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THE CLINICAL UTILITY OF WIDEBAND ABSORBANCE TYMPANOMETRY IN ADULTS LIVING WITH HIV

A dissertation submitted to

The Department of Speech Pathology and Audiology

School of Human and Community Development

Faculty of Humanities

University of Witwatersrand,

Johannesburg

In fulfilment of the requirement of the degree

Master of Arts in Audiology



By

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DECLARATION

I declare that this dissertation is my own and unaided work. I am solely responsible for its content and the conclusions presented. This work has only been submitted for the degree of Master of Arts (Audiology) at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other university.



_____

Ben Sebothoma

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Date

This work is dedicated to my late mother, Maria Mosadi Sebothoma who spent her whole life teaching me about the importance of education.

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LIST OF ABBREVIATIONS

ART	Antiretroviral therapy
ASHA	American Speech-Hearing Association
BSA	British Society of Audiology
CDC	Centres for Disease Control and Prevention
CD4	Cluster of differentiation 4
CEO	Chief Executive Officer
CHL	Conductive Hearing loss
EAM	External Auditory Meatus
ECV	Ear Canal volume
EMLM	Elias Motsoaledi Local Municipality
HREC	Human Research Ethics Committee
Hz	Hertz
KHz	Kilohertz
HIV	Human Immunodeficiency Virus
MHL	Mixed hearing loss
NCG	Ndlovu Care Group
NWA	Ndlovu Wits Audiology
TM	Tympanic Membrane
UNAIDS	Joint United Nations Programme on HUV/AIDS
WAI	Wideband acoustic Immittance
WBA	Wideband absorbance tympanometry
WBR	Wideband reflectance tympanometry
WHO	World Health Organisation

DEFINITION OF TERMS

Clinical Utility: The ability of the diagnostic test to improve health outcomes relative to the current best alternative. It consists of sensitivity, specificity, positive and negative predictive values

HIV: The human immunodeficiency virus is an infection that affects the CD4 cells and cause AIDS

Middle ear pathologies: Disorders that affect the structure(s) of the middle ear system and alter their functioning.

Sensitivity: Ability of a test to correctly identify people who are known to have a disease. In the present study, sensitivity will refer to measures of the middle system such a standard tympanometry and WAI that are able to correctly identify adults with middle ear pathologies.

Specificity: Ability of a test to correctly identify people without a particular disease. In the present study, specificity will refer to the ability of Wideband Acoustic immittance and standard tympanometry that are able to correctly identify adults without middle ear pathology.

Tympanogram: A graphical representation of the tympanometric results plotted on a chart.

Tympanometry: An audiological measure developed to assess the integrity of the middle ear system. This measure uses four clinical parameters (ear canal, compliance, pressure and gradient) to determine whether the middle ear system is functioning normally.

Wideband absorbance tympanometry (WBA): A type of wideband acoustic immittance that measure the amount of sound energy absorbed by the middle ear system

Wideband acoustic immittance (WAI): A family of wideband measures which includes wideband absorbance tympanometry (WBA) and wideband reflectance tympanometry (WBR).

Wideband reflectance tympanometry (WBR): A type of wideband acoustic immittance that measure the amount of sound energy reflected back into the external auditory meatus

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ABSTRACT

Background: Studies suggest that wideband acoustic immittance (WAI) has higher sensitivity and specificity in the identification of middle ear pathologies than the tympanometry with 226Hz. However, most of the research on WAI emerges from the Western and Australian countries, primarily focusing on the paediatric population. There is limited scientific knowledge on WAI in adults, particularly those living with human immunodeficiency virus (HIV). Given that people living with HIV are known to be prone to various middle ear pathologies varying in severities (subtle to chronic) due to their weakened immune system, it was deemed valuable to investigate the clinical utility of wideband tympanometry in this population.

Purpose: The aim of this study was to evaluate the clinical utility of WAI in identifying middle ear pathologies in adults living with HIV.

Participants: A non-probability purposive sampling method was used to recruit 99 adults diagnosed with HIV who were between the ages of 18 and 72 years, with a mean age of 46 years. All participants were recruited from Elias Motsoaledi Local Municipality (EMLM), Sekhukhune district, Limpopo province and were attending Ndlovu medical centre for their treatments.

Method: A prospective quantitative, non-experimental, correlational design was employed. All participants underwent an audiological test battery which included case history information using a self-developed extracted sheet, video-otoscopy, tympanometry with 226Hz probe tone, wideband absorbance tympanometry using click stimulus, and pure tone audiometry. All measures were conducted in a sound treated room.

