbid conditions. The test procedures that were utilized also measured balance function related to real-world conditions (ABC scale, ABC-Z scale and high frequencies of the HIMP), thereby balance function results may better represent various real-life situations.

Data analysis

All data were captured in an Excel spreadsheet. Data capturing was verified for accuracy. The data analysis was performed on SAS Release 9.4 (SAS Institute, 2017). The statistical procedures used in the current study are presented in Table 8.

Table 8

Statistical procedures

Statistical procedures	Rationale and application in the current study
Descriptive statistics - Measures of central tendency: Mean values - Measures of variability: Range and standard deviation (SD)	Descriptive statistics were used to summarize and describe the collected data in a succinct manner (Ali & Bhaskar, 2016; Rubin, 2013). Mean values provided a summary of the nominal quantities, including sample characteristics such as age, whilst the range and standard deviation were used to represent data distribution (Rubin, 2013). Measures of central tendency and variability were calculated in Excel.
- Agreement between two variables: McNemar Test	The McNemar Test does not measure independence but rather the differences between two paired variables (Hazra & Gogtay, 2016). This test was used to establish the agreement between ABC scores and HIMP results.
Probability (hypothesis) statistics - Test of mean differences: Two-sample *t*-test - Test of percentage differences: Fisher's exact test	Probability testing is used to determine significance between groups or categorical data (Hazra & Gogtay, 2016). All probability tests were two-sided and p values ≤ 0.05 were considered as statistically significant. The two-sample *t*-test was used to establish significance between mean values [e.g. mean pure tone averages (PTAs)], whilst the Fisher's exact test was used to determine significance of percentages (e.g. occurrence of tinnitus).

Chapter 4: Results

Introduction

The results of the current study are presented in this chapter in accordance with the main aim of the study, namely to describe the audiological and peripheral vestibular characteristics of HIV-positive individuals and to compare these findings with that of a group of HIV-negative individuals (control group). Firstly, the audiological results were presented, followed by the results of the balance function tests. A significance level of ≤ 0.05 was used for all statistical tests, unless specified otherwise.

Audiological characteristics of the two participant groups

The first sub-aim was to describe the audiological characteristics of HIV-positive individuals (participant group 1) and that of an HIV-negative control group (participant group 2).

Self-reported auditory symptoms

During the case history (Appendix G) participants were asked to describe any problems related to their ears or hearing abilities. The prevalence and type of auditory symptoms reported in both participant groups are presented in Figure 7. Some participants reported more than one symptom.

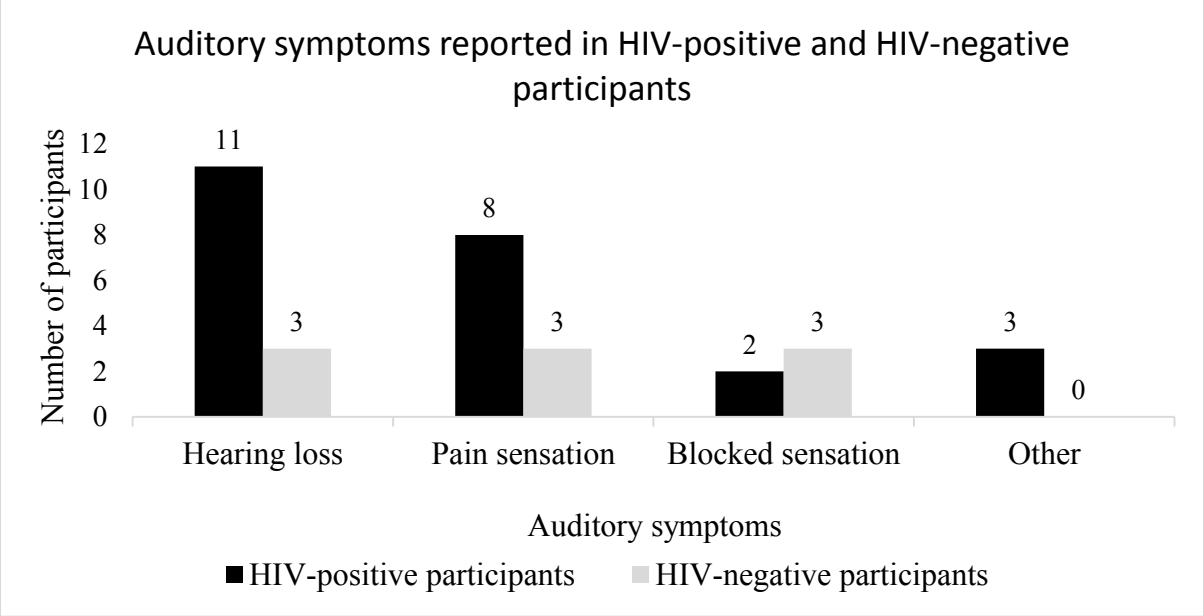


Figure 7. Prevalence and type of auditory symptoms reported by HIV-positive and HIV-negative participants.

Participant group 1

In this group, 33% ($n_1 = 20$) of participants reported some type of auditory symptom with most indicating hearing loss ($n_1 = 11$) and pain ($n_1 = 8$). The category *other* included symptoms such as a history of blisters or bumps in the ear canal, and/or discharge.

Participant group 2

Twenty-five percent of participants ($n_2 = 8$) in this group reported auditory symptoms. Hearing loss ($n_2 = 3$), pain ($n_2 = 3$), and a blocked sensation ($n_2 = 3$) were most often reported.

No statistically significant difference was found between the two participant groups regarding the prevalence of self-reported auditory symptoms ($p = 0.48$; Fisher's exact test).

Tinnitus

The nature of tinnitus experienced was recorded as occurrence (constant or intermittent), side (bilateral or unilateral), and pitch (low or high frequency) (Figure 8).

Participant group 1

Just over half of participants (57%; $n_1 = 34$) reported the presence of some type of tinnitus. The most prevalent nature of tinnitus reported was intermittent (45%; $n_1 = 27$), bilateral (48%; $n_1 = 29$), and high frequency (35%; $n_1 = 21$).

Participant group 2

Tinnitus was reported in 34% of participants ($n_2 = 11$). All these participants reported bilateral tinnitus. Similar to the HIV-positive group, intermittent (28%; $n_2 = 9$) high-frequency tinnitus (19%; $n_2 = 6$) was most prevalent.

In summary, the prevalence of tinnitus in the HIV-positive participant group and HIV-negative participant group was 57% and 34% respectively. A statistically significant difference was confirmed by the Fisher's exact test ($p = 0.05$).

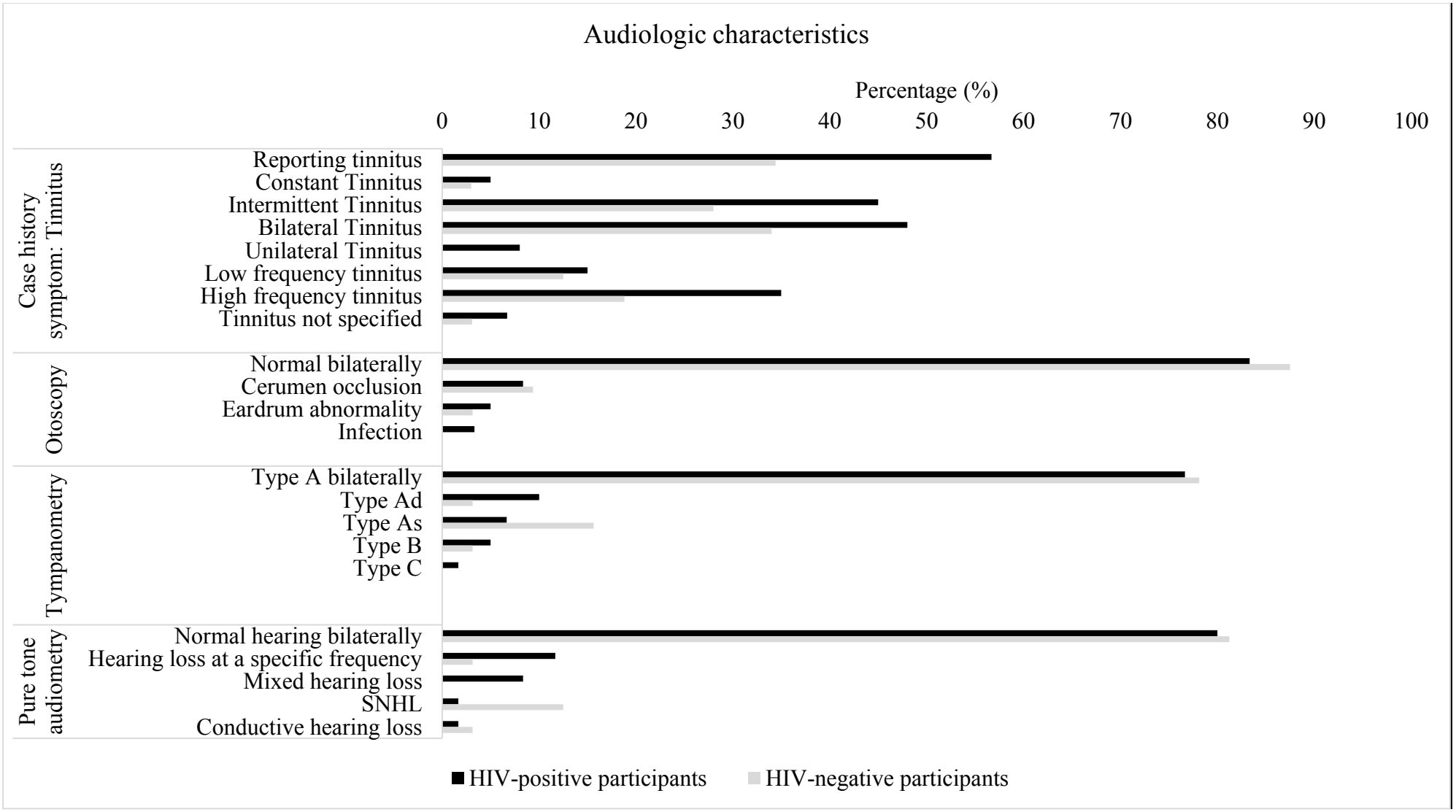


Figure 8. Visual illustration of auditory characteristics of HIV-positive participants (n_1 = 60) and HIV-negative participants (n_2 = 32).

Otoscopy

Normal otoscopy was classified according to the criteria discussed in Table 6.

Participant group 1

The results indicated that the majority of participants (83%; $n_1 = 100$ ears) presented with normal otoscopy bilaterally (Table 9).

Participant group 2

Bilateral normal otoscopy was observed in 88% ($n_2 = 56$ ears) of participants. Only one participant (3%) presented with an abnormal tympanic membrane, which was unilateral and attributed to a retracted tympanic membrane observed in the right ear (Table 9).

The results indicate that there is no statistically significant difference in the otoscopy findings between the two participant groups ($p = 0.17$; Fisher's exact test). The otoscopy and tympanometry results are reported separately for the left and right ears in Table 9.

Table 9

Otoscopy and tympanometry results

	Participant groups			
	HIV-positive group (n_1 = 60; 120 ears) % (n_1)		**HIV-negative group** (n_2 = 32; 64 ears) % (n_2)	
Otoscopy				
Normal bilaterally	83% (50)		88% (28)	
	Left ears (n_1 = 60)	**Right ears** (n_1 = 60)	**Left ears** (n_2 = 32)	**Right ears** (n_2 = 32)
Normal	87% (52)	93% (56)	94% (30)	88% (28)
Cerumen occlusion	7% (4)	5% (3)	6% (2)	9% (3)
Infection	3% (2)	0 (0%)	0% (0)	0% (0)
Tympanic membrane abnormalities	3% (2)	1 (2%)	0% (0)	3% (1)
Tympanometry				
Type A bilaterally	77% (46)		78% (25)	
	Left ears (n_1 = 60)	**Right ears** (n_1 = 60)	**Left ears** (n_2 = 32)	**Right ears** (n_2 = 32)
Type A	83% (50)	92% (55)	84% (27)	84% (27)
Type B	3% (2)	2% (1)	0% (0)	3% (1)
Type C	2% (1)	0% (0)	0% (0)	0% (0)
Type As	7% (4)	2% (1)	13% (4)	9% (3)
Type Ad	5% (3)	5% (3)	3% (1)	3% (1)

Tympanometry

The criteria suggested by Jerger (1970) (Table 6) were used to classify middle ear function.

Participant group 1

The results indicated that the majority of participants (77%; n_1 = 92 ears) in this group presented with normal Type A tympanograms bilaterally (Table 9).

Participant group 2

A Type A tympanogram was measured bilaterally in 79% (n_2 = 50 ears) of participants (Table 9).

In both participant groups, a Type A tympanogram was most prevalent, followed by an abnormality related to static compliance (Type As). Statistical analysis confirmed an insignificant difference in middle ear function between the two groups as determined by the Fisher's exact test (p = 1.00).

Pure tone audiometry

The pure tone audiometry results were classified according to the pure tone average, configuration (symmetrical or asymmetrical), nature (SNHL, conductive or mixed), and degree (mild, moderate, severe, or profound) of hearing loss. The criteria discussed in Table 6 used to classify the degree of hearing impairment.

Participant group 1

The mean pure tone average (PTA) for all left ears was 12.6 dB (±11.8; range: 0 – 65) and 12.3 dB (±9.2; range: 1.7 - 53.3) for all right ears. The vast majority of participants (90%; n_1 = 108 ears) presented with hearing within normal limits bilaterally according to their pure tone average. These results are presented separately for all left and right ears in Table 10.

Table 10

Pure tone audiometry

	Participant groups			
	HIV-positive group ***(n*$_1$ **= 60; 120 ears) % (*** n_1**)**		**HIV-negative group** **(*** n_2 **= 32; 64 ears) % (*** n_2**)**	
Hearing within normal limits bilaterally across frequency spectrum (250 Hz-8 kHz)	80% (48)		81% (26)	
Hearing within normal limits bilaterally based on pure tone average (>25 dB HL)	90% (54)		94% (30)	
Symmetrical hearing configuration	83% (50)		91% (29)	
Asymmetrical hearing configuration	17% (10)		9% (3)	
	Left ears (* n_1 **= 60)**	**Right ears (*** n_1 **= 60)**	**Left ears (*** n_2 **= 32)**	**Right ears (*** n_2 **= 32)**
Hearing within normal limits	83% (50)	85% (51)	91% (29)	81% (26)
Conductive hearing loss	0% (0)	2% (1)	0% (0)	3% (1)
SNHL	2% (1)	2% (1)	6% (2)	13% (4)
Mixed hearing loss	7% (4)	3% (2)	0% (0)	0% (0)
Hearing loss (>25 dB HL) at specific frequencies (2 kHz – 8 kHz)	8% (5)	8% (5)	3% (1)	3% (1)

Participant group 2

The audiograms presented with a mean PTA of 11.4 dB (±6.2; range: 0 - 21.7) and 13.7 dB (±7; range: 0 – 30) for the left and right ears respectively. Bilateral hearing within

normal limits, calculated according to the pure tone average, was most prevalent (94%; n_2 = 60 ears) (Table 10).

No statistically significant difference was found between the HIV-positive and HIV-negative groups in respect of the mean PTA of the left ears (p = 0.52; two-sample t-test). Likewise, no statistically significant difference was found between the two groups in respect of the right ears (p = 0.42; two-sample t-test).

Prevalence of hearing loss

The second sub-aim of the study was to determine the prevalence of HIV-positive individuals who present with hearing loss and compare this prevalence with hearing loss to that of an HIV-negative control group.

This prevalence was calculated according to the presence of an abnormal PTA (500 Hz, 1 kHz, and 2 kHz) of >25 dB HL.

The prevalence of hearing loss in participant group 1 was 10% (n_1 = 6) and 6% (n_2 = 2) in participant group 2. This difference was not statistically significant (p = 0.70; Fisher's exact test).

In summary, the majority of participants in both groups presented with hearing within normal limits bilaterally.

Hearing loss and tinnitus prevalence compared to previous studies

The third sub-aim of the study was to compare the prevalence of hearing loss and tinnitus in the current study with previous studies. This comparison is reported in Table 11.

Table 11

Comparison of prevalence of hearing loss and tinnitus in the current study with previous studies

Study	**Prevalence of hearing loss % (*n*)**	***p*-value when compared to prevalence of current study (10%; $n_1 = 6$)**	**Prevalence of tinnitus reported % (*n*)**	***p*-value when compared to prevalence of current study (57%; $n_1 = 34$)**
Chandrasekhar et al. (2000)	29 (15)	< 0.05*	26 (13)	< 0.05*
Khoza and Ross (2002)	23(35)	< 0.05*	23 (35)	< 0.05*
Van der Westhuizen et al. (2013)	14 (28)	0.51*	26 (52)	< 0.05*

Note. * = Fisher's exact test (p-value ≤ 0.05 was considered statistically significant)

The prevalence of hearing loss was only slightly higher than that reported by Van der Westhuizen et al. (2013), but significantly higher than that reported by Chandrasekhar et al. (2000) and Khoza and Ross (2002). The overall prevalence of tinnitus in the current study was significantly higher than previously reported. The current study also found that the prevalence of tinnitus was higher in CDC category 2 and category 3 compared to CDC category 1, however, this difference was not statistically significant ($p = 0.23$; two-sample t-test).

Auditory results and associated history of HIV-positive participants with hearing loss

To gain a better understanding of the factors that could contribute to these results, various characteristics were investigated, including the auditory history, ARV treatment, HIV category, as well as secondary symptoms of the 12 participants that presented with a hearing loss (Table 12).

No shared characteristics could be identified, thereby confirming that hearing loss in HIV-positive individuals may be attributed to various factors. These may include middle ear infections, presence of co-morbid conditions, and may occur irrespective of any ARV regimen, treatment duration or CDC category.

Table 12

Auditory results and associated history of HIV-positive participants presenting with hearing loss

Participant No	Type of hearing loss	Auditory history	Tinnitus	ARV regimen #	Duration on ARVs (years)	CDC category	Most recent viral load (copies/mL)	Secondary symptoms
3	Mild sloping hearing loss starting at 8 kHz	Occasional pain in left ear	Occasional high frequency	EFV; FTC; TDF	1	3 A	Not available	None
7	Bilateral mild mixed hearing loss	Struggles with hearing bilaterally for the last 4 years. Occasional discharge from left ear reported	Occasional low frequency in left ear	d4t; NVP; 3TC	5	2 A	82	None
8	Unilateral mild hearing loss at 3 kHz and a mild hearing loss at 4 kHz in the contralateral ear	No problems reported	None	EFV; FTC; TDF	1	2 A	<50	None
9	Unilateral mild hearing loss at 3 kHz and 6 to 8 kHz. Mild hearing loss at 2 kHz and 8 kHz in the contralateral ear	Participant reported that hearing has deteriorated since HIV diagnosis	Occasional high frequency	EFV; FTC; TDF	3	2 C	<50	Oesophageal candidiasis

Participant No	Type of hearing loss	Auditory history	Tinnitus	ARV regimen #	Duration on ARVs (years)	CDC category	Most recent viral load (copies/mL)	Secondary symptoms
10	Unilateral severe mixed hearing loss with a mild to severe hearing loss at 4 kHz to 8 kHz in the contralateral ear	Chronic middle ear infections since childhood (left ear)	Reported, not specified	AZT; EFV; 3TC	1	1 A	124	None
12	Unilateral mild hearing loss at 8 kHz	Occasional pain in left ear	Occasional low frequency	AZT; EFV; 3TC	2	2 C	<50	Pulmonary TB
31	Moderate unilateral mixed hearing loss	Pain, discharge, and hearing problems reported in the right ear	None	d4t; NVP; 3TC	13	3 C	Not available	Herpes Simplex
32	Unilateral mild hearing loss at 4 kHz and 6 kHz	No problems reported	Occasional high frequency	EFV; TDF; 3TC	3	2 A	<50	None
34	Mild bilateral SNHL	Struggled with hearing loss since childhood	Occasional low and high frequency	AZT; NVP; 3TC	7	2 C	<50	Pulmonary TB
48	Moderate mixed unilateral hearing loss	Problems with left ear since childhood	None	EFV; FTC; TDF	3	1 A	Not available	None
51	Unilateral mild hearing loss at 3, 6, and 8 kHz	Participant reported an infection in the	Occasional high frequency	EFV; FTC; TDF	2	2 A	Not available	None

Participant No	Type of hearing loss	Auditory history	Tinnitus	ARV regimen #	Duration on ARVs (years)	CDC category	Most recent viral load (copies/mL)	Secondary symptoms
		left ear during childhood						
57	Unilateral moderate to severe mixed hearing loss, with a unilateral moderate to severe conductive hearing loss in contralateral ear	Long-standing hearing loss. Participant also has a history of noise exposure from work	Occasional high frequency	EFV; FTC; TDF	1	1 A	Not available	None

Note. The abbreviations used in this table are described below.

#: EFV = Efavirenz; FTC = Emtricitabine; TDF = Tenofovir; d4T = Stuvadine; NVP = Nevirapine; 3TC = Lamivudine; AZT = Zidovudine

Balance characteristics of the two participant groups

The fourth sub-aim was to describe the balance characteristics of HIV-positive individuals and to compare these findings to that of an HIV-negative control group as determined with subjective (ABC scale/ABC-Z scale) and objective (HIMP) measures.

Self-perceived balance confidence level (ABC scale)

The balance confidence level as measured with the ABC and/or ABC-Z scale was calculated for each participant and evaluated according to the criteria for physical function, as suggested by Powell and Myers (1995) as well as Lajoie and Gallagher (2004) (Table 6).

Participant group 1

Half of the participants ($n_1 = 30$) in the HIV-positive group reported 100% balance confidence. The mean balance confidence score (93.4%) (Table 13) indicated a high level of physical function (>80%) (Powell & Myers, 1995) and a low risk of future falls (≤ 67%) (Lajoie & Gallagher, 2004). The ABC scale results are presented in Table 13.

Table 13

ABC scale results

	Participant groups	
	HIV-positive group (n_1 = 60)	**HIV-negative group (n_2 = 32)**
Mean ABC scores	1493.8	1590
Significance of mean ABC scores	*$p < 0.01$	
SD	±191.9	±24.1
Range	530 – 1600	1510 – 1600
Mean balance confidence	93.4%	99.4%
	HIV-positive group % (n_1)	**HIV-negative group % (n_2)**
ABC score categories (Powell & Myers, 1995)		
>80%	90% (54)	100% (32)
50-80%	8% (5)	0% (0)
<50%	2% (1)	0% (0)
Higher risk for future falls (≤ 67%)	3% (2)	0% (0)

Note. * = Two-sample *t*-test (*p*-value of ≤ 0.05 was considered statistically significant)

Participant group 2

The majority of participants (81%; $n_2 = 26$) scored 100% balance confidence. The lowest ABC score was 1510 (Table 13) indicating a balance confidence of 94.4%. Therefore all HIV-negative participants reported a high level of physical function (>80%) (Powell & Myers, 1995).

The mean ABC scores were significantly lower ($p < 0.01$; two-sample *t*-test) in the HIV-positive group than in the HIV-negative group. However, there was no statistically significant difference between the two groups in prevalence of scores indicating a high risk for future falls (≤ 67%) ($p = 0.54$; Fisher's exact test).

HIMP

During the HIMP, the presence of possible covert and/or overt catch-up saccades across various velocities tested, was evaluated for each SSC on the left and right side (Table 14). The criteria discussed in Table 6 were used to evaluate the HIMP results.

Participant group 1

A bilateral normal HIMP response was measured in the majority of participants (95%; $n_1 = 57$).

Participant group 2

All participants in this group (100%; $n_2 = 32$) presented with a normal HIMP response bilaterally.

The HIMP results for both groups are presented in Table 14.

Table 14

HIMP results

	Participant groups			
	HIV-positive group (n_1 = 60) % (n_1)		**HIV-negative group (n_2 = 32) % (n_2)**	
Bilateral normal HIMP results	95% (57)		100% (32)	
Unilateral normal HIMP results	5% (3)		0% (0)	
Presence of catch-up saccades and SCC affected				
	Left ears (n_1 = 60)	**Right ears (n_1 = 60 ears)**	**Left ears (n_2 = 32 ears)**	**Right ears (n_2 = 32 ears)**
Covert catch-up saccades	0% (0)	0% (0)	0% (0)	0% (0)
Overt catch-up saccades	2% (1) posterior SCC	0% (0)	0% (0)	0% (0)
Combination covert and overt catch-up saccades	3% (2) lateral SCC	0% (0)	0% (0)	0% (0)
Abnormal VOR gain				
Lateral canal	2% (1)	0% (0)	0% (0)	0% (0)
Anterior canal	0% (0)	0% (0)	0% (0)	0% (0)
Posterior canal	2% (1)	0% (0)	0% (0)	0% (0)

Catch-up saccades which met the criteria for consistency, direction, latency, and velocity, were present in only 5% (n_1 = 3) of individuals in participant group 1. The mean age of participants who presented with an abnormal HIMP response was 40 years, which is comparable to the mean age of this participant group (mean = 41 years; ± 5.3). There was, however, a statistically significant difference in mean age between the two participant groups

($p = 0.00$; two-sample *t*-test). Furthermore, the velocities used to obtain these abnormal HIMP results were also comparable to participants with normal HIMP results.

The mean VOR gains and asymmetries of the HIMP are presented for both participant groups in Table 15.

Table 15

Mean VOR gains and asymmetries of the HIMP

	Participant groups			
	HIV-positive group (n_1 = 60)		**HIV-negative group (n_2 = 32)**	
	Left ears (n_1 = 60)	**Right ears (n_1 = 60 ears)**	**Left ears (n_2 = 32 ears)**	**Right ears (n_2 = 32 ears)**
Lateral SCC				
Mean VOR gain	0.96	1.02	0.94	1.02
SD	±0.1	±0.1	±0.1	±0.1
Range	0.66 - 1.18	0.76 – 1.28	0.7 – 1.26	0.82 – 1.37
Mean asymmetry (%)	7.3		8.8	
SD	±5		±5.2	
Range	0 - 21		0 - 23	
Anterior SCC				
Mean VOR gain	0.89	0.90	0.87	0.91
SD	±0.1	±0.1	±0.1	±0.1
Range	0.65 – 1.16	0.67 – 1.05	0.71 – 1.16	0.78 – 1.08
Mean asymmetry (%)	7.8		8.6	
SD	±5.9		±5.3	
Range	0 - 27		1 – 18	
Posterior SCC				
Mean VOR gain	0.90	0.90	0.97	0.91
SD	±0.1	±0.1	±0.1	±0.1
Range	0.67 – 1.09	0.7 – 1.12	0.7 – 1.17	0.73 – 1.15
Mean asymmetry (%)	7.9		12.3	
SD	±5.9		±7.6	
Range	0 - 27		0 - 31	

Although the mean VOR gain of the left anterior SCC was within normal limits for participant group 1, this gain was observed to be lower compared to the other SCCs in 32% (n_1 = 19) of participants.

Similarly, the VOR gain of the left anterior SCC (Table 15) was observed to be lower in 41% (n_2 = 13) of HIV-negative participants.

The mean VOR gain of the left posterior SCC was significantly lower in the HIV-positive group compared to the HIV-negative group ($p < 0.01$; two-sample *t*-test), whilst the mean values of the other SCCs did not differ significantly between the two groups ($p > 0.05$; two-sample *t*-test).

Prevalence of reduced semi-circular canal function (anterior, posterior and lateral SCCs) and its afferent neural pathways

The fifth sub-aim was to determine the prevalence of HIV-positive individuals and an HIV-negative control group who present with reduced semi-circular canal function (anterior, posterior, and lateral SCCs), and its afferent neural pathways. The prevalence was calculated according to the presence of catch-up saccades (covert and/or overt), which was determined by analysing the raw HIMP data.

The prevalence of abnormal HIMP results in participant group 1 was 5% (n_1 = 3), whilst no individuals in participant group 2 presented with any HIMP abnormalities. This prevalence of abnormality in the HIV-positive group was not statistically significant (p = 0.54; Fisher's exact test). The prevalence of peripheral vestibular impairment in the current study (5%; n_1 = 3) was significantly lower ($p < 0.01$; Fisher's exact test) than reported by Heinze et al. (2014) (45.3%; n = 24).

Vestibular results and associated history in HIV-positive participants with balance impairment

In order to evaluate the factors associated with balance impairment, the vestibular history, vestibular results (subjective and objective), and HIV history (ARV regimen, CDC category, and secondary symptoms) were explored (Table 16).

No specific characteristic was identified in all these participants, as four various ARV regimens were used and participants were distributed among four different CDC categories. Although pulmonary TB was the only secondary symptom, this was only present in 33% (n_1 = 2) of participants.

Table 16

Balance results and associated history of HIV-positive participants with balance impairment

Participant No	**Vestibular history**	**ABC score (%)**	**Presence of catch-up saccades**	**Canal with saccades "**	**Mean VOR gain of this canal**	**HIMP Asymmetry (%)**	**ARV regimen #**	**Duration on ARVs (years)**	**CDC category**	**Most recent viral load (copies/mL)**	**Secondary symptoms**
*10	Reported occasional spinning sensation whilst sitting	33.3	None	None	N/A	N/A	AZT; EFV; 3TC	1	1A	124	None
24	Reported occasional spinning sensation	58.3	None	None	N/A	N/A	EFV; FTC; TDF	13	3C	<50	Pulmonary TB
28	None	90	Combination covert and overt saccades	LL	0.85	14	EFV; FTC; TDF	1	3A	94	None

Participant No	Vestibular history	ABC score (%)	Presence of catch-up saccades	Canal with saccades "	Mean VOR gain of this canal	HIMP Asymmetry (%)	ARV regimen #	Duration on ARVs (years)	CDC category	Most recent viral load (copies/mL)	Secondary symptoms
*34	Sometimes experiences dizziness for a few seconds	95	None	None	N/A	N/A	AZT; NVP; 3TC	7	2C	<50	Pulmonary TB
47	None	97.5	Overt saccades	LP	0.67	17	FTC; NVP; TDF	2	3A	75	None
56	None	96.3	Combination covert and overt saccades	LL	0.76	10	EFV; FTC; TDF	1	3A	<20	None

Note. The abbreviations used in this table are described below.

*: Participants with hearing loss as presented in Table 12

": LL = Left lateral; LP = Left posterior

#: AZT = Zidovudine; EFV = Efavirenz; 3TC = Lamivudine; FTC = Emtricitabine; TDF = Tenofovir disoproxil fumarate; NVP = Nevirapine

Agreement between the ABC scores and the HIMP results

The final sub-aim was to determine the agreement between subjective self-reported balance function and an objective peripheral vestibular function test.

The ABC scores and HIMP results showed a strong agreement as indicated by the McNemar test ($p = 0.32$) in the HIV-positive group (85% agreement). It should be noted, however, that all three HIV-positive participants that presented with a HIMP abnormality scored > 80% on the ABC scale. In the HIV-negative group there was perfect agreement (100%) between the results on both tests and therefore the McNemar test could not be calculated.

Chapter 5: Discussion

Introduction

This chapter provides a critical discussion regarding the results in accordance with the sub-aims of the study and relates these findings to the literature.

Auditory symptoms and audiological characteristics

The most noteworthy finding regarding auditory symptoms in the current study, was the significantly higher prevalence of tinnitus in the HIV-positive group compared to the HIV-negative control group. Tinnitus may be associated with hearing loss (Khoza-Shangase & Van Rie, 2016), however, the latter symptom was self-reported less frequently compared to the self-reporting of tinnitus. Khoza and Van Rie (2016) attributed this finding to two possible mechanisms. Firstly, hearing loss may co-occur with tinnitus, however, the degree of hearing impairment may be mild and insufficient for the individual to notice, specifically when such hearing loss affects only the higher frequencies; or the tinnitus may be related to non-auditory pathologies (Khoza-Shangase & Van Rie, 2016). In the current study high-frequency hearing loss (2 kHz-8 kHz) correlated with high-frequency tinnitus in 50% of HIV-positive individuals ($n_1 = 4$) who presented with hearing loss; however, this type of tinnitus was also reported by participants with hearing that was within normal limits. As tinnitus typically represents the frequency where hearing is most affected (Castillo & Roland, 2007), high-frequency audiometry (> 8 kHz) may have revealed a higher prevalence of hearing loss.

The increased tinnitus prevalence in the current study may be attributed to detailed tinnitus categories used, including occasional or consistent low-frequency or high-frequency tinnitus, or tinnitus which the participant was not able to describe as low or high frequency. Although the difference in tinnitus prevalence between the different CDC categories was insignificant, the increased prevalence in CDC category 2 and category 3 correlates with the study by Van der Westhuizen et al. (2013). This finding may be related to the direct damage

caused by HIV to auditory structures (Stearn & Swanepoel, 2010), which may have increased at more progressive stages of infection (Van der Westhuizen et al., 2013).

The comparable audiological results between the two participant groups were surprising, considering that earlier studies had reported a high prevalence of SNHL in HIV-positive individuals (Chandrasekhar et al., 2000; Khoza & Ross, 2002; Teggi et al., 2008; Van der Westhuizen et al., 2013). The findings from the current study may be attributed to earlier ARV treatment initiation which may have preserved hearing function (Schouten et al., 2006). Furthermore, 88% (n_1 = 53) of HIV-positive participants were using a first-line ARV protocol, which has been associated with less-toxic effects (WHO, 2013). In addition, 58% (n_1 = 35) of participants were asymptomatic, therefore the effects of secondary conditions and their treatment protocols were limited. These findings may also be attributed to effective management protocols employed by the NMC aimed at optimizing treatment and adherence levels of HIV-positive individuals, which include regular follow-up appointments for blood work and counselling sessions. The increased prevalence of SNHL reported by other studies may also be attributed to different criteria used to classify this type of hearing loss. Although not evident from previous studies, hearing impairment which affects only specific higher frequencies may have been classified as SNHL, whilst the current study separately classified hearing loss according to reduced hearing sensitivity (>25 dB HL) only at specific high frequencies (e.g. 8 kHz). Of interest however, is the finding that participants in the current study who presented with hearing loss at specific higher frequencies, were all using an ARV protocol which included EFV.