Data Analysis: Data was analysed through both descriptive and inferential statistics. Sensitivity and specificity were determined by receiver operative characteristics (ROC)

analysis. All the analysis were conducted using IBM statistical Package for Social Sciences version 24

Results: The occurrence of middle ear pathologies in adults living with HIV was 11% (n=17) based on ENT diagnosis. A significantly lower occurrence of middle ear pathologies (11%, n=13) was obtained from tympanometry with 226Hz**.** The sensitivity and specificity of wideband absorbance tympanometry is generally high in the present study. The sensitivity of wideband absorbance tympanometry was higher (91%) than the sensitivity of tympanometry with 226Hz (23.5%) prone tone and clinical examination (30.8%), ($p<0.001$) in identifying middle ear pathologies in adults living with HIV. The sensitivity of wideband absorbance tympanometry was significantly higher compared with the sensitivity of tympanometry with 226Hz probe tone and clinical examination in higher frequencies. However, there was a comparable specificity of wideband absorbance tympanometry (90%), with tympanometry with 226Hz (93.8%) and clinical examination 91.2%) across various frequencies.

Conclusion: Middle ear pathologies in adults living with HIV exist despite the use of HAART treatment. This study demonstrated the clinical utility of wideband absorbance tympanometry when assessing middle ear pathologies in adults living with HIV. Therefore, this study highlights the need to use wideband absorbance tympanometry, in combination with other middle ear measures such as video otoscopy, to accurately identify middle ear pathologies in adults living with HIV. **Keywords**: adults, clinical utility, HIV, wideband absorbance tympanometry,

CHAPTER 1: INTRODUCTION

Background

Clinical utility of wideband acoustic immittance (WAI) has been established in the scientific literature. Published literature indicates that WAI has high sensitivity and specificity in the identification of various middle ear pathologies than conventional tympanometry with single probe tone frequency; such as 226Hz or 1000Hz) (Beers et al, 2010; Kaf, 2011; Terzi et al., 2015). Despite this evidence, there is limited published research on the clinical utility of WAI in specific conditions and populations such as in adults living with human immunodeficiency virus (HIV) HIV remains one of the biggest challenges to ear and hearing care in South Africa (Khoza-Shangase, 2017). Therefore, the current study intended to expand knowledge on the clinical utility of WAI (Feeney et al., 2013) in adults living with HIV where middle ear pathology has been documented as one of the presenting otological manifestations (Obasineke et al., 2014; Van der Westhuizen et al., 2013).

The incidence of middle ear pathologies has been reported to be increasing; particularly in developing countries such as South Africa (Biagio, Swanepoel, Laurent, Lundberg, 2014; Ramma & Sebothoma, 2016). This constant increase is linked to the multiplicity of risk factors; risk factors which may not necessarily be predominant in developed countries. For instance, in a meta- analysis conducted by Zhang and colleagues (2014), low socioeconomic background and low educational level of the mothers were reported to be associated with the development of middle ear pathologies Published evidence has indicated that HIV increases the risk of middle ear pathologies by causing the CD4 cell count to decline in the body and incapacitates the immune system (Vajpayee, Negi & Kurapati, 2013). This allows the viruses and bacteria to enter the middle ear system and cause middle ear pathologies (Van der Westhuizen, Swanepoel, Heinze & Hofmeyer, 2013).

The link between HIV and middle ear pathologies (Obasineke et al., 2014) is concerning given that HIV has become a pandemic particularly in African countries; with South Africa being dubbed the epicentre of the virus (Statistics South Africa [SSA], (2017); WHO, 2015). The rates of infection continuing to increase rapidly with evidence of new infections each year (UNAIDS, 2014; Gómez-Olivé et al., 2013). This link between HIV and middle ear pathologies exists despite the reported efficacy of the current antiretroviral therapy (ART) that is able to lower the HIV viral load, prevent HIV replication, and improve the immune system (Morsheimer, Dramowski, Rabbie & Cotton, 2014; Mwaba, Ngoma, Kusanthan & Menon, 2015; Vos et al., 2017). This constant increase in HIV infections may exacerbate the prevalence and nature of middle ear pathologies in the country (Van der Westhuizen et al., 2013). If these pathologies are left undiagnosed and untreated, or diagnosed late, further complications may occur.