Previous reports have also suggested that otitis media may be more prevalent in HIV-positive individuals (Lalwani & Sooy, 1992), resulting in conductive hearing loss (Khoza, 2007). However, conductive hearing loss was not only least prevalent in the current study, concurring with earlier studies (Khoza & Ross, 2002; Van der Westhuizen et al., 2013), but

the occurrence thereof was also identical between the two participant groups. The reduced prevalence of conductive hearing loss in the current study may also be related to earlier ARV treatment initiation, which has been linked with reduced occurrence of opportunistic infections such as otitis media (WHO, 2016).

Prevalence of hearing loss

The hearing loss prevalence in HIV-positive individuals was less than that reported by earlier studies (Chandrasekhar et al., 2000; Khoza & Ross, 2002; & Van der Westhuizen et al., 2013). Differences in hearing loss prevalence between the current study and previous studies may be attributed to various factors. This slight insignificant difference between the prevalence of the current study and that reported by Van der Westhuizen et al. (2013) may be attributed to the use of ARVs. In their study only patients classified as CDC category 3 were receiving ARVs, whilst all participants in the current study were receiving ARVs irrespective of CDC category. In addition to ARV treatment initiation, the distribution of participants among various CDC categories and the presence of secondary conditions may also influence prevalence. The majority of participants in the study conducted by Chandrasekhar and colleagues (2000) was distributed among CDC category 2 (38%; n = 19) and CDC category 3 (44%; n = 22), whilst the minority of participants were in CDC category 1 (18%; n = 9). Therefore, as many participants were in the later progressive stages of infection, which has been associated with increased risk of developing hearing loss (Khoza & Ross, 2002; Van der Westhuizen et al., 2013), their significantly higher prevalence is not surprising. Furthermore, Khoza and Ross (2002) reported that almost all the HIV-positive subjects (91%; n = 137) in their study had a history of secondary conditions which may have contributed to their higher hearing loss prevalence, whilst in the current study 58% (n_1 = 35) of participants were classified in CDC category A, thereby indicating absence of any secondary conditions. In addition to the effect of different sample sizes, Chandrasekhar et al. (2000) (N = 50); Khoza

and Ross (2002) *(N* = 150); Van der Westhuizen et al. (2013) *(N* = 200); current study (n_1 = 60), various test batteries used which evaluate different aspects of the auditory system, may also play a role in prevalence differences. For example, Khoza and Ross (2002) included the ABR, which is able to evaluate neural integrity of the auditory system (Matas et al., 2010); Van der Westhuizen et al. (2013) included OAEs, which are sensitive for detecting ototoxic damage (Ranjan & Bhat 2008); whilst the current study did not include either of these measures. Finally, these differences may also be attributed to the criteria used to classify hearing loss. In the study conducted by Van der Westhuizen et al. (2013) and the current study, hearing loss was classified as a PTA > 25 dB HL, whilst Khoza and Ross (2002) classified hearing loss as any threshold > 25 dB HL; when applying this criterion to the current study, the prevalence is increased to 22% (n_1 = 13).

Balance characteristics

Subjective measure

The ICF framework recommends that various aspects of function should be evaluated in order to better understand the impact of an impairment (WHO, 2001b). By including the ABC scale, the perceived effects of a vestibular impairment on daily function could be evaluated.

The findings from the current study support previous reports that HIV is not a strong indicator for perceived fall risk caused by vestibular dysfunction (CROI, 2015; Erlandson et al., 2012; Erlandson et al., 2016). Some studies have, however, indicated that higher fall risk in HIV-positive individuals may be related to the presence of multiple co-occurring conditions (e.g. chronic pain, diabetes, hypertension) and use of multiple medications to treat these conditions rather than HIV sero-status (Erlandson et al., 2012; Erlandson et al., 2016). In the current study, four HIV-positive participants were using medication for hypertension, whilst another was using pain killers on a regular basis. Of these participants only one, being

treated for hypertension, scored within the moderate range (ABC scale) of physical function (72.5%), whilst the others (n_1 = 4) scored a high level of physical function (>80%). Owing to the small size of the study sample with these co-occurring conditions, a conclusion regarding this link was not possible in the current study.

Objective measure

The HIMP was selected for the current study based on its many advantages as well as to supplement available research conducted in HIV-positive individuals utilizing the caloric test (Castello et al., 1998; Grimaldi et al., 1993; Hausler et al., 1991; Heinze et al., 2014; Mathews et al., 2012; Teggi et al., 2008; Teggi et al., 2006). Although no shared characteristics were identified in participants with hearing loss, mutual findings in all participants with HIMP abnormalities included: older than 35 years (mean = 39.9 years; ±0.58); current ARV protocol consisting of FTC and TDF as well as current or prior treatment with EFV; treatment duration of less than 3 years (mean = 1.3 years; ±0.58); in CDC category 3A; hearing within normal limits; and normal balance confidence as suggested by their ABC scores. Other participants also presented with some of these characteristics, however, this complete profile was specific only to the three individuals with abnormal HIMP results.

The higher VOR gain of the right lateral and right anterior SCCs in both participant groups is consistent with a previous study, which attributed this occurrence to the geometry of the test procedure and measuring the response from the right eye (McGarvie et al., 2015). McGarvie et al. (2015) suggested that during the rightward head movement, a slightly bigger demand for eye rotation on this side exists to maintain fixation on the target. As a result, a larger VOR gain can be expected for rightward head movements compared to the left. Furthermore, the significantly lower mean VOR gain of the left posterior SCC in the HIV-positive group, may be attributed to the higher mean age of this group (mean = 41.4 years;

±5.3) compared to the control group (mean = 32.5 years; ±9.1); as increased age has been associated with a reduction in VOR gain of the posterior SCC (McGarvie et al., 2015).

Prevalence of reduced semi-circular canal function (anterior, posterior and lateral SCCs) and its afferent neural pathways

The insignificant difference in prevalence of peripheral vestibular function between HIV-positive and HIV-negative individuals supports findings from an earlier study (Cohen et al., 2012). Cohen and colleagues (2012) attributed this outcome to the effect of ARVs, which may strengthen immunity and reduce the occurrence of vestibular impairments. Their study also excluded all participants who presented with any vestibular complaints and therefore, many of these subjects may have been centrally compensated (Heinze et al., 2014) or without any vestibular impairment. The current study did not exclude HIV participants based on self-perceived dizziness after their HIV diagnosis, however, as was evident from the case history as well as ABC scores, the majority of HIV-positive participants did not experience any vestibular symptoms. Therefore, participants in the current study may also have been centrally compensated or without vestibular impairment. However, contrary to the study conducted by Cohen et al. (2012), a diagnostic test procedure was utilized to identify sub-clinical peripheral vestibular impairments.

The significantly higher prevalence of peripheral vestibular impairment reported by Heinze et al. (2014) may be attributed to history of opportunistic infections or previous ototoxic exposure, which was not available to the authors at the time of data collection. Heinze et al. (2014) reported that prevalence of peripheral vestibular impairment decreased at more advanced stages of infection, which was attributed to the effect of ART as more subjects in the advanced stages of infection were using ARVs. Considering possible secondary conditions, history of ototoxic medications, and that not all HIV-positive subjects were receiving ARVs, this increased prevalence reported by Heinze et al. (2013) is not

unexpected. In the current study, just over half of the participants were confirmed by medical records as CDC category A. Therefore, reduced prevalence of peripheral vestibular impairment may be attributed to limited effects of secondary conditions and their associated treatment. Contrary to previous studies, the current study was also conducted during the new ARV era of earlier treatment initiation, which has been associated with many health benefits (WHO, 2016). Furthermore, at the study site where the data were collected, extra precautions are taken in order to improve and maintain treatment adherence (e.g. HIV counselling sessions). In addition, more than half of the participants (65%; $n_1 = 39$) who had recently been tested for their current viral loads had < 50 copies/mL of the virus. Therefore, the consistent and effective management of these individuals may have contributed to the reduced prevalence of peripheral vestibular impairments.

The current findings may also differ from previous studies due to different test batteries that were utilized. Heinze and colleagues (2013) included the caloric test to report a significantly higher occurrence of unilateral impairment in the HIV-positive group compared to the HIV-negative group. Teggi et al. (2008) also used the caloric test to report that peripheral vestibular impairment was a prevalent finding across various progressive stages of HIV infection. However, it was not evident from the latter study whether any ARVs had been utilized. Therefore, the natural progression of the virus in the absence of any treatment, may also have contributed to these findings. Both Heinze et al. (2014) and Teggi et al. (2008) also conducted the HIT test. Although this procedure is limited in terms of subjective interpretation, detecting only overt catch-up saccades, and providing information regarding lateral SCC function (Curthoys et al., 2011), similar to the current study, no significant difference between HIV-positive and HIV-negative subjects was reported.

Agreement between the ABC scores and the HIMP results

The strong agreement between the ABC and the HIMP was not surprising considering that both tests evaluate aspects of balance function (confidence versus physical function) used during everyday activities. A possible explanation why all participants with abnormal HIMP results scored normal balance confidence (ABC scale) pertains to the degree of vestibular impairment. It may be possible that balance impairments, as suggested by the HIMP, have been noticed by these participants but were not yet sufficient for it to impact their balance confidence. Furthermore, a variety of factors may influence balance confidence, including the presence and duration of vestibular symptoms, self-reported psychological impairments (depression and anxiety) (Marchetti et al., 2011), and presence of co-morbid conditions and medications used to treat them (Erlandson et al., 2012; Erlandson et al., 2016). As none of the participants with HIMP abnormalities presented with any of these characteristics, unaffected ABC scores may be expected.

Summary

The audiological as well as vestibular results were comparable in both groups. Findings from the current study may suggest that HIV does not typically affect higher frequencies of the VOR pathway as indicated by the HIMP results. These findings have also been suggested by previous studies (Heinze et al., 2014; Teggi et al., 2008) using the bedside assessment (HIT). From the literature, it seems that lower frequencies of the VOR mechanism, as suggested by caloric studies, may be more vulnerable to HIV and its secondary effects. Therefore, peripheral vestibular impairment may have been more prevalent in the current study but was not identified by the HIMP procedure. However, as hearing impairment as well as fall risk was also comparable between the two groups, it may be possible that these impairments were less frequent as a result of new ARV guidelines and optimal intervention and management strategies employed by the current study site. A strong

agreement existed between balance confidence and physical function in the majority of participants as suggested by the ABC scores and the HIMP results.

Chapter 6: Conclusion

Introduction

This chapter presents the conclusion of the study, which was drawn from the results obtained according to the various sub-aims. In this section the critical reflection, implications, and recommendations for future research are also addressed.

Summary of the research findings

From the test battery, tinnitus was more prevalent in the HIV-positive group compared to the HIV-negative control group. The remainder of the audiological test battery was comparable between the two groups and therefore the prevalence difference of hearing loss was insignificant. Furthermore, differences in fall risk and HIMP abnormalities between the two groups were also insignificant. The reduced prevalence of audiological and vestibular abnormalities in the current study may be attributed to new ARV guidelines and effective management strategies. However, the strength of this conclusion is limited as a comprehensive test battery was not conducted. A strong agreement was found between the ABC scores and the HIMP results in both participant groups.

Critical evaluation of the study

Strengths

- This study included a large sample size, allowing generalization of the findings to the population in the Sekhukhune district (rural community).
- To the knowledge of the researcher, this is the first study conducted in South Africa utilizing the HIMP test to evaluate peripheral vestibular function in HIV-positive individuals.
- ARV regimens, as well as secondary conditions of each participant were listed, therefore the combined direct and indirect effect of HIV on the peripheral vestibular system were investigated.

- The ABC-Z scale was included, therefore reduced scores were less likely to be attributed to language barriers.

Limitations

- A cross-sectional research design was utilized, therefore the causal relationships could not be established. This type of research design provided an overview of the current auditory and vestibular function, whereas the use of a longitudinal research design could allow for changes within subjects to be observed, ultimately providing a better understanding regarding the effects of HIV and its treatment regimen.
- Another limitation of the current study pertains to the differences between the two participant groups, including the sample sizes and the fact that participants were not age- and gender-matched.
- HIV status was self-reported in the HIV-negative control group and not confirmed by a blood serology test.
- A test battery that may be more sensitive to detecting ototoxic damage was not included (e.g. OAEs). Therefore, possible ototoxic hearing loss as a result of ARVs and medications used for opportunistic infections may have been underreported.
- The entire peripheral vestibular system was not tested, therefore peripheral impairment may have been present in more individuals but was not identified by the HIMP.

Implications

Clinical implications

The findings from the current study provide evidence that tinnitus may be more prevalent in HIV-positive individuals than previously reported in the literature. As the focus of the current study was a portion of the peripheral vestibular system, it may be possible that

vestibular impairment affecting other structures was not identified, therefore the inclusion of a more comprehensive test battery may have identified a larger prevalence of impairments.

The main focus is often placed on the management of HIV itself and other co-occurring conditions rather than the symptoms experienced as a result thereof (balance and hearing impairments) (Teggi et al., 2008). The ignorance of these symptoms is concerning when considering the impact it may have on QoL. Therefore, it remains essential to increase awareness among health care professionals regarding tinnitus, hearing, and balance problems in order to ensure effective referral and management of HIV-positive individuals at all levels of healthcare, including the public as well as the private sector.

Policy implications

Considering that hearing loss was self-reported less frequently than tinnitus and the standard audiological test battery was comparable between the two participant groups, the inclusion of a test battery which is sensitive to detecting ototoxic hearing loss may identify more impairments. Therefore, as suggested by Campbell (2007), in addition to conventional audiometry, including the assessment of ultra-high frequencies (> 8 kHz) and OAEs may be valuable. In an ideal setting these tests should be conducted before the initiation of any treatment regimen in order to serve as a baseline to compare changes in hearing abilities and to determine effective intervention (AAA, 2009). This process may ultimately reduce the effect that hearing loss may have on communication abilities and therefore QoL. However, as such equipment may not always be available, asking the individual regarding these characteristics during the case history or using tinnitus surveys may prove valuable in order to collaborate with the medical team regarding possible treatment regimen changes, and counselling the individual regarding the need to monitor hearing abilities. As tinnitus in HIV-positive participants may also be related to non-auditory (Khoza-Shangase & Van Rie,

2016) pathologies, the evaluation thereof remains crucial not only to implement tinnitus management strategies but also to establish the need for referral.

Furthermore, the current study concurs with previous research that a comprehensive vestibular test battery should be used to evaluate the entire vestibular system (Eza-Nuñez et al., 2014; Bell et al., 2015; Redondo-Martínez et al., 2016). By adding test procedures such as the cVEMP and oVEMP as well as tests evaluating the central vestibular system (e.g. oculomotor tests), more comprehensive information regarding the effects of HIV on various vestibular structures may be obtained. Although the inclusion of a comprehensive vestibular test battery may be ideal, the availability of this equipment may be limited at all levels of healthcare, especially in the public health sector. Therefore, the use of questionnaires and bedside assessments may be valuable in all contexts. By including these assessments in the standard consultation with HIV-positive individuals, more referrals may be made and management of these individuals may be optimized.

Recommendations for future research

The following recommendations may be valuable to expand on the current research:

Employing a longitudinal research method may be valuable in order to determine a causal relationship between HIV and its treatment regimen on auditory and vestibular function. Studies could also evaluate the association between treatment adherence levels and the occurrence of auditory and vestibular disturbances in HIV-positive individuals. The inclusion of a similar HIV-positive and HIV-negative sample size, as well as age- and gender-matched participants in both groups, may improve generalization of the test results. Confirming HIV sero-status in all HIV-negative individuals by blood serology tests may also eliminate any possibility of assigning an individual to the wrong participant group.

As the prevalence of tinnitus was significantly higher in the HIV-positive group, future studies could focus on tinnitus management strategies as well as investigating the

contributing factors, including the use of specific medication, and nature of tinnitus experienced with the use of more specific tests such as frequency and intensity matching.

Inclusion of OAEs and high-frequency audiometry in the test battery may also provide more insight regarding possible ototoxic hearing loss and therefore the effects of new ARV protocols on the auditory system as well as the nature of tinnitus experienced. The inclusion of VEMPS, in addition to the HIMP test may be valuable in order to evaluate the complete peripheral vestibular system in HIV-positive individuals. Furthermore, the addition of calorics may also complement the test battery. The caloric test may provide diagnostic value, especially in participants with a normal HIMP where peripheral vestibular involvement is suspected. More research is required in HIV-positive individuals using the HIMP test. This test could also be complemented by the SHIMP (Suppression Head Impulse) test in order to evaluate residual vestibular function through VOR suppression (Halmagyi et al., 2017). The effect of confounding variables, such as diabetes and medications used to treat these conditions on fall risk in HIV-positive individuals, could also be better investigated by including a larger sample size with such conditions.

In conclusion, from the current study it is evident that more auditory and vestibular research is required in HIV-positive individuals using a comprehensive test battery; especially now that new ARV treatment guidelines, which recommend earlier treatment initiation and use of less-toxic drugs (WHO, 2015; WHO, 2016) have been implemented. Although the management of the life-threatening virus is often the first concern, neglecting to manage the effects of this virus can be just as debilitating and adversely affect QoL. Although the inclusion of a comprehensive test battery may not always be feasible due to various reasons, using questionnaires and bedside assessments may be valuable. Furthermore, increasing awareness among medical staff regarding the possible effects of HIV

on both auditory and vestibular function as well as the presenting symptoms, may contribute toward more effective management and ultimately enhance QoL.

References

Agrup, C., Gleeson, M., & Rudge, P. (2007). The inner ear and the neurologist. *Journal of Neurology, Neurosurgery and Psychiatry, 78*(2), 114-122.

Ali, Z., & Bhaskar, S. B. (2016). Basic statistical tools in research and data analysis. *Indian Journal of Anaesthesia, 60*(9), 662-669.

American Academy of Audiology. (2009). Position statement and clinical practice guidelines: Ototoxicity monitoring. Retrieved from www.audiology.org/resources/documentlibrary/Documents/OtoMonPositionGuideline.pdf

Amico, P., Aran, C., & Avila, C. (2010). HIV spending as a share of total health expenditure: An analysis of regional variation in a multi-country study. *PLOS ONE, 5*(9), e12997.

Ansari, N. A., Kombe, A. H., Kenyon, T. A., Hone, N. M., Tappero, J. W., Nyirenda, S. T., Binkin, N. J., & Lucas, S. B. (2002). Pathology and causes of death in a group of 128 predominantly HIV-positive patients in Botswana, 1997–1998. *International Journal of Tuberculosis and Lung Disease, 6*(1), 55–63.

Arlinger, S. (2003). Negative consequences of uncorrected hearing loss—A review. *International Journal of Audiology, 42*(*Suppl*. 2), 17-20.

Arya, R., Thawani, P., & Rangasayee, R. (2016). Vertigo in ICF framework: A pilot study. *International Journal of Community Health and Medical Research, 2*(2), 32-37.

Assuiti, L. F. C., Lanzoni, G. M., Dos Santos, F. C., Erdmann, A. L., & Meirelles, B. H. S. (2013). Hearing loss in people with HIV/AIDS and associated factors: An integrative review. *Brazilian journal of otorhinolaryngology, 79*(2), 248-255.

Azia, I. N., Mukumbang, F. C., & Van Wyk, B. (2016). Barriers to adherence to antiretroviral treatment in a regional hospital in Vredenburg, Western Cape, South Africa. *Southern African Journal of HIV Medicine, 17*(1), 476.

Badke, M. B., Miedaner, J. A., Shea, T. A., Grove, C. R., & Pyle, G. M. (2005). Effects of vestibular and balance rehabilitation on sensory organization and dizziness handicap. *Annals of Otology Rhinology and Laryngology*, *114*(1 Pt 1), 48-54.

Baha, H. (2016). An introduction of descriptive analysis, its advantages and disadvantages. Unpublished Thesis, Leuphana University of Lüneburg.

Bajpai, S., Bajpai, R. C., & Chaturvedi, H. K. (2015). Evaluation of inter-rater agreement and inter-rater reliability for observational data: An overview of concepts and methods. *Journal of the Indian Academy of Applied Psychology, 41*(3), 20-27.

Baloh, R. W., Ying, S. H., & Jacobson, K. M. (2003). A longitudinal study of gait and balance dysfunction in normal older people. *Archives of Neurology, 60*(6), 835-839.

Bardien, S., De Jong, G., Schaaf, H. S., Harris, T., Fagan, J., & Petersen, L. (2009). Aminoglycoside-induced hearing loss: South Africans at risk. *South African Medical Journal, 99*(6), 44-441.

Barin, K. (October, 2014a). ICS Impulse vHIT: Clinical applications. Retrieved from http://www.icsimpulse.com/how-it-works#additional. (2017, September 28). Otometrics: How it works. [Video File]. Retrieved from https://www.youtube.com/watch?time_continue=794&v=ihEnKWc1Q88

Barin, K. (October, 2014b). ICS Impulse vHIT: Interpretation of test results. Retrieved from http://www.otometrics.com/en-AU/solutions/balance-assessment/ics-impulse-vhit#top. (2017, September 28). Otometrics: How it works. [Video File]. Retrieved from https://www.youtube.com/watch?time_continue=319&v=9HVbT0EBJDE

Barnighausen, T., Hosegood, V., Timaeus, I. M., & Newell, M. L. (2007). The socio-economic determinants of HIV incidence: Evidence from a longitudinal, population-based study in rural South Africa. *AIDS, 21*(*Suppl.* 7), S29-S38.

Bauman, N. G. (2003). Ototoxicity—the hidden menace. Part I: Lives in upheaval. Retrieved from http://www.hearnet.com/features/articles/Ototoxic_Drugs_Exposed.pdf

Beers, S. L., & Abramo, T. J. (2004). Otitis externa review. *Pediatric Emergency Care, 20*(40), 250-256.

Belli, G. (2008). Nonexperimental quantitative research. Retrieved from https://www.k4health.org/sites/default/files/migrated_toolkit_files/0470181095-1.pdf

Berg, K. O., Maki, B. E., Williams, J. I., Holliday, P. J., & Wood-Dauphinee, S. L. (1992). Clinical and laboratory measures of postural balance in an elderly population. *Archives of Physical Medicine and Rehabilitation, 73*(11), 1073-1080.

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

Bess, F. H., & Humes, L. E. (2008). *Audiology: The fundamentals* (4th ed.). Philadelphia; PA: Lippincott Williams & Wilkins.

Birchall, M. A., Wight, R. G., French, P. D., Cockbain, Z., & Smith, S. J. (1992). Auditory function in patients infected with the human immunodeficiency virus. *Clinical Otolaryngology & Allied Sciences, 17*(2), 117-121.

Black, F. O., Pesznecker, S., & Stallings, V. (2004). Permanent gentamicin vestibulotoxicity. *Otology & Neurotology, 25*(4), 559-569.

Blum, L., & Korner-Bitensky, N. (2008). Usefulness of the berg balance scale in stroke rehabilitation: A systematic review. *Physical Therapy, 88*(5), 559–566.

Botner, E. M., Miller, W. C., & Eng, J. J. (2005). Measurement properties of the activities-specific balance confidence scale among individuals with stroke. *Disability and Rehabilitation, 27*(4), 156-163.

Brandt, T., & Dieterich, M. (1993). Vestibular falls. *Journal of Vestibular Research: Equilibrium and orientation, 3*(1), 3–14.

Cameron, M. H., & Huisinga, J. (2013). Objective and subjective measures reflect different aspects of balance in multiple sclerosis. *Journal of Rehabilitation Research & Development, 50*(10), 1401-1410.

Campbell, K. C. M. (2007). *Pharmacology and ototoxicity for audiologists*. New York, US: Thompson/Delmar Learning.

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 and Laryngology, 107*(12), 1054-1060.

Castillo, M. P., & Roland, P. S. (2007). Disorders of the auditory system. In R. J. Roeser, M. Valente, & H. Hosford-Dunn (Eds.), *Audiology Diagnosis* (pp. 3 & 78). Stuttgart, BW: Thieme Medical Publishers.

Cattaneo, D., Regola, A., & Meotti, M. (2006). Validity of six balance disorders scales in persons with multiple sclerosis. *Disability & Rehabilitation, 28*(12), 789–795.

CDC. (1992). 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. *Center for Disease Control and Prevention, 18*(41(RR-17): 1-19).

CDC. (2013). Descriptive and analytical studies [PDF document]. Retrieved from, https://www.cdc.gov/globalhealth/healthprotection/fetp/training_modules/19/desc-and-analytic-studies_ppt_final_09252013.pdf

Census. (2011). Municipal report Limpopo. Retrieved from, http://www.statssa.gov.za/census/census_2011/census_products/LP_Municipal_Report.pdf

Chandrasekhar, S. S., Conelly, P. E., Brahmbatt, S. S., Shah, C. S., Kloser, P. C., & Baredes, S. (2000). Otologic and audiologic evaluation of human immunodeficiency virus-infected patients. *American Journal of Otolaryngology Head and Neck Medicine and Surgery, 21*(1), 1-9.

Chandrasekhar, S.S., Siverls, V., & Sekhar, H. K. (1992). Histopathologic and ultra-structural changes in the temporal bones of HIV-infected human adults. *American Journal of Otolaryngology, 13*(3), 207-214.

Chang, N. N-Y., Hiss, M. M., Sanders, M. C., Olomu, O. U., MacNeilage, P. R., Uchanski, R. M., & Hullar, T. E. (2014). Vestibular perception and the vestibulo-ocular reflex in young and older adults. *Ear and hearing, 35*(5), 565-570.

Chin, J. (2007). HIV/AIDS Prevention. *The AIDS pandemic: The collision of epidemiology with political correctness* (p. 160). Oxford, SEA: Radcliffe Publishing.

Chinsongkram, B., Chaikeeree, N., Saengsirisuwan, V., Viriyatharakij, N., Horak, F. B., & Boonsinsukh, R. (2014). Reliability and validity of the balance evaluation systems test (BESTest) in people with subacute stroke. *Physical Therapy, 94*(11), 1632-1643.

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

Clark-Carter, D. (2009). *Quantitative psychological research: The complete student's comparison* (3rd ed.). Hove; UK: Psychology Press.

Cloete, A., Strebel, A., Simbayi, L., Van Wyk, B., Henda, N., & Nqeketo, A. (2010). Challenges faced by people living with HIV/AIDS in Cape Town, South Africa: Issues for group risk reduction interventions. *AIDS Research and Treatment*, 2010 (ID 420270). Retrieved from, https://www.hindawi.com/journals/art/2010/420270/

Cohen, D. (2006). Poverty and HIV/AIDS in sub-Saharan Africa. *HIV/AIDS Electronic Library*, Paper No.: 27. Retrieved from,

http://www.undp.org/content/dam/aplaws/publication/en/publications/hiv-aids/poverty-and-hiv-aids-in-sub-saharan-africa/87.pdf?download

Cohen, E. B., Durstenfeld, A., & Roehm, P. C. (2014). Viral causes of hearing loss: A review for hearing health professionals. *Trends in Hearing, 18*, 1-17.

Cohen, H. S., & Kimball, K. T. (2008). Usefulness of some current balance tests for identifying individuals with disequilibrium due to vestibular impairments. *Journal of Vestibular Research, 18*(5), 295-303.

Cohen, H. S., Cox, C., Springer, G., Howard, J. H., Young, M., 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), e38419.

Collinson, M., Wolff, B., Tollman, S., & Kahn, K. (2006). Trends in internal labour migration from the rural Limpopo province, male risk behaviour, and implications for spread of HIV/AIDS in rural South Africa. *Journal of Ethnic and Migration Studies, 32*(4), 633-648.

Conference on Retroviruses and Opportunistic Infections. (2015). Balance confidence predicts falls better than physical function testing in HIV+ men. 2015. Seattle, Washington. Abstract 786.

Cox, J.A., Lukande, R. L., Lucas, S., Nelson, A.M., Van Marck, E., & Colebunders, R. (2010). Autopsy causes of death in HIV-positive individuals in sub-Saharan Africa and correlation with clinical diagnoses. *AIDS Reviews, 12*(4), 183–194.

Craig, J. (2016, March). Vestibular evoked myogenic potentials (VEMP): How do I get started? *AudiologyOnline*, Article 16713. Retrieved from http://www.audiologyonline.com

Crumley-Welsh, W. (2013, July 22). ICS Impulse – revolutionizing vestibular assessment. *AudiologyOnline*, Article 12003. Retrieved from http://www.audiologyonline.com/

Crumley-Welsh, W. (2016, September). LARP RALP. Retrieved from http://www.icsimpulse.com/how-it-works#vhit. (2017, September 28). Otometrics: How it works. [Video File]. Retrieved from https://www.youtube.com/watch?time_continue=7&v=xt-prupr884

Curthoys, I. S., MacDougall, H. G., Manzari, L., Burgess, A. M., Bradshaw, A. P., McGarvie, L.A., Halmagyi, G. M., & Weber, K. P. (2011). Clinical application of a new objective test of semicircular canal dynamic function – the video head impulse test (vHIT): A safe, simple and fast clinical vestibular test. Retrieved from, http://www.centroequilibra.com/uploads/2/1/2/3/2123449/2.6.isc_.otometrics_01.pdf

Curthoys, I. S., MacDougall, H. G., McGarvie, L. A., Weber, K. P., Szmulewicz, D., Manzari, L., Burgess, A. M., & Halmagyi, G. M. (2014). The video head impulse test (vHIT). In G. P. Jacobson, & N. T. Shephard (Eds.) (2nd ed.), *Balance function assessment and management* (p. 416). San Diago, CA: Plural publishing.

Deeks, S. G., Lewin, S. R., & Havlir, D. V. (2013). The end of AIDS: HIV infection as a chronic disease. *Lancet, 382*(9903), 1525-1533.

Den Boon, S., Van Lill, S. W. P., Borgdorff, M. W., Enarson, D. A., Verver, S., Bateman, E. D., Irusen, E., Lombard, C. J., White, N. W., De Villiers, C., & Beyers, N. (2007). High prevalence of tuberculosis in previously treated patients, Cape Town, South Africa. *Emerging Infectious Diseases, 13*(8), 1189-1194.

Dickins, J. R. E., & Graham, S. S. (1990). Meniere's disease: 1983 – 1989. *American Journal of Otology, 11*(1), 51-65.

Domenech, J., Fuste, J., & Traserra, J. (1996). Equilibrium and auditory disorders in patients affected by HIV-1. *Revue Neurologique, 24*(136), 1623-1626.

Duggal, P., & Sarkar, M. (2007). Audiologic monitoring of multi-drug resistant tuberculosis patients on aminoglycoside treatment with long term follow-up. *Biomed Central Ear Nose Throat Disorders, 7*(5), 1–7.

Enloe, L. J., & Shields, R. K. (1997). Evaluation of health-related quality of life in individuals with vestibular disease using disease-specific and general outcome measures. *Physical Therapy, 77*(9), 890-903.

Erlandson, K. M., Allshouse, A. A., Jankowski, C. M., Duong, S., MaWhinney, S., Kohrt, W. M., & Campbell, T. B. (2012). Risk factors for falls in HIV-infected persons. *Journal of Acquired Immune Deficiency Syndrome, 61*(4), 484-489.

Erlandson, K. M., Plankey, M. W., Springer, G., Cohen, H. S., Cox, C., Hoffman, H. J., Yin, M. T., & Brown, T. T. (2016). Fall frequency and associated factors among men and women with or at risk for HIV infection. *HIV medicine, 17*(10), 740-748.

Eza-Nuñez, P., Fariñas-Alvarez, C., & Perez-Fernandez, N. (2014). The caloric test and the video head-impulse test in patients with vertigo. *The Journal of International Advanced Otology, 10*(2), 144-149.

Farid, A. S., El-Abd, S. M., & Abou-Elew, M. H. (2003). Monothermal caloric test its value in assessment of vestibular function. *International Congress Series, 1240*, 1319-1324.

Fielder, H., Denholm, S. W., Lyons, R. A., & Fielder, C. P. (1996). Measurement of health status in patients with vertigo. *Clinical Otolaryngology and Allied Sciences, 21*(2), 124-126.

Food and Agriculture Organization of the United Nations. (2017). The impact of HIV/AIDS on rural households and land issues in southern and eastern Africa. Retrieved from http://www.fao.org/wairdocs/ad696e/ad696e04.htm#fnB3

Ganyaza-Twalo, T., & Seager, J. (2005). Literature review on poverty and HIV/AIDS: Measuring the social and economic impacts on households. Retrieved from http://www.wsu.ac.za/hsrc/html/ganyaza-twalo.pdf

Gillespie, S. (2008). Poverty, food insecurity, HIV vulnerability and the impacts of AIDS in sub-Saharan Africa. *IDS Bulletin, 39*(5), 10-18.

Godwin, M., Ruhland, L., Casson, I., MacDonald, S., Delva, D., Birtwhistle, R., Lam, M., & Seguin, R. (2003). Pragmatic controlled clinical trials in primary care: The struggle between external and internal validity. *BMC Medical Research Methodology, 22*(3), 28.

Goebel, J. A. (2008). Practical anatomy and physiology. In J. A. Goebel (Ed.), *Practical management of the dizzy patient* (2nd ed., p. 32). Philadelphia; PA: Lippincott Williams & Wilkins.

Greater Sekhukhune District Municipality Profile. (2011). Retrieved from https://www.google.co.za/url?sa=t&rct=j&q=&esrc=s&source=web&cd=2&cad=rja&uact=8&ved=0ahUKEwjMy8XgwbDUAhUlJsAKHTBXBRcQFggrMAE&url=http%3A%2F%2Fwww.nda.agric.za%2FdoaDev%2F22SMS%2Fdocs%2FPROFILES%25202011%2520GREATER%2520SEKHUKHUNE.docx&usg=AFQjCNFFqEqfzkpv8mjfT9MxgtkxdU7l3Q

Grill, E., Bronstein, A., Furman, J., Zee, D. S., & Müller, M. (2012). International classification of functioning, disability and health (ICF) core set for patients with vertigo, dizziness and balance disorders. *Journal of Vestibular Research, 22*(5-6), 261-271.