Literature indicates that if middle ear pathologies are not detected and treated early, transient conductive hearing loss (CHL) may occur (Chao et al., 2012; Iacovou et al., 2012; Sanjar, Queiroz & Miziara, 2011; Tshifularo, Govender, & Monama, 2013; Van der Westhuizen et al., 2013; Williams, 1987). CHL is a temporary hearing loss that results from dysfunction of one or more structural elements of the middle ear system (Martin & Clark, 2015). However, the prolongation of middle ear pathologies in the middle ear system can cause further damage such as permanent sensori/neural hearing loss (SNHL) (Kolo, Salisu, Yaro & Nwaorgu, 2012) and life threatening conditions such as meningitis (Sharma, Jaiswal, Banerjee, & Garg, 2015).

The consequence of the aforementioned complications may be dire and far reaching. For example, hearing loss of any type and severity has been shown to affect the psychosocial well-being, causes communication difficulties especially in the presence of background noise, affects vocational abilities, and impacts overall quality of life (Anderson, Parkerbery-Clark,

White-Schwoch, Drehobl & Kraus, 2013;). In order to prevent the long term effects of hearing loss, the world health organisation (WHO) (2016) recommends that preventative measures such as early identification initiatives should be implemented.

Tympanometry with single probe tone (e.g. 226Hz, 678Hz, 1000Hz,) is a longstanding measure of middle ear function (Jerger, 1970) and continues to be used even today in diagnostic audiology and otology clinics across the world to identify middle ear pathologies (British Society of Audiology [BSA], 2013; Hunter & Sanford, 2015; Margolis & Sally, 1999). Hearing screening programmes are also incorporating the use of tympanometry with single probe tone in the testing protocols to identify middle ear pathologies (Mahomed-Asmail, Swanepoel and Eikelboom, 2016).

The widespread acceptance and use of tympanometry with single probe tone appears to stem from the fact that it is an objective and affordable measure that is quick and easy to administer and obtain results from (BSA, 2013). Tympanometry often takes a few seconds to complete, and does not require any active participation from the patient (Bess and Humes, 2003). Furthermore, tympanometry can also be conducted by non-health professionals with sufficient training (Erkkola-Anttinen, Tähtinen, Laine & Ruohola, 2014). These characteristics indicate that tympanometry with single probe tone does not require specialised skills, and therefore can be operated by many individuals. Although tympanometry is the most commonly used measure for evaluating middle ear pathologies, and has been shown to have high sensitivity and specificity in identifying middle ear pathologies, some researchers argue that it does not accurately identify middle ear pathologies (Kaf, 2011; Hunter et al., 2017; Shahnaz & Polka, 1997).

There is a growing body of literature indicating that tympanometry with single probe has poor sensitivity and specificity in identifying middle ear pathologies, particularly middle ear pathologies that have slightly changed the mechanical aspects of the tympanic membrane

such as those in Down's syndrome (Kaf, 2011) and pathologies affecting the ossicular chain such as otosclerosis (Browning, Swan & Gatehouse, 1985; Shahnaz & Polka (1997). Earlier studies employing tympanometry with a wide range of frequencies demonstrated that the 2 kHz to 4 kHz range serves as the sensitive indicator for middle ear pathologies (Piskorski, Keefe, Simmons & Gorga, 1999). It is therefore not surprising that tympanometry employing a single low frequency tone such as 226Hz or 1 kHz probe tone may not provide accurate identification of middle ear pathologies.

Literature attributes the lack of sensitivity and specificity of tympanometry with single probe tone to its inability to detect subtle changes of the middle ear resonance frequency (RF) (Iacovou, Vlastarakos, Ferekidis & Nikolopoulos, 2013; Vanaja & Manjula, 2003). Studies on multifrequency tympanometry (Margolis & Goycoolea, 1993; Shahnaz, 2007; Shahnaz & Polka, 1997) have shed some light on the nature and characteristics of the RF of the middle ear system. The RF is a crucial clinical parameter that indicates balance between *mass* and *stiffness* of the middle ear system (Shahnaz & Bork, 2008; Terzi, et al., 2017). Its frequencies range approximately from 750Hz through to 2000Hz in individuals with normal middle ear function (Funasaka, Funai & Kumakawa, 1984; Özgür et al., 2016; Shahnaz & Davies, 2006; Shahnaz & Polka, 1997). Therefore, a slight shift of the RF due to either subtle middle ear pathologies or pathology affecting the ossicular chain may not be detectable through the use of tympanometry with a single probe tone (Kaf, 2011). In HIV, subtle middle ear pathologies may occur; and poor and/or late diagnosis of these may lead to delayed intervention (Obasineke et al., 2014).