Grimaldi, L. M. E., Luzi, L., Martino, G. V., Furlan, R., Nemni, R., Antonelli, A., Canal, N., & Pozza, G. (1993). Bilateral eighth cranial nerve neuropathy in human immunodeficiency virus infection. *Journal of Neurology, 240*(6), 363-366.

Hain, T. C. (2012). Vestibular testing. Retrieved from http://american-hearing.org/disorders/vestibular-testing/. Accessed on 12 December, 2017.

Hain, T. C. (2017). Vestibular evoked myogenic potential (VEMP) testing - cervical (SCM). Retrieved from https://www.dizziness-and-balance.com/testing/vemp.html. Accessed on 12 December, 2017.

Hain, T. C., & Helminski, J. O. (2014). Anatomy and physiology of the normal vestibular system. In S. J. Herdman, & R. Clendaniel (Eds.), *Vestibular Rehabilitation* (4th ed.). *Chapter 1* (pp. 1-13). Philadelphia; PA: F. A. Davis Publications.

Hajimia, H. (2014). *Research method-sampling* [PowerPoint Slides]. Retrieved from https://www.slideshare.net/hafizahhajimia/research-method-sampling

Halmagyi, G. M., & Curthoys, I. S. (1988). A clinical sign of canal paresis. *Archives of Neurology, 45*(7), 737-739.

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.

Harris, T., & Heinze, B. (2013). Tuberculosis (TB), aminoglycoside and HIV-related hearing loss. *Open Access Guide to Audiology and Hearing Aids for Otolaryngologists*: Retrieved from https://vula.uct.ac.za/access/content/group/27b5cb1b-1b65-4280-9437-a9898ddd4c40/Tuberculosis%20_TB_%2C%20HIV%20and%20aminoglycoside%20related%20hearing%20loss%20_ototoxicity_.pdf

Harsha, W. J., Philips, J. O., & Backous, D. D. (2008). Clinical anatomy and physiology. In P. C. Weber (Ed.), *Vertigo and disequilibrium: A practical guide to diagnosis and management* (p. 413). Stuttgart; BW: Thieme Medical Publishers.

Hart, C.W., Cokely, C.G., Schupbach, J., Dal Canto, M.C., & Coppleson, L.W. (1989). Neurotologic findings of a patient with acquired immune deficiency syndrome. *Ear and hearing, 10*(1), 68–76.

Hausler, R., Vibert, D., Koralnik, I. J., & Hirschel, B. (1991). Neuro-otological manifestations in different stages of HIV infection. *Acta Otolaryngologica,* (*Suppl.* 481), 515-521.

Hazra, A., & Gogtay, N. (2016). Biostatistics series module 4: Comparing groups – categorical variables. *Indian Journal of Dermatology, 61*(4), 385-392.

HPCSA. (2002). Standards of practice in audiology. Retrieved from http://www.hpcsa.co.za/Uploads/editor/UserFiles/downloads/conduct_ethics/audiology_standards_for_slh.pdf

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., 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 and Otology*, *125*(9), 881–890.

Hendelman, W. J., Humphreys, P., & Skinner, C. R. (2017). *The integrated nervous system: A systematic diagnostic case-based approach*. Boca Raton, Florida: CRC Press.

Hizli, Ö., Hizli, P., Kaya, S., Monsanto, R. D., Paparella, M. M., & Cureoglu, S. (2016). Histopathologic ear findings of syphilis: A temporal bone study. *European Archives of Otorhinolaryngology, 273*(9), 2443-2449.

Hofmeyr, L. (2015). HIV and AIDS. Retrieved from http://lmhofmeyr.co.za/conditions/dizziness-and-balance-disorders/hiv-and-aids/

Hofmeyr, L. M., & Baker, M. (2010). Balance disorders associated with HIV/AIDS. In D. W. Swanepoel, & B. Louw (Eds.), *HIV/AIDS related communication, hearing and swallowing disorders* (pp.289- 349). San Diego; Oxford; Brisbane: Plural Publishing.

Holbein-Jenny, M. A., Billek-Sawhney, B., Beckman, E., & Smith, T. (2005). Balance in personal care home residents: a comparison of the berg balance scale, the multi-directional reach test, and the activities-specific balance confidence scale. *Journal of Geriatric Physical Therapy, 28*(2), 48-53.

Horak, F. B., Wrisley, D. M., & Frank, J. (2009). The balance evaluation systems test (BESTest) to differentiate balance deficits. *Physical Therapy, 89*(5), 484–498.

Hotz, M., Harris, F., & Probst, R. (1994). Otoacoustic emissions: An approach for monitoring aminoglycoside-induced ototoxicity. *Laryngoscope, 104*(9), 1130–1134.

Institute for Health Metrics and Evaluation. (2016). Growth in maternal and child health funding outpaces spending on HIV, TB, and malaria. Retrieved from http://www.healthdata.org/news-release/growth-maternal-and-child-health-funding-outpaces-spending-hiv-tb-and-malaria. Accessed on 8 December, 2017.

Integrated Development Plan. (2017). IDP review 2017-2018: Sekhukhune District Municipality. Retrieved from http://www.sekhukhunedistrict.gov.za/sdm-admin/documents/Sekhukhune%20District%20Draft%202017-18%20IDP-Budget.pdf

Jacobs, J. V., & Kasser, S. L. (2012). Balance impairment in people with multiple sclerosis: Preliminary evidence for the balance evaluation systems test. *Gait & Posture 36*(3), 414-418.

Jacobson, G. P., & Newman, C. W. (1990). The development of the dizziness handicap inventory. *Archives of Otolaryngology Head & Neck Surgery, 116*(4), 424-427.

Jacobson, G. P., & Newman, C.W. (1997). Background and technique of caloric testing. In G. P. Jacobson, C. W. Newman, & J. M. Kartush (Eds.), *Handbook of balance function testing* (pp.156-160). San Diego; London: Singular publishing group.

Jerger, J. (1970). Clinical experience with impedance audiometry. *Archives of otolaryngology, 92*(4), 311-324.

Johnson, A. S., Hu, X., & Dean, H. D. (2010). Epidemiologic differences between native-born and foreign-born black people diagnosed with HIV infection in 33 U.S. states, 2001–2007. *Public Health Reports, 125*(*Suppl.* 4), 61-69.

Kallail, K. J., Downs, D. W., & Scherz, J. W. (2008).Communication disorders in individuals with HIV/AIDS. *Kansas Journal of Medicine, 1(3), 62-69.*

Kamanji, R. (2016). Zulu translation and cross cultural adaptation of the activities-specific balance confidence (ABC) scale. Unpublished Masters, University of the Witwatersrand.

Kaufman, K. R., Brey, R. H., Chou, L. S., Rabatin, A., Brown, A. W., & Basford, J. R. (2006). Comparison of subjective and objective measurements of balance disorders following traumatic brain injury. *Medical Engineering and Physics 28*(3), 234-239.

Kegelmeyer, D. A., Kloos, A. D., Thomas, K. M., & Kostyk, S. K. (2007). Reliability and validity of the Tinetti mobility test for individuals with Parkinson disease. *Physical Therapy 87*(10), 1369-1378.

Khoza, K. (2007). An investigation and monitoring of the auditory status of a group of adults with AIDS receiving anti-retroviral and other therapies attending a provincial hospital HIV/AIDS clinic in Johannesburg, South Africa. Unpublished PhD, University of the Witwatersrand.

Khoza, K., & Ross, E. (2002). Auditory function in a group of adults with HIV/AIDS in Gauteng, South Africa. *South African Journal of Communication Disorders, 49*, 17-27.

Khoza-Shangase, K. (2011). Highly active antiretroviral therapy: Does it sound toxic? *Journal of Pharmacy and Bioallied Sciences, 3*(1), 142–153.

Khoza-Shangase, K., & Van Rie, K. J. (2016). 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.

Kohan, D., Hammerschlag, P.E., & Holliday, R.A. (1990). Otologic diseases in AIDS patients: CT correlation. *Laryngoscope*, *100(12)*, 1326–1330.

Lacovou, E., Vlastarakos, P. V., Papacharalampous, G., Kampessis, G., & Nikolopoulos, T. P. (2012). Diagnosis and treatment of HIV-associated manifestations in otolaryngology. *Infectious Disease Reports*, *4*(1), e9.

Lajoie, Y., & Gallagher, S. P. (2004). Predicting falls within the elderly community: Comparison of postural sway, reaction time, the berg balance scale and ABC scale fallers and non-fallers. *Archives of Gerontology and Geriatrics, 38*(1), 11-26.

Lalwani, A. K., & Sooy, C. D. (1992). Otologic and neurotologic manifestations of acquired immunodeficiency syndrome. *Otolaryngologic Clinics of North America, 25*, 1183-1197.

Larsen, C. R. (1998). *HIV-1 and communication disorders: What speech and hearing professionals need to know*. San Diego; London: Singular Publishing Group.

Lasisi, O. A. (2005). Otolaryngological manifestations of HIV/AIDS: A review. *Annals of Ibadan Postgraduate Medicine*, 3(1), 33-39.

Leddy, A. L., Crowner, B. E., & Earhart, G. M. (2011). Utility of the mini-BESTest, BESTest, and BESTest sections for balance assessments in individuals with Parkinson disease. *Journal of Neurology and Physical Therapy, 35*(2), 90-97.

Legters, K., Whitney, S. L., Porter, R., & Buczek, F. (2005). The relationship between the activities-specific balance confidence scale and the dynamic gait index in peripheral vestibular dysfunction. *Physiotherapy Research International 10*(1), 10-22.

Lewis, C. (1993). Balance, gait test proves simple yet useful. *Bulletin of Faculty of Physical Therapy, 2*(10), 9, 40.

Limpopo Provincial Treasury. (2012). Socio-economic review and outlook. Retrieved from http://policyresearch.limpopo.gov.za/bitstream/handle/123456789/939/SOCIO%20ECONOMIC%20REVIEW%202012.pdf?sequence=2

Lord, S. R., Allen, G. M., Williams, P., & Gandevia, S. C. (2001). Risk of falling: Predictors based on reduced strength in persons previously affected by polio. *Archives of Physical Medicine and Rehabilitation, 83*(6), 757-763.

Lord, S. R., Caplan, G. A., Colagiuri, R., Colagiuri, S., & Ward, J. A. (1993). Sensori-motor function in older persons with diabetes. *Diabetic Medicine, 10*(7), 614–618.

Lord, S. R., Clark, R. D., & Webster, I. W. (1991). Physiological factors associated with falls in an elderly population. *Journal of the American Geriatrics Society, 39*(12), 1194–1200.

Lord, S. R., Menz, H. B., & Tiedemann, A. (2003). A physiological profile approach to falls risk assessment and prevention. *Physical Therapy, 83*(3), 237-52.

Lord, S. R., Ward, J. A., Williams, P., & Anstey, K. (1994). Physiological factors associated with falls in older community-dwelling women. *Journal of the American Geriatrics Society, 42*(10), 1110–1117.

Lubbe, D. E. (2004). HIV and ENT. *Continuing medical education: Your SA Journal of CPD*, 250-253.

Lurie, M. N. (2000). Migration and AIDS in southern Africa: A review. *Southern African Journal of Science, 96*(6), 343-369.

Macambira, Y. K., Carnaúba, A. T., Fernandes, L. C., Bueno, N. B., & Menezes, P. L. (2017). Aging and wave-component latency delays in oVEMP and cVEMP: A systematic review with meta-analysis. *Brazilian Journal of Otorhinolaryngology, 83*(4), 475-487.

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), e61488.

MacDougall, H. G., Weber, K. P., McGarvie, L. A., Halmagyi, G. M., & Curthoys, I. S. (2009). The video head impulse test: Diagnostic accuracy in peripheral vestibulopathy. *Neurology*, *73*(14), 1134–1141.

Maes, L., Dhooge, I., D'haenens, W., Bockstael, A., Keppler, H., Philips, B., Swinnen, F., & Vinck, B. M. (2010). The effect of age on the sinusoidal harmonic acceleration test, pseudorandom rotation test, velocity step test, caloric test, and vestibular evoked myogenic potential test. *Ear and Hearing, 31*(1), 84-94.

Mafora, M. H., & Anim, F. D. K. (2014). Socio-economic analysis of land reform projects at Elias Motsoaledi local municipality in the Limpopo province of South Africa: comparing the degree of contribution to food security. Dissertation Retrieved from UNISA Institutional Repository.

Majumi, M. N., Aparajit, B. D., & Mohammed, E. H. (2014). Relevance of balance measurement tools and balance training for fall prevention in older adults. *Journal of Clinical Gerontology and Geriatrics, 5*(2), 31-35.

Mak, M. K., & Pang, M. Y. (2009). Balance confidence and functional mobility are independently associated with falls in people with Parkinson's disease. *Journal of Neurology, 256*(5), 742-749.

Mak, M. K., Lau, A. L., Law, F. L., & Cheung, C. C. (2007). Validation of the Chinese translated activity-specific balance confidence scale. *Archives of Physical Medicine and Rehabilitation*, *88*(4), 496-503.

Maki, B. E., Holliday, P. J., & Topper, A. K. (1994). A prospective study of postural balance and risk of falling in an ambulatory and independent elderly population. *Journal of Gerontology, 49*(2), M72–M84.

Mao, H. F., Hsueh, I. P., Tang, P. F., Sheu, C. F., & Hsieh, C. L. (2002). Analysis and comparison of the psychometric properties of three balance measures for stroke patients. *Stroke 33*(4), 1022-1027.

Marchetti, G. F., Whitney, S. L., Redfern, M. S., & Furman, J. M. (2011). Factors associated with balance confidence in older adults with health conditions affecting the balance vestibular system. *Archives of Physical Medicine and Rehabilitation, 92*(11), 1884-1891.

Marcusen, D.C., & Sooy, C.D. (1985). Otolaryngologic and head and neck manifestations of acquired immunodeficiency syndrome (AIDS). *Laryngoscope, 95(4),* 401-405.

Marques, A. P., Mendes, Y. C., Taddei, U., Pereira, C. A., & Assumpcao, A. (2013). Brazilian-Portuguese translation and cross cultural adaptation of the activity-specific balance confidence (ABC) scale. *Brazilian Journal of Physical Therapy, 17*(2), 170-178.

Marra, C. M., Wechkin, H. A., Longstreth, W. T., Rees, T. S., Syapin, C. L., & Gates, G. A. (1997). Hearing loss and antiretroviral therapy in patients infected with HIV-1. *Archives of Neurology, 54*(4), 407-410.

Martin, F. N., & Clark, J. G. (2003). *Introduction to audiology* (8th ed.). Boston: Allyn & Bacon.

Matas, C. G., Silva, S. M., Marcon Bde, A., & Gonçalves, I. C. (2010). Electrophysiological manifestations in adults with HIV/AIDS submitted and not submitted to antiretroviral therapy. Retrieved from http://www.scielo.br/pdf/pfono/v22n2/en_v22n2a07.pdf

Mathews, S. S., Albert, R. R., & Job, A. (2012). Audio-vestibular function in HIV infected patients in India. *Indian Journal of Sexually Transmitted Diseases, 33*(2), 98–101.

McCaslin, D. L., Dundas, J. A., & Jacobson, G. P. (2008). The bedside assessment of the vestibular system. In G. P. Jacobson, & N.T. Shepards (Eds.), *Balance function assessment and management* (*pp. 63-97*). San Diego, Oxford, Brisbane: Plural publishing.

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*, Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4495346/pdf/fneur-06-00154.pdf

McHugh, M. L. (2012). Interrater reliability: The kappa statistic. *Biochemia Medica, 22*(3), 276-282.

McLeod, S. A. (2013). What is validity? Retrieved from www.simplypsychology.org/validity.html

McNabb, C. (2009). *Descriptive research methodologies* [PowerPoint Slides]. Retrieved from https://www.slideshare.net/hamidehkarimy/descriptive-method-2163479?ref=https://cirt.gcu.edu/research/developmentresources/research_ready/descriptive/advan_disadvan

Michel, J., & Matlakala, M. C. (2013). The challenges experienced by nongovernmental organisations with regard to the roll-out of antiretroviral therapy in KwaZulu-Natal. *South African Family Practice, 55*(3), 264–269.

Michel, J., Matlakala, M. C., English, R., Lessells, R., & Newell, M.-L. (2013). Collective patient behaviours derailing ART roll-out in KwaZulu-Natal: Perspectives of health care providers. *AIDS Research and Therapy*, *10*(1), 20.

Mogotlane, S. M., Chauke, M. E., Van Rensburg, G. H., Human, S. P., & Kganakga, C. M. (2010). A situational analysis of child-headed households in South Africa. *Curationis, 33*(3), 24-32.

Moller, A. R. (2013). The ear. In A. R. Moller*, Hearing: Anatomy, physiology, and disorders of the auditory system* (3rd ed.) (pp. 3-49). San Diego; CA: Plural Publishing.

Mondal, M. N. I., & Shitan, M. (2013). Factors affecting the HIV/AIDS epidemic: an ecological analysis of global data. *African Health Sciences, 13*(2), 301-310.

Monzani, D., Casolari, L., Guidetti, G., & Rigaletti, M. (2001). Psychological distress and disability in patients with vertigo. *Journal of Psychosomatic Research, 50*(6), 319-323.

Murray, J., Sonnenberg, P., Nelson, G., Bester, A., Shearer, S., & Glynn, J. R. (2007). Cause of death and presence of respiratory disease at autopsy in an HIV-1 sero-conversion cohort of southern African gold miners. *Aids, 21*(*Suppl*. 6), S97–S104.

Ndlovu Care Group. (2015). Retrieved from http://www.ndlovucaregroup.co.za/about_ndlovu/history.html

Niccolai, L. M., Toussova, O. V., Verevochkin, S. V., Barbour, R., Heimer, R., & Kozlov, A. P. (2010). High HIV prevalence, suboptimal HIV testing, and low knowledge of HIV-positive serostatus among injection drug users in St. Petersburg, Russia. *AIDS and Behaviour 14*(4), 932–941.

Nilsagård, Y., Carling, A., & Forsberg. A. (2012). Activities-specific balance confidence in people with multiple sclerosis. *Multiple Sclerosis International, 2012*, 1-8.

Padgett, P. K., Jacobs, J. V., & Kasser, S. L. (2012). Is the BESTest at its best? A suggested brief version based on interrater reliability, validity, internal consistency, and theoretical construct. *Physical Therapy, 92*(9), 1197–1207.

Paiva, C. E., Barroso, E. M., Carneseca, E. C., De Pádua Souza, C., Dos Santos, F. T., López, R. V. M., & Paiva, S. B. R. (2014). A critical analysis of test-retest reliability in instrument validation studies of cancer patients under palliative care: a systematic review. *BMC Medical Research Methodology (Open Access)*, 14(8). Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3899385/pdf/1471-2288-14-8.pdf

Pappas, D. G., Roland, J. T., 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.

Patel, H. R., & Joseph, J. M. (2016). Questionnaire designing process: A review. *Journal of Clinical Trials, 6*(2), 255. Retrieved from https://www.omicsonline.org/open-access/questionnaire-designing-process-a-review-2167-0870-1000255.pdf

Petito, C. K. (1988). Review of central nervous system pathology in human immunodeficiency virus infection. *Annals of Neurolology*, *23*(*Suppl*. 1), S54–S57.

Petrak, M. R., Bahner, C., & Beck, D. L. (2013). Video head impulse testing (vHIT): VOR analysis of high frequency vestibular activity. Retrieved from http://www.hearingreview.com/2013/08/video-head-impulse-testing-vhit-vor-analysis-of-high-frequency-vestibular-activity/

Phelan, C., & Wren, J. (2005). Exploring reliability in academic assessment. Retrieved from https://www.uni.edu/chfasoa/reliabilityandvalidity.htm

Powell, L. E., & Myers, A. M. (1995). The activities-specific balance confidence (ABC) scale. *Journal of Gerontology: Medical Sciences, 50*(1), M28-34.

Prasad, H. K. C., Bhojwani, K. M., Shenoy, V., & Prasad, S. C. (2006). HIV manifestations in otolaryngology. *American Journal of Otolaryngology, 27*(3), 179-185.

Rana, F. S., Hawken, M. P., Mwachari, C., Bhatt, S. M., Abdullah, F., Ng'ang'a, L. W., Power, C., Githui, W. A., Porter, J. D., & Lucas, S. B. (2000). Autopsy study of HIV-1-positive and HIV-1-negative adult medical patients in Nairobi, Kenya. *Journal of Acquired Immune Deficiency Syndromes, 24*(1), 23–29.

Ranjan, R., & Bhat, J. S. (2008). DPOAE in HIV infected adults. *Online Journal of Health and Allied Sciences, 7*(1), 9. Retrieved from http://www.ojhas.org/issue25/2008-1-9.htm

Redondo-Martínez, J., Bécares-Martínez, C., Orts-Alborch, M., García-Callejo, F. J., Pérez-Carbonell, T., & Marco-Algarra, J. (2016). Relationship between video head impulse test (vHIT) and caloric test in patients with vestibular neuritis. *Acta Otorrinolaringologica Espanola, 67*(3), 156-161.

Reyes-Contreras, L., Silva-Rojas, A., Ysunza-Rivera, A., Jimenez-Ruiz, G., Berruecos-Villalobos, P., & Romo-Gutierrez, G. (2002). Brainstem auditory evoked response in HIV-infected patients with and without AIDS. *Archives of Medical Res*earch, *33*(1), 25-28.

Rogers, C., & Petersen, L. (2011). Aminoglycoside-induced balance deficits: A review of vestibulotoxicity. *South African Family Practice*, *53*(5), 419-424.

Roland, J. T., & Cohen, N. L. (1998). Vestibular and auditory ototoxicity. In C. W. Cummings, J. M. Frederickson, L. A. Harker, C. J. Krause, D. F. Schuller, & M. A.

Richardson (Eds.), *Otolaryngology & head and neck surgery*, (3rd ed.) (pp. 3186-3197). Missouri; US: Mosby Incorporated.

Rosengren, S. M., Welgampola, M. S., & Colebatch, J. G. (2010). Vestibular evoked myogenic potentials: Past, present and future. *Clinical Neurophysiology, 121*(5), 636-651.

Rubin, A. (2013). *Statistics for evidence-based practice and education* (3rd ed.). Belmont, CA: Cengage Learning.

Rzewnicki, I., Olszewska, E., & Rogowska-Szadkowska, D. (2012). HIV infections in otolaryngology. *Medical Science Monitor*, *18*(3), RA17–RA21.

Salbach, N. M., Mayo, N. E., Robichaud-Ekstrand, S., Hanley, J. A., Richards, C. L., & Wood-Dauphinee, S. (2006). Balance self-efficacy and its relevance to physical function and perceived health status after stroke. *Archives of Physical Medicine and Rehabilitation, 87*(3), 364-70.

Sanna, M. (2002). The normal tympanic membrane. In A. Russo, G. De Donato, A. Caruso, & A. Taibah. (Eds.), *Color Atlas of Otoscopy: From diagnosis to surgery* (2nd ed.) (pp. 4-5). Stuttgart; BW: Thieme Medical Publishers.

Schellack, N., & Naude, A. (2012). An overview of pharmacotherapy-induced ototoxicity. *South African Family Practice, 55*(5), 357-365.

Schmid, A. A., Van Puymbroeck, M., Altenburger, P. A., Dierks, T. A., Miller, K. K., Damush, T. M., & Williams, L. S. (2012). Balance and balance self-efficacy are associated with activity and participation after stroke: a cross-sectional study in people with chronic stroke. *Archives of Physical Medicine and Rehabilitation, 93*(6), 1101-1107.

Schneider, W. H. (2005). The establishment of institutional review boards in the U.S. background and history. Retrieved from http://www.iupui.edu/~histwhs/G504.dir/irbhist.html

Schouten, J. T., Lockhart, D. W., Rees, T. S., Collier, A. C., & Marra, C. M. (2006). A prospective study of hearing changes after beginning zidovudine or didanosine in HIV-1 treatment-naïve people. *BMC Infectious Diseases 6*, 28.

Sedgwick, P. (2014). Cross sectional studies: Advantages and disadvantages. Retrieved from https://fhs.mcmaster.ca/anesthesiaresearch/documents/Sedgwick2014Crosssectionalstudies-advantagesanddisadvantages.pdf

Selimoglu, E. (2007). Aminoglycoside-induced ototoxicity. *Current Pharmaceutical Design, 13*(1), 119-126.

Setswe, G. (2016). *Three decades of the HIV epidemic in South Africa* [PowerPoint Slides]. Retrieved from http://www.hsrc.ac.za/uploads/pageContent/7164/3%20decades%20of%20HIV%20epidemic%20in%20SA.pdf

Sharp, P. M., & Hahn, B. H. (2011). Origins of HIV and the AIDS pandemic. *Cold Spring Harbor Perspectives in Medicine, 1*(1), a006841.

Shively, W. P. (2017). *The craft of political research*, (10th ed.). New York; NY: Routledge.

Shumway-Cook, A., Baldwin, M., Polissar, N. L., & Gruber, W. (1997). Predicting the probability for falls in community-dwelling older adults. *Physical Therapy 77*(8), 812-819.

Simdon, J., Watters, D., Bartlett, S., & Connick, E. (2001) Ototoxicity associated with use of nucleoside analog reverse transcriptase inhibitors: A report of 3 possible cases and review of the literature. *Clinical Infectious Diseases 32*, 1623-1627.

Smith, M. E., & Canalis, R. F. (1989). Otologic manifestations of AIDS: The otosyphilis connection. *Laryngoscope, 99*(4), 365–372.

Smith, P. F., & Darlington, C. L. (2013). Personality changes in patients with vestibular dysfunction. *Frontiers in Human Neuroscience, 29*(7), 678.

Song, J. J., Lee, H. M., Chae, S. W., & Hwang, S. J. (2005). Bilateral otosyphilis in a patient with HIV infection. *European Archives of Otorhinolaryngology, 262*(12), 972–974.

Sonnenberg, P., Copas, A., Glynn, J. R., Bester, A., Nelson, G., Shearer, S., & Murray, J. (2011). The effect of HIV infection on time off work in a large cohort of gold miners with known dates of seroconversion. *Occupational and Environmental Medicine, 68*(9), 647–652.

Soyuer, F., & Ozturk, A. (2007). The effect of spasticity, sense and walking aids in falls of people after chronic stroke. *Disability and Rehabilitation, 29*(9), 679-687.

Statistics South Africa. (2015a). Mid-year population estimates 2015. Retrieved from https://www.statssa.gov.za/publications/P0302/P03022015.pdf

Statistics South Africa. (2015b). Poverty on the rise in South Africa. Retrieved from http://www.statssa.gov.za/?*p*=10334

Statistics South Africa. (2016). Sekhukhune district municipality: IDP review. Retrieved from http://www.sekhukhunedistrict.gov.za/sdm-admin/documents/Sekhukhune%20District%20Draft%202017-18%20IDP-Budget.pdf

Stearn, N., & Swanepoel, D. W. (2010). Sensory and neural auditory disorders associated with HIV/AIDS. In D.W. Swanepoel, & B. Louw (Eds.), *HIV/AIDS related communication, hearing and swallowing disorders*. (pp. 243-288). San Diego, Oxford, Brisbane: Plural Publishing.

Steckler, A., & McLeroy, K. R. (2008). The importance of external validity. *American Journal of Public Health, 98*(1), 9-10

Steinert, J. I., Cluver, L., Melendez-Torres, G. J., & Romero, R. H. (2016). Relationships between poverty and AIDS illness in South Africa: An investigation of urban and rural households in KwaZulu-Natal. *Global Public Health, 12*(9), 1183-1199.

Swanepoel, D. W., & Louw, B. (2010). Global perspective on HIV/AIDS and associated communication, hearing and swallowing disorders. In D.W. Swanepoel, & B. Louw (Eds.), *HIV/AIDS related communication, hearing and swallowing disorders*. (pp. 1-10). San Diego, Oxford, Brisbane: Plural Publishing.

Taylor, S., & Asmundson, G. J. G., (2008). Internal and external validity in clinical research. In D. McKay (Ed.), *Handbook of Research Methods in Abnormal and Clinical Psychology* (p. 24). Los Angeles; CA: Sage Publications

Teggi, R., Ceserani, N., Luce, F.L., Lazzarin, A., & Bussi, M. (2008). Otoneurological findings in human immunodeficiency virus positive patients. *The Journal of Otology and Laryngology, 122*(12), 1289–1294.

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

Theunissen, E. A. R., Dreschler, W. A., Latenstein, M. N., Rasch, C. R. N., Van der Baan, S., De Boer, J. P., Balm, A. J. M., & Zuur, C. L. (2014). A new grading system for ototoxicity in adults. *Annals of Otology, Rhinology & Laryngology, 123*(10), 711-718.

Tinetti, M. E., Williams, T. F., & Mayewski, R. (1986). Fall risk index for elderly patients based on number of chronic disabilities. *American Journal of Medicine, 80*(3), 429-434.

Tladi, L. S. (2006). Poverty and HIV/AIDS in South Africa: An empirical contribution. *Sahara Journal, 3*(1), 369-381.

Topper, A. K., Maki, B. E., & Holliday, P. J. (1993). Are activity-based assessments of balance and gait in the elderly predictive of risk of falling and/or type of fall? *Journal of the American Geriatrics Society, 41*(5), 479–487.

Tseng, A. L., Dolovich, L., & Salit, I. E. (1997). Azithromycin-related ototoxicity in patients infected with human immunodeficiency virus. *Clinical Infectious Diseases, 24*(1), 76-77.

UNAIDS. (2016). HIV countries: South Africa. Retrieved from http://www.unaids.org/en/regionscountries/countries/southafrica. Accessed on 7 December, 2017.

UNAIDS. (2017a). Fact sheet: Global statistics. Retrieved from http://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf. Accessed on 7 December, 2017.

UNAIDS. (2017b). Ending aids: Progress towards the 90-90-90 targets. Retrieved from http://www.unaids.org/sites/default/files/media_asset/Global_AIDS_update_2017_en.pdf

U.S. Food and Drug Administration (2017, November 12). ICS chartr EP 200 with VEMP. Retrieved from https://www.accessdata.fda.gov/cdrh_docs/pdf14/k143670.pdf

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*(1), 37-43.

Vargus-Adams, J. N., & Majnemer, A. (2014). International classification of functioning, disability and health (ICF) as a framework for change: Revolutionizing rehabilitation. *Journal of Child Neurology, 29*(8), 1030-1035.

Weber, K. P., Aw, S. T., Todd, M. J., McGarvie, L. A., Curthoys, I. S., & Halmagyi, G. M. (2008). Head impulse test in unilateral vestibular loss. *Neurology, 70* (6), 454-463.

Weder, S., Senn, P., Caversaccio, M., & Vibert, D. (2013). Cochleovestibular deficit as first manifestation of syphilis in a HIV-infected patient. *Case Reports in Neurology, 5*(1), 62–67.

Whitney, S. L., Hudak, M. T., & Marchetti, G. F. (1999). The activities-specific balance confidence scale and the dizziness handicap inventory: A comparison. *Journal of Vestibular Research, 9*(4), 253-259.

Whitney, S. L., Wrisley, D. M., Brown, K. E., & Furman, J. M. (2004). Is perception of handicap related to functional performance in persons with vestibular dysfunction? *Otology & Neurotology, 25*(2), 139–143.

Whitney, S. L., Wrisley, D. M., Marchetti, G. F., Gee, M. A., Redfern, M. S., & Furman, J. M. (2005). Clinical measurement of sit-to-stand performance in people with balance disorders: Validity of data for the five-times-sit-to-stand test. *Physical Therapy, 85*(10), 1034–1045.

Whitney, S. L., Wrisley, D. M., & Furman, J. (2003). Concurrent validity of the berg balance scale and the dynamic gait index in people with vestibular dysfunction. *Physiotherapy Research International 8*(4), 178-186.

Whitney, S. L., & Rossi, M. M. (2000). Efficacy of vestibular rehabilitation. *Otolaryngologic clinics of North America, 33*(3), 659-672.

World Health Organization (2001a). Strengthening mental health promotion. Geneva, World Health Organization (Fact sheet, No. 220).

World Health Organization. (2001b). The international classification of functioning, disability and health (ICF). Retrieved from http://www.who.int/classifications/icf/en/

World Health Organization. (2007a). Case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and

children. Retrieved from http://www.who.int/hiv/pub/guidelines/HIVstaging150307.pdf

World Health Organization. (2007b). Towards universal access: Scaling up priority HIV/AIDS interventions in the health sector: Progress report. Retrieved from http://www.who.int/hiv/mediacentre/universal_access_progress_report_en.pdf

World Health Organization. (2013). What ART regimen to start with (first-line ART): Consolidated ARV guidelines. Retrieved from http://www.who.int/hiv/pub/guidelines/arv2013/art/whatregimentostart/en/

World Health Organization. (2015). HIV/AIDS. Geneva. Retrieved from http://www.who.int/mediacentre/factsheets/fs360/en/

World Health Organization. (2016). Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Retrieved from http://apps.who.int/iris/bitstream/10665/208825/1/9789241549684_eng.pdf?ua=1

World Medical Association. (2013). WMA declaration of Helsinki: Ethical principles for medical research involving human subjects. Retrieved from https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/

Yetişer, S., & Ince, D. (2017). Caloric analysis of patients with benign paroxysmal positional vertigo. *The Journal of International Advanced Otology, 13*(3), 390-393.

Zingler, V., Cnyrim, C., & Jahn, K. (2007). Causative factors and epidemiology of bilateral vestibulopathy in 255 patients. *Annals of Neurology, 61*(6), 524–532.