The continuous use of tympanometry with a single probe tone in individuals living with HIV could therefore lead to misdiagnosis; either from false positive or false negative results. The consequences of misdiagnosis can significantly create costs for the individual, family, the health care system, and the society at large (Ahmed, Shapiro & Bhattacharyya,

2013). For example, while less severe middle ear pathologies [for example, acute otitis media (AOM)] can be treated at the primary health care (PHC) clinic with simple antibiotics; severe middle ear pathologies such as chronic suppurative otitis media (CSOM) require specialised services such as ENT specialists who are extremely limited in developing countries such as South Africa (Fagan & Jacobs, 2009). Accessing such services may be difficult for individuals who are unemployed and living in poverty (Pullen, 2015). Therefore, an alternative measure that has high sensitivity and specificity, and can accurately diagnose middle ear pathologies while still at the less severe stage is warranted.

Currently, physicians such as ENT specialists use clinical examination techniques that are reported to have high sensitivity and specificity in identifying middle ear pathologies. These clinical examination techniques include pneumatic otoscopy, video otoscopy, otomicroscopy, and radiological imaging such as computed tomography (CT scan) and Magnetic resonance imaging (MRI scan) (Baigio et al., 2013; Trojanowska et al., 2012; Veillon et al., 2000). Unlike acoustic immittance, clinical examination may be regarded as the subjective measure of middle ear status – not function. Moreover; these measures require the tester to have extensive knowledge of the anatomy, physiology, and pathophysiology of the head and neck region in order to identify changes in one or more areas involved (Khater, Fahmy, El Shahat, & Khater, 2015).

It is therefore clear that even though clinical examinations of middle ear pathology may be available; their exclusive reliance on professional expertise raise implications for access in resource limited contexts such as South Africa where these experts and/or specialists are limited in number – and are not equally distributed across the country (Fagan & Jacobs, 2009). As a result, an alternative measure with high sensitivity and specificity that does not require extensive training, demonstrates function, and can be used by many ear

health professionals (and trained non-professionals) in various settings outside the healthcare setting, for example schools, mines, is needed.

Wideband acoustic immittance (WAI) has emerged in the literature as the favourite measure to potentially replace tympanometry with a single probe tone (Sanford, Hunter, Feeney, & Nakajima, 2013). Several studies have demonstrated that WAI can accurately identify middle ear pathologies, including subtle pathologies and pathologies affecting the ossicular chain (Hunter, Prieve, Kei & Sanford, 2013; Hunter, Bagger-Sjöbäck, Lundberg, 2008; Keefe & Simmons, 2003; Shahnaz & Polka, 1997). Kaf, (2011) noted that 63% of individuals who presented with normal tympanograms had abnormal results on WAI. Although WAI holds promise as an alternative measure of middle ear function because of its accuracy in identifying middle ear pathologies, available evidence is mainly from the Western and Australian countries, and focuses primarily on the paediatric population (Aithal, Kei, Driscoll, Khan & Swanston, 2015; Aithal et al., 2017; Hunter et al., 2017; Hunter, et al., 2010; Hunter, Tubaugh, Jackson & Propes, 2008; Hunter et al., 2008; Wali, Mazlan & Kei, 2017). Currently, there is limited information on the sensitivity and specificity of WAI in adults living with HIV; hence the importance of the current study within the South African context where HIV/AIDS remains a significant public health challenge.

Outline of the thesis:

Chapter 1: This chapter provides the background to the study by indicating the gap in the literature while providing rationale for the current study.

Chapter 2: This chapter provides relevant and comprehensive literature review on HIV/AIDS and auditory pathologies, with a specific focus on middle ear pathologies. The potential long term effects of unidentified and untreated middle ear pathologies are also presented. This chapter culminates in an argument on the need for investigating sensitivity and specificity of measures for assessing middle ear pathologies.

Chapter 3: This chapter discusses the most common measures of middle ear function; with a specific focus on their clinical utility.

Chapter 4: This chapter provides details on the methodology adopted in the current study.

Chapter 5: This chapter presents findings of the study in accordance with the study objectives. Relevant tables and graphs to summarise and illustrate the results are presented.