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

Comparison of balance assessment scales and questionnaires

Balance assessment tool	Reliability	Validity	Sensitivity and specificity	Diagnosis	Purpose
The Dizziness Handicap Inventory (DHI) (Jacobson & Newman, 1990)	Satisfactory test retest reliability has been reported, for total score and sub-scale scores, in patients with vestibular dysfunction (Jacobson and Newman, 1990).	Concurrent validity: In subjects with vestibular dysfunction, the DHI shows excellent correlation with the Activities-specific Balance Confidence Scale (ABC) (Whitney, Hudak, & Marchetti, 1999). Content validity: DHI scores have been considerably worse in patients experiencing more frequent dizziness, (Jacobson & Newman, 1990; Fielder, Denholm, Lyons, & Fielder, 1996) and greater impairment of functional abilities (Whitney, Wrisley, Brown, & Furman, 2004).	This scale has been shown to be sensitive in detecting changes in vestibular function associated with vestibular rehabilitation (Enloe & Shields, 1997; Badke, Miedaner, Shea, Grove, & Pyle, 2005).	- Vestibular Disorders (Jacobson & Newman, 1990) - Elderly (Witney et al., 1999) - Multiple Sclerosis (Cattaneo, Regola, & Meotti, 2006) - Traumatic Brain Injury (Kaufman et al., 2006)	Administered in order to evaluate the functional handicapping effects of dizziness on daily living, as well as emotional consequences of this impairment (Jacobson & Newman, 1990).

Balance assessment tool	Reliability	Validity	Sensitivity and specificity	Diagnosis	Purpose
Physiological Profile Approach (PPA) (Lord, 1996)	Acceptable inter-rater reliability has been reported (Lord, Menz, & Tiedemann, 2003). High test retest reliability for the vision, muscle force, reaction time, and balance tests, whilst moderate reliability has been reported for the sensory tests (Lord et al., 2003).	The PPA provides validated measures to discriminate between fallers and non-fallers, and accurately measures aspects of balance (Lord et al., 2003).	The PPA is able to differentiate between fallers versus non-fallers with 75% accuracy (Lord, Ward, Williams, & Anstey, 1994).	- Vestibular disease (Brandt & Dieterich, 1993) - Elderly (≥65 years) (Lord, Clark, & Webster, 1991) - Peripheral neuropathy (Lord, Caplan, Colagiuri, Colagiuri, & Ward, 1993) - Muscle-wasting conditions (such as polio) (Lord, Allen, Williams, & Gandevia, 2001)	Used to identify physiological mechanisms responsible for balance impairment (Lord et al., 2003).

Balance assessment tool	Reliability	Validity	Sensitivity and specificity	Diagnosis	Purpose
The Balance Evaluation Systems Test (BESTest) (Horak, Wrisley, & Frank, 2009)	Excellent inter-rater reliability reported in community dwelling adults, with and without balance deficits (Horak et al., 2009).	Concurrent validity: In community dwelling adults, with and without balance impairment, the BESTest showed excellent correlation with the Activities-specific Balance Confidence Scale (ABC) (Horak et al., 2009). Construct validity: Subjects with balance impairments obtain scores significantly poorer than healthy subjects (Horak et al., 2009).	Adequate ability to detect fallers (86% sensitivity), with 95% specificity to identify non-fallers (Padgett, Jacobs, & Kasser, 2012).	-Balance deficits (Horak et al., 2009) -Subacute stroke (Chinsongkram et al., 2014) - Multiple Sclerosis (Jacobs & Kasser, 2012) - Parkinson's Disease (Leddy, Crowner, & Earhart, 2011)	Evaluates how six various postural control systems are affected by functional imbalance (Horak et al., 2009).

Balance assessment tool	Reliability	Validity	Sensitivity and specificity	Diagnosis	Purpose
Tinetti Balance and Gait Assessment (Tinetti, Williams, & Mayewski 1986)	Good inter-rater reliability has been reported. Agreement by different administrators has been measured in over 85% of the items. Scores that differ, are usually less than 10% (Lewis, 1993).	Validity of this scale has been reported for older adults, and patients with specific chronic conditions (Tinetti et al., 1986; Kegelmeyer, Kloos, Thomas, & Kostyk, 2007; Soyuer & Ozturk, 2007).	Excellent sensitivity has been reported, 93% of fallers are identified, however, this scale showed poor specificity of only 11% (Topper, Maki, & Holliday, 1993; Maki, Holliday, & Topper, 1994).	- Older adults (Tinetti et al., 1986) - Stroke patients (Soyuer & Ozturk, 2007) - Parkinson's Disease (Kegelmeyer et al., 2007)	Evaluates characteristics of balance and gait in elderly patients (Tinetti et al., 1986).

Balance assessment tool	Reliability	Validity	Sensitivity and specificity	Diagnosis	Purpose
Berg Functional Balance Scale (BBS) (Berg, Wood-Dauphinee, Williams, & Gayton, 1989)	Excellent inter-rater reliability when used for community-dwelling elderly (Berg, Maki, Williams, Holliday, & Wood-Dauphinee, 1992) and institutionalized older adults (Holbein-Jenny, Billek-Sawhney, Beckman, & Smith, 2005).	Adequate predictive validity reported for vestibular dysfunction when compared to the Dynamic Gait Index (Whitney, Wrisley, & Furman, 2003).	By considering history of falls in the elderly population, the sensitivity of the BBS has been reported as 91% with 82% specificity (Shumway-Cook, Baldwin, Polissar, & Gruber, 1997).	- Vestibular dysfunction (Cohen & Kimball., 2008) - Geriatric population (Berg et al., 1992) - Stroke patients (Mao, Hsueh, Tang, Sheu, & Hsieh, 2002)	Evaluates static and dynamic balance in older adults during functional tasks (Berg et al., 1992; Blum & Korner-Bitensky, 2008).

Balance assessment tool	Reliability	Validity	Sensitivity and specificity	Diagnosis	Purpose
Activities-Specific Balance Confidence Scale (ABC) (Powell & Myers, 1995)	Good test retest reliability in older adults has been reported for the overall scale as well as the individual items (Powell & Myers, 1995).	Criterion validity: Adequate to excellent correlation with other balance assessment tools in patients with vestibular disorders has been reported, including the BESTest (Horak et al., 2009) and DGI (Legters, Whitney, Porter, & Buczek, 2005). Construct validity: Restricted mobility (Powell & Myers, 1995) and fall-risk (Lajoie & Gallagher, 2004) have been associated with significantly lower ABC scores. In a study comparing the validity of various scales (Five-Times-Sit-to-Stand Test, ABC and Dynamic Gait Index), the authors reported that the ABC scale showed the best sensitivity to identify subjects with a balance disorder (Whitney et al., 2005).	Scores of >67% could accurately predict fall-risk 84% of the time, whilst the scale could identify non-fallers with an 87% specificity (Lajoie & Gallagher, 2004). In another study, the ABC scale was able to accurately identify 80% of subjects with a balance disorder (Whitney et al., 2005).	- Vestibular disorders (Whitney et al., 1999) -Elderly (Powell & Myers, 1995) -Strokes (Botner, Miller, & Eng, 2005) - Multiple sclerosis (Nilsagård, Carling, & Forsberg, 2012) - Parkinson's Disease (Mak & Pang, 2009)	Used to assess subjective confidence during everyday activities, without falling or experiencing unsteadiness (Powell & Myers, 1995).

Appendix B

The Activities-specific Balance Confidence (ABC) Scale (Powell & Myers, 1995)

"*How confident are you that you will not lose your balance or become unsteady when you*:"

1. walk around the house? __%
2. walk up or down stairs? __%
3. bend over and pick up a slipper from the front of a closet floor? __%
4. reach for a small can off a shelf at eye level? __%
5. stand on your tiptoes and reach for something above your head? __%
6. stand on a chair and reach for something? __%
7. sweep the floor? __%
8. walk outside the house to a car parked in the driveway? __ %
9. get into or out of a car? __%
10. walk across a parking lot to the mall? __%
11. walk up or down a ramp? __%
12. walk in a crowded mall where people rapidly walk past you? __%
13. are bumped into by people as you walk through the mall? __%
14. step onto or off an escalator while you are holding onto a railing? __ %
15. step onto or off an escalator while holding onto parcels such that you cannot hold onto the railing? __%
16. walk outside on icy sidewalks? __%

Appendix C

The Zulu translated ABC scale (Kamanji, 2016)

1. ...uhamba endlini? __%
2. ...ukhuphuka noma wehla ngezitebhisi? __%
3. ...ugoba futhi ucosha ophaca endaweni yakho yokugcina izimpahla? __%
4. ...welula ingalo uthatha ithini elincane eshalofini eliqondene namehlo ngokuphakama? __%
5. ...ucokama futhi welula ingalo ukuze uthathe into esendaweni engaphezu kwekhanda? __%
6. ...uma phezu kwesihlalo futhi uthatha okuthile? __%
7. ...ushanela phansi? __%
8. ...uphumela ngaphandle uya emotweni emi ngaphandle kwesango? __%
9. ...ungena noma uphuma emotweni? __%
10. ...uhamba unqamula phakathi kwezimoto ezimile uyongena ezitolo? __%
11. ...uhamba ukhuphuka noma wehla endaweni ewumqansa? __%
12. ...uhamba ezitolo eziphithizelayo lapho abantu bekudlula beshesha? __%
13. ...abantu behamba bekushayisa njengoba uhamba ezitolo? __%
14. ...ugibela noma wehla kwi-escalator (izitebhisi ezihambayo) ubambelele ezinsimbini zayo? __%
15. ...ugibela noma wehla kwi-escalator (izitebhisi ezihambayo) uphethe izinto uze ungakwazi nokubambelela ezinsimbini zayo? __%
16. ...uhamba ngaphandle ezindaweni ezineqhwa phansi noma kwi pavement/phansi? __%

Appendix D

Ndlovu study advert

VOLUNTEERS NEEDED FOR A RESEARCH STUDY at Ndlovu Wits Audiology Clinic

Study title: ***Vestibular function in adults with HIV***

We are conducting a research study to describe the balance abilities of HIV-positive adults.

Eligibility criteria:

- Males and females
- Aged 18 years to 50 years
- Diagnosed with HIV

Participants' hearing will be tested with an otoscope, tympanometry and pure tone audiometry. Balance abilities will be tested with a questionnaire and video-goggles.

Hearing and balance tests will take approximately **one hour** to complete and are **free of charge**. None of the tests are harmful. Remember that your name will **NOT** be identified in the research study.



If you are willing to take part in this study, please visit Ndlovu Wits Audiology Clinic on Thursday to Friday from 08h00 to 03h00 or consult me on **079 697 1266** for further information.

Appendix E

Data collection form

Participant No.: _____

Date of assessment: _____ Date of birth: _____
Gender: M / F

HIV HISTORY

ARVs	Yes	No	Current viral load	CD4 + count	CDC Category
Duration of treatment (years)	1-5			✓	
	6-10			✓	
	11 +			✓	
ARV regimen (tick relevant)	Efavirenz (EFV)		Tenofovir disoproxil fumarate (TDF)	Nevirapine (NVP)	Other
	Emtricitabine (FTC)		Zindovudine (AZT)	Stuvadine (d4T)	
Other medication					

VESTIBULAR HISTORY

Have you ever had any balance problems prior to the HIV diagnosis? Y / N

If yes, please describe the problems:

	Y	N		Y	N
Unsteadiness			Light-headedness		
World spinning around you			Spinning Sensation		
Falling to one side (L / R / Both)					

Did they give you a specific diagnosis of the balance problem? (Such as vestibular neuritis)

_____
_____
_____
_____
_____

AUDITORY HISTORY

Do you currently experience difficulty hearing? Y / N

If yes, please explain:

_____
_____
_____
_____
_____

Have you ever had any ear operations before? Y / N

If yes, please specify (when, why, outcome):

_____
_____
_____
_____

Have you experienced any ear ache / discharge from your ears recently? Y / N

If yes, please describe (symptoms, onset, duration, treatment, whether it has been resolved):

_____
_____
_____
_____

MEDICAL HISTORY

Have you ever been diagnosed with one of the following?

Condition	Y	N	
Cancer			Treatment received and duration
Tuberculosis Circle relevant TB MDR-TB XDR-TB			Treatment received and duration
Other			Please list the condition(s): Treatment received and duration

AUDIOLOGIC ASSESSMENTS

Otoscopic examination

Ear	Normal	Cerumen occlusion		Perforation*	*Foreign object	Discharge*	Other
		Partial	Complete*				
Right							
Left							

*If present refer patient for medical management

Tympanometry

Ear	ECV	Pressure	Static compliance	Type
Right				
Left				

Audiogram

Unilateral / Bilateral

Symmetrical / Asymmetrical

Ear	Type	Degree	Configuration
Right			
Left			

BALANCE ASSESSMENTS

Test procedure			
ABC scale	Total ABC score: _____ % Balance confidence: _____		
Presence of abnormal catch-up saccades:			
HIMP		Covert saccades	Overt saccades
	Right Lateral:		
	Left Lateral:		

		Covert saccades	Overt saccades
	Right anterior:		
	Left anterior:		
	Right posterior:		
	Left posterior:		
	VOR gain		
Right Lateral:			
Left Lateral:			
Right anterior:			
Left anterior:			
Right posterior:			
Left posterior:			

Appendix F

Participant informed consent form

I hereby agree to participate in this study on the 'Vestibular function in adults with HIV'. The purpose and procedures have been explained to me. I understand the following:

- Participation is voluntary and I may choose to withdraw from the study at any time without negative consequences.
- All my personal information will be kept confidential.
- My medical records will be reviewed

Full name/s and surname of participant: _____

Participant signature: _____ Date: _____

Researcher signature: _____Date: _____

Appendix G

Ndlovu Case history form

Ndlovu Wits Audiology Clinic - Case History Form: Adult

Patient's Details

Name and Surname: _____

File Number: _____

Date of birth: _____ Age: _____

Telephone No 1: _____

Telephone No 2: _____

Home Language: _____

Why did you come to see me today? / Can you tell me about your ears and your hearing?

_____
_____
_____
_____

When did you first notice this problem and did anything happen that you think may have caused it?

_____
_____
_____

Has the problem changed since it started?

_____
_____

Is there anyone in your family that has a hearing problem?

_____
_____
_____

Have you ever had your ears tested before? Results?

_____
_____
_____
_____

Do you ever experience the following (which ear, does it differ between the ears and how often);
Dizziness?

_____

Pain in your ears?

_____

Discharge from your ears?

_____

Ringing in your ears (frequency, duration, etc.)?

_____

Where do you work?

_____

_____

Are you exposed to loud noises at home / work/ social currently or previously? For how long?

_____

_____

Medical History

Have you ever experienced any head, neck or ear trauma?

_____

_____

_____

Have you ever had an operation on your ears, head or neck?

_____

_____

_____

Have you had any of the following?

Asthma	
Cardiac Disease	
Cancer	
Chicken Pox	
Encephalitis	
Epilepsy, convulsions, seizures	
German measles (rubella)	
Malaria	
Measles	
Meningitis	
Mumps	
TB	
Earache (provide details)	
Ear Infections (provide details)	
Discharge from the ears (provide details)	
High Temperatures	
Other	

What medicines are you currently taking?

_____

_____

Is there anything else you want to tell me about your ears / hearing that we have not yet spoken about?

_____

_____

Developed: January 2014

Appendix H

Human Research Ethics Committee (Medical) approval letter



R14/49 Miss Alison Millar

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M160150

NAME: (Principal Investigator)	Miss Alison Millar
DEPARTMENT:	Speech Pathology and Audiology Ndlovu Medical Centre Limpopo Province
PROJECT TITLE:	Vestibular Function in Adults with HIV/AIDS
DATE CONSIDERED:	29/01/2015
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Karin Joubert
APPROVED BY:	Professor P. Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	04/07/2016

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary in Room 10004,10th floor, Senate House/2nd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand. I/We fully understand the the conditions under which I am/we are authorised to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated,from the research protocol as approved, I/we undertake to resubmit to the Committee. I **agree to submit a yearly progress report.** The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. in this case, the study was initially review in January and will therefore be due in the month of January each year.

Principal Investigator Signature

Date 20.07.16

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix I

Ndlovu Medical Centre approval letter

NDLOVU MEDICAL TRUST
P.O. Box 14, Groblersdal, 0470
Republic of South Africa

NDLOVU CARE GROUP
Community Program with a Difference

To whom it may concern,

Permission to conduct research: Ndlovu Care Group

This letter serves to grant permission to **Ms. Alison Millar,** a Masters student at the University of the Witwatersrand to conduct her research titled: **Vestibular function in adults with HIV/AIDS** at the Ndlovu Medical Centre and Audiology Department, Elandsdoorn Limpopo.

The insurance costs of the equipment as well as the consumables will be covered by the Ndlovu Wits Audiology clinic.

Please do not hesitate to contact me should you need any further information.

Yours Sincerely,



Dr HA Tempelman
CEO Ndlovu Care Group
02 February 2016

Tel: +27 (0) 13 262 9000 • Fax: +27 (0) 13 262 3488 • info@ndlovu.com • www.ndlovucaregroup.com
NPO: 018-534-NPO • PBO: 930007417 • Reg no: IT 10661/98 • Vat Reg No: 4560236059
Ndlovu Care Group: CEO Hugo Tempelman • FM Lourens Deverenge
Board of Trustees:
Chairperson: Prof Geert H Bijkam Non Executive Members: Ronald Vos, Lynn van der Elst, Sagie Pillay, Dr Eugene Sidlo Executive Member: Dr Hugo Tempelman

Appendix J

Limpopo Department of Health and Social Development approval letter

LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

DEPARTMENT OF HEALTH

Enquiries: Latif Shamila (015 293 6650) Ref:4/2/2

Millar Alison
Human Research Ethics Committee

Greetings,

RE: Vestibular Function in Adults with HIV/AIDS

The above matter refers.