Chapter 6: This chapter provides a discussion of each of the findings in accordance with the objectives of the study with the use of relevant literature to substantiate and/or compare results to existing evidence.

Chapter 7: This final chapter offers conclusions to the study, which includes identification of strengths and weakness in the study design and analysis; while raising implications and offering recommendations for future directions.

CHAPTER 2: LITERATURE REVIEW

The purpose of this chapter was to review the literature and provide the context of the study. The literature will begin by providing the background of HIV including the prevalence and treatment of HIV. The association between HIV and auditory pathologies including middle ear will be reviewed and discussed. This section will be followed by a discussion of various measures of middle ear function that are commonly used in clinical settings. Lastly, the effects of middle ear pathologies will be presented at the end of this chapter.

2.1 Human immunodeficiency virus

HIV is currently in its third year of existence since it was first reported. The Centre for Disease control and Prevention (CDC) (2001) has reported that the first cases of HIV were first discovered among homosexual men in the United States of America (USA) in the early 1980s. However, in South Africa the first cases of HIV were more prevalent in younger women than in men (Karim, Churchyard, Karim & Lawn, 2009). Although reports indicated that HIV affects all individuals regardless of age, gender, ethnicity, and socioeconomic background (Hargreaves et al., 2002; UNAIDS, 20016); in South Africa, women still present with the highest rate of HIV infection [Kharsany et al., 2015; Statistics South Africa (SSA), 2017].

HIV is a virus that is known to weaken the immune system through impairing CD4 cells, and belongs to the family of lentivirus genus which includes the retroviridae (Turner & Summers, 1999). The HIV genome consists of two identical single-stranded RNA, and its DNA is generated by the reverse transcription (Engelman & Cherepanov, 2012). As the HIV virus enters the human body, it targets the CD4 cells (Luckheeram, Zhou, Verma & Xia, 2012) and binds their viral envelope glycoprotein (gp120) and the amino-terminal

immunoglobulin domain of the CD4 cells (Mkhize-Kwitshana, Mabaso & Walzl, 2014; Turner & Summers, 1999). Subsequently, HIV creates a new HIV DNA by converting the viral RNA into DNA. Once the HIV exists in the cell, replication begins and further weakens the immune system (Engelman & Cherepanov, 2012). As a result, the body becomes incapacitated and unable to fight infections (Atiya & Masege, 2015; Vajpayee, Negi & Kurapati, 2013).

Literature reports that there are a number of opportunistic infections associated with HIV (Hemkens & Bucher, 2014; Rodriguez-Arboli et al., 2017; Sandhu & Samra, 2013; Van Heerden et al., 2017). Among the reported infections and diseases, tuberculosis is the most common opportunistic infection resulting from HIV (Karo et al. (2017; Manjareeka & Nanda, 2013). Internationally, Sun et al. (2015) found the prevalence of TB to be 10.5% in individuals diagnosed with HIV. Studies conducted in South Africa have indicated a higher prevalence of TB in individuals diagnosed with HIV. The TB prevalence can be as high as 63% among individuals living with HIV (South African National AIDS Council [SANAC], 2017)

2.2 Subtypes of HIV

HIV comprises of two types, namely, HIV type 1 (HIV-1) and HIV type 2 (HIV-2). Although the subtypes of HIV have similarities; such as the fact that both are able to weaken the immune system, and that both have similar mode of transmission (CDC, 2005; Patel et al., 2014; WHO, 2017), they were also both believed to have derived from the non-human primates (Klimas, Koneru & Fletcher, 2008). However, these types of HIVs were reported to be distinct on many levels. First, the types of HIVs differ on the encoding of proteins that are necessary to enhance their replication. For example, HIV-1 encodes viral protein U (vpu) gene (Gonzáz, 2015), while HIV-2 encodes vpx gene (Reeves & Doms, 2002). Furthermore,

while HIV-1 is more prevalent in the Sub-Saharan countries (UNAIDS, 2016); HIV-2 is more predominant to the Western African countries (Kerina, Babill, & Muller, 2013). Despite the varying types of HIV, the prevalence of HIV has been a public health concern globally.