1. Permission to conduct the above mentioned study is hereby granted.
2. Kindly be informed that:-
   - Research must be loaded on the NHRD site (http://nhrd.hst.org.za) by the researcher.
   - Further arrangement should be made with the targeted institutions, after consultation with the District Executive Manager.
   - In the course of your study there should be no action that disrupts the services.
   - After completion of the study, it is mandatory that the findings should be submitted to the Department to serve as a resource.
   - The researcher should be prepared to assist in the interpretation and implementation of the study recommendation where possible.
   - The above approval is valid for a 3 year period.
   - If the proposal has been amended, a new approval should be sought from the Department of Health.
   - Kindly note, that the Department can withdraw the approval at any time.

Your cooperation will be highly appreciated.

Head of Department

Date 15/09/2016.

18 College Street, Polokwane, 0700, Private Bag x9302, POLOLKWANE, 0700
Tel: (015) 293 6000, Fax: (015) 293 6211/20 Website: http/www.limpopo.gov.za

Appendix K

Participant information sheet



Good day,

My name is Alison Millar. I am a research student at the University of Witwatersrand and I am conducting research on the balance function in adults with HIV. In this study, I want to find out how many people with HIV have balance problems. This will assist audiologists to help people with HIV who have balance problems.

I would like to invite you to participate in the study; however, before you agree you need to understand what will be expected of you.

If you agree to take part in the study we will look at your medical file to get information regarding the current medication you are using. We will then ask you some questions regarding your medical history, your hearing and balance. After this we will test your hearing and assess your balance.

The hearing test will include the following procedures:

- We will look into your ears with a light (otoscope), to see your ear canal and eardrum.
- You will then listen to different sounds through earphones and if you hear the sound, you will press a button.

The balance test will include the following procedures:

- Glasses with a camera inside will be placed on your eyes and your head will be moved into different directions while you focus your eyes on a target.

The assessment will be done whilst you are waiting to see the doctor for your monthly appointment. You will keep your place in the queue and as soon as the tests are done you will see the doctor. The tests will take 1 hour to complete. Your participation in this study is voluntary. You may decide not to continue with the testing at any time without penalty. If we find that you have a problem with your ears or hearing, you will be referred to the doctor or audiologist at Ndlovu for management (free of charge). Once we have completed the testing, we will explain the results to you.

Please note that your name will not be used in the study; instead a number will be used. This is to ensure that nobody gets to know that you were part of this study. If you wish to be informed of the results of the study, please feel free to request these and they will be provided to you. The data will be kept in a password-protected computer file and only the researchers will have access to it. The raw data will be destroyed after 5 years.

If you decide to take part in this study, you will be asked to sign a form to confirm that you understand the purpose of the research and are willing to participate in the study.

The results of the study will be made available to the Ndlovu Care Group and Department of Health and Social Development.

If you need any more information, please contact me on 079 6971266 or email: millar.ali@gmail.com or my research supervisor Dr Karin Joubert on 011 717 4561 or email:

karin.joubert@wits.ac.za. Alternatively, you may contact the administrator of the Human Research Medical Ethics Committee at the University of the Witwatersrand, Mr Langutani Masingi, on 011 717 1234 or email: langutani.masingi@wits.ac.za or the chairperson, Prof. Cleaton-Jones, on 011 717 2301 for any additional enquiries.

Yours sincerely,

Alison Millar

Appendix L

Booth calibration certificate 2016

Amtronix PTY LIMITED
Amtronix - breaking the sound barrier
Reg No. 1977/001577/07

P O Box 26318
East Rand 1462
Gauteng, South Africa
Tel: 0861 amtronix (268766)
Tel: 011 894 4632
Fax: 011 894 4629
info@amtronix.co.za
www.amtronix.co.za
Support: 0861 amtronix

Name and Address:			Calibration Certificate Number:
Ndlovu Medical Trust HAART P O Box 14 Groblersdal 0485			0 42562

	Audiometer	Left Earphone	Right Earphone
Make:	N/A	N/A	N/A
Model:	N/A	N/A	N/A
Serial Number:	N/A	N/A	N/A
Chassis Number:	N/A	Bone Conductor No:	N/A
Insert Earphones	N/A		
HDA Earphones	N/A	N/A	N/A

Calibration Site:	Audio room	Audiometer/Booth Number:	1
For Compliance With:	Audiometer - SANS 10154		
Calibration Expiry Date:	2017/07/11	Function:	Fixed Installation

Calibration Equipment:		Calibration Date
Artificial Mastoid:	N/A	
Sound Level Meter:	Rion NL-32 # 00703326	Dec-15
Sound Level Calibrator:	Rion NC-73 # 10738079	Dec-15
1/3 Octave Filter:	Rion NX-22RT # 736747J	Dec-15
Frequency Counter	Extech EX505 # 0791999	Dec-15
Artificial Ear:	G.R.A.S RA0039 # 89539	Dec-15
Microphones:	90547/106337	Dec-15

This certificate becomes invalid if either the audiometer or its earphones or inserts are:

i. Subjected to any misuse or rough handling
ii. Subjected to repairs, including replacement of an earphone or insert
iii. Moved from site of calibration by road, rail or air, unless the procedures in SANS10154:2006 Annex A are followed.

Remarks: This Audiometer is hereby certified calibrated in accordance with ISO R389 and/or ANSI S3.6 and/or SANS 10154:2006. IEC 645-1,-2, including booth to SANS 10182. This audiometer complies to Type2 and/or Type3 and/or Type4 specifications. Calibration level are available on request.

This certificate is valid for 12 Months (365 Days)

Customer Notes:

All equipment in good operating order.

Modalities calibrated are:	Air Conduction: N/A	Bone conduction: N/A
	Free Field Speakers: N/A	Inserts: N/A

Filters:	NB N/A	SN N/A	WN N/A	Speech N/A
Booth Tested Fan Off:	Yes	SANS 10182 (Booth)	Booth type: AX2 Wooden	

	Hz	AP	8K	4K	2K	1K	500	250	125
Booth Certified to required levels	dB	44.7	12.4	11.3	9.9	8.7	9.6	17.5	25.9

CALIBRATION OFFICER:	Date & Time:
Jacques Ewald	2016/07/11 12:13

African Management Software
NeuroCom Balance + Rehab
EasyOne Spirometers
Titmus Vision
ICS Medical
Amplivox Med Acoustics
Tremetrics Audiometers
Madsen Audiometers

Directors: S.C Hardy S.J.Geier

Whilst every precaution is taken to ensure the accuracy of the calibration, Amtronix (Pty) Ltd or its representatives shall not be held liable for any errors, whether in fact or opinion.

Appendix M

Booth calibration certificate 2017

Amtronix PTY LIMITED
Amtronix - breaking the sound barrier
Reg No. 1977/001577/07

P O Box 26318
East Rand 1462
Gauteng, South Africa
Tel: 0861 amtronix (268766)
Tel: 011 894 4632
Fax: 011 894 4629
info@amtronix.co.za
www.amtronix.co.za
Support: 0861 amtronix

Name and Address:

Ndlovu Wits Audiology Clinic
Stand no. 938
Elandsdoorn
Dennilton

Calibration Certificate Number: 42871

	Audiometer	Left Earphone	Right Earphone
Make:	N/A	N/A	N/A
Model:	N/A	N/A	N/A
Serial Number:	N/A	N/A	N/A
Chassis Number:	N/A	**Bone Conductor No:**	N/A
Insert Earphones	N/A		
HDA Earphones	N/A		

Calibration Site:	Audio room	**Audiometer/Booth Number:**	1
For Compliance With:	Audiometer - SANS 10154		
Calibration Expiry Date:	2018/05/16	**Function:**	Fixed Installation

Calibration Equipment:		**Calibration Date**
Artificial Mastoid:	Bruel & Kjaer 4930 # 526213	Dec-16
Sound Level Meter:	Rion NL-52 # 00142576	Sep-16
Sound Level Calibrator:	Rion NC-74 # 35046845	Sep-16
1/3 Octave Filter:	Rion NH-25 # 32604	Sep-16
Frequency Counter	ACM - 800 #2013-001	Sep-16
Artificial Ear:	Larson Davis AEC201 # 0266	Sep-16
Microphones:	06397/148554	Sep-16

This certificate becomes invalid if either the audiometer or its earphones or inserts are:

i. Subjected to any misuse or rough handling
ii. Subjected to repairs, including replacement of an earphone or insert
iii. Moved from site of calibration by road, rail or air, unless the procedures in SANS10154:2006 Annex A are followed.

Remarks: This Audiometer is hereby certified calibrated in accordance with ISO R389 and/or ANSI S3.6 and/or SANS 10154:2006. IEC 645-1,-2, including booth to SANS 10182. This audiometer complies to Type2 and/or Type3 and/or Type4 specifications. Calibration level are available on request.

This certificate is valid for 12 Months (365 Days)

Customer Notes:

All equipment in good operating order.

Modalities calibrated are:		**Air Conduction:**	N/A	**Bone conduction:**	N/A
		Free Field Speakers:	N/A	**Inserts:**	N/A
Filters:	**NB** N/A	**SN** N/A	**WN** N/A	**Speech**	N/A
Booth Tested Fan Off:	Yes	SANS 10182 (Booth)	Booth type: 0		

	Hz	AP	8K	4K	2K	1K	500	250	125
Booth Certified to required levels	dB	49.3	14.5	11.3	9	10.2	9.2	19.9	25.9

CALIBRATION OFFICER: Heinz Schneider

Date & Time: 2017/05/16 15:26

Whilst every precaution is taken to ensure the accuracy of the calibration, Amtronix (Pty) Ltd or its representatives shall not be held liable for any errors, whether in fact or opinion.

African Management Software
NeuroCom Balance + Rehab
EasyOne Spirometers
Titmus Vision
ICS Medical
Amplivox Med Acoustics
Tremetrics Audiometers
Madsen Audiometers
Directors: SC Hardy S.J.Geier

Appendix N

Interacoustics tympanometer and audiometer (Titan) calibration certificate (2016-2017)

Interacoustics

Calibration Certificate

Ndlovu Wits Audiology Clinic

Date of Calibration: **13/12/2016**

Detailed Information of Equipment Calibrated

DISCRIPTION		MAKE	MODEL	SERIAL NO.
Audiometer		Interacoustics	AS608	SN0910465
	Earphone Right	Telephonics	DD45	WT093056
	Earphone Left	Telephonics	DD45	WT093054
HDA200		Interacoustics	AD629	SN0912716
Middle ear analyzer		Interacoustics	Titan	SN0911419
		Interacoustics	MT10-2	SN0912291
Audio Booth verification			N/A	N/A

List of Compliances

Item	Specification in Compliance to	Compliance Yes/No
Audiometer	Item is certified as being in calibration in accordance	Yes
Free Fields	Item is certified as in calibration in accordance with ISO 389-7	Yes
Audiometric Booth	Item is certified that the environment of the audio booth meets the requirements set forth by the publication SABS	Yes
Middle ear analyzer	Item is certified as being in calibration in accordance with EN61027 for Impedance	Yes

MEASURING EQUIPMENT

Sound Level Meter:	Rion NA-28	Serial No: 10351705
Artificial Ear:	B & K, Type 4153	Serial No: 1365968
Microphone:	GRAS	Serial No: 16063
Calibrator:	B & K, Type 4230	Serial No: 298552
Frequency Counter:	Extech 350	Serial No: 07051406
Artificial Mastoid:	B & K 4930	Serial No: 391079
Manometer:	MHC1	

Signature of Calibration Officer: Lulama Sikwebu

Trained and Accredited by Interacoustics Denmark, 2015

Ref: 291015

Interacoustics Trading as Oticon SA
39 Van Vuuren Rd, Constantia Kloof, Roodepoort
Phone: +27 11 675 6104 | Fax: +27 86 627 4004
E-mail: info@interacoustics.co.za | www.interacoustics.com

Appendix O

Amtronix tympanometer (Madsen Otoflex) calibration certificate 2016

Amtronix PTY LIMITED
Amtronix - breaking the sound barrier Reg No. 1977/001577/07

P O Box 26318
East Rand 1462
Gauteng, South Africa
Tel: 0861 amtronix (268766)
Tel: 011 894 4632
Fax: 011 894 4629
info@amtronix.co.za
www.amtronix.co.za
Support: 0861 amtronix

Name and Address:			**Calibration Certificate Number:**
Ndlovu Medical Trust HAART P O Box 14 Groblersdal 0485			958711 42562
	Tympanometer		
Make:	GN Otometrics		
Model:	Otoflex 100	Probe Serial Number: 959001	
Serial Number:	958711	Contra Headset Type: 0	
Calibration Site:	Audio room	Contra Headset S/N: N/A	
For Compliance With:	SANS 10154 (Audiometer)		
Calibration Expiry Date:	2017/07/11	Function:	Fixed Installation
Calibration Equipment:			**Calibration Date**
Artificial Mastoid:	N/A		
Sound Level Meter:	Rion NL-32 # 00703326		Dec-15
Sound Level Calibrator:	Rion NC-73 # 10738079		Dec-15
1/3 Octave Filter:	Rion NX-22RT # 736747J		Dec-15
Frequency Counter	Extech EX505 # 0791999		Dec-15
Artificial Ear:	G.R.A.S RA0039 # 89539		Dec-15
Microphones:	90547/106337		Dec-15

This certificate becomes invalid if either the audiometer or its earphones or inserts are:

i. Subjected to any misuse or rough handling
ii. Subjected to repairs, including replacement of an earphone or insert
iii. Moved from site of calibration by road, rail or air, unless the procedures in SANS10154:2006 Annex A are followed.

Remarks: This Audiometer is hereby certified calibrated in accordance with ISO R389 and SANS 10154:2006. IEC 645-1,-2, including booth to SANS 10182. This audiometer complies to Type 3 and/or Type 4 specifications.

This certificate is valid for 12 Months (365 Days)

Customer Notes:
All equipment in good operating order.

Modalities calibrated are:	**IPSI:**	**Yes**	**CONTRA:**	**No**

CALIBRATION OFFICER	**Date & Time:**
Jacques Ewald	2016/07/11 11:15

Whilst every precaution is taken to ensure the accuracy of the calibration, Amtronix (Pty) Ltd or its representatives shall not be held liable for any errors, whether in fact or opinion.

Appendix P

Amtronix tympanometer (Madsen Otoflex) calibration certificate 2017

Amtronix PTY LIMITED
Amtronix – breaking the sound barrier

P O Box 26318
East Rand 1462
Gauteng, South Africa
Tel: 0861 amtronix (268766)
Tel: 011 973 2684
Fax: 011 395 2598
info@amtronix.co.za
www.amtronix.co.za
Support: 0861 amtronix

Reg No. 1977/001577/07

Name and Address:	Calibration Certificate Number:
Ndlovu Wits Audiology Clinic Stand no. 938 Elandsdoorn Dennilton	958712 42871

	Tympanometer	Contra Earphone	IPSI
Make:	Madsen / GN Otometrics		Otoflex
Model:	Otoflex		959030
Serial Number:	958712		
Calibration Site:	Audio room		
Calibration Site:	Fixed Installation		
For Compliance With:	SANS 10154		
Calibration Expiry Date:	2018/05/17	Function:	Fixed Installation

Calibration Equipment:		Calibration Date
Artificial Mastoid:	Bruel & Kjaer 4930 # 526213	Dec-16
Sound Level Meter:	Rion NL-52 # 00142576	Sep-16
Sound Level Calibrator:	Rion NC-74 # 35046845	Sep-16
1/3 Octave Filter:	Rion NH-25 # 32604	Sep-16
Frequency Counter	ACM - 800 #2013-001	Sep-16
Artificial Ear:	Larson Davis AEC201 # 0266	Sep-16
Microphones:	06397/148554	Sep-16

This certificate becomes invalid if either the audiometer or its earphones or inserts are:

i. Subjected to any misuse or rough handling
ii. Subjected to repairs, including replacement of an earphone or insert
iii. Moved from site of calibration by road, rail or air, unless the procedures in SANS10154:2006 Annex A are followed.

Remarks: This Tympanometer/Audiometer is hereby certified calibrated in accordance with ISO R389 and SANS 10154:2006. IEC 645-1,-2 and in accordance with the specification of the manufacturer. This audiometer complies to Type 3 and/or Type 4 specifications.

This certificate is valid for 12 Months (365 Days)

Customer Notes:
All equipment in good operating order.

Tympanometer Modalities calibrated :	**IPSI**	Yes	**Contra Earphone**	N/A
Audiometer Modalities calibrated :	**AC**	N/A	**BC**	N/A

CALIBRATION OFFICER

Heinz Schneider

Date & Time:
2017/05/16 14:33

Whilst every precaution is taken to ensure the accuracy of the calibration, Amtronix (Pty) Ltd or its representatives shall not be held liable for any errors, whether in fact or opinion.

African Management Software
NeuroCom Balance + Rehab
Satellite Spirometers
EasyOne Spirometers
Tinnus Vision
ICS Medical
Amplivox Med Acoustics
Tremetrics Audiometers
Madsen Audiometers
Directors: S.C.Hardy S.J.Geier