2.3 Prevalence of HIV

A recent report has indicated that in 2015 there were 36.7 million people [34.0 million – 39.8 million] living with HIV in the whole world (UNAIDS, 2016). This number has increased by over 3 million from 2010 (UNAIDS, 2016). In 2013 in the United States of America, there were 1.1 million people living with HIV (Huang et al., 2015). Similar rates of HIV were also reported in the United Kingdom with 101 200 people reported to have been diagnosed with HIV in 2015 (Public Health England, 2016). In Canada the number of people with HIV is smaller when compared with those of the USA and UK (Bourgeois et al., 2017).

Unlike the developed countries, the prevalence of HIV has been reported to be very high in developing countries, in which South Africa is one of them. Sub-Saharan countries have been reported to be the most affected regions, accounting for approximately 70% of the world epidemic (UNAIDS, 2016). In South Africa, the number of people living with HIV has been reported to have almost doubled in the last 15 years; increasing from 4 million in 2002 to 7 million in 2017 (SSA, 2017).

2.4 HIV treatment

Antiretroviral therapy (ART) was introduced in the early 1990s to control the spread and replication of HIV (Johnson & Hirsch, 1990; Pau & George, 2013). Meintjes et al. (2017) reported that ART inhibits one of the enzymes that are necessary for the replication, integration and maturation of HIV. The enzymes include the reverse transcriptase, integrase, or protease. As a result, inhibiting these enzymes prevents the replication of HIV, lowers the

viral load, and ultimately improves the immunological status of those living with HIV (Misker, Demissie, & Mellie, 2014; Morsheimer, Dramowski, Rabbie & Cotton, 2014; Mwaba, Ngoma, Kusanthan & Menon 2015). Consequently, individuals who are taking ART as part of their treatment for HIV can have an extended life expectancy and live a near or normal life (Johnson et al., 2013). Due to these clinical benefits, ART is therefore important for those living with HIV.

The South African National Department of Health (NDOH) (2015) ART guidelines state that pregnant mothers who are diagnosed with HIV and children under the age of 5 years, regardless of their CD4 cell count, and adults and adolescent with CD4+ counts ≤500 cells/µl should be enrolled into ART programmes. However, recently the world health organisation has released a guideline stipulating that *all* individuals living with HIV should receive ART regardless of WHO clinical stage and CD4 cell count (WHO, 2016). The WHO guidelines are in agreement with the UNAIDS 90-90-90 targets on HIV, which state that by the year 2030, 90% of infected individuals will be diagnosed; 90% be on treatment, and 90% be virally suppressed (UNAIDS, 2014). Despite the minor differences in the criteria for enrolling into ART, the efforts and initiatives demonstrate the urgent need and determination to combat HIV epidemic in the world.

2.5 HIV and audiological pathologies

Auditory pathologies appear to be common among individuals living with HIV. A systematic review conducted by Araújo and colleagues (2012) revealed that auditory pathologies are common in individuals living with HIV. In the same review, the auditory pathologies are divided into auditory symptoms which include most commonly include tinnitus, otalgia, and vestibular associated symptoms; and clinical test results indicating

hearing loss. Below is a discussion of studies that investigated the association between HIV and various auditory pathologies

2.5.1 HIV and hearing loss

Hearing loss is one of the common sensory symptoms characterised by impedance of stimulus into the ear and beyond and is demonstrated through audiometric measures such as pure tone (Martin & Clark, 2015). Individuals with hearing loss complain of difficulty perceiving speech, which leads to difficulty communicating in challenging environments (Anderson et al., 2013). The association between HIV and hearing loss has been reported in the literature (Assuiti et al., 2013; Ensink & Kuper, 2017; Khoza & Ross, 2002). The prevalence of hearing loss appears to range from 10% to 61% in the adult population depending on the sample size and methodology used (Fokou et al., 2015; Khoza & Ross, 2002; Khoza-Shangase, 2011; Van der Westhuizen et al., 2013). Despite these variability, it is evident that hearing loss is common among adult individuals living with HIV. Along with the prevalence of hearing loss reports, the types of hearing losses have also been established.

2.5.2 HIV and types of hearing loss

Individuals living with HIV were found to have different types of hearing losses. Individuals living with HIV were found to have higher rates of sensorineural hearing loss (SNHL) compared to other types of hearing loss (Fakou et al., 2015; Van Westhuizen et al., 2013). While there is no consensus on the causes of SNHL in this population, various studies (Khoza-Shangase, 2011; Khoza-Shangase, 2014) that have utilised distortion product otoacoustic emission (DPOAE) – a measure of outer hair cells function (Dhar & Hall, 2012), have demonstrated the potential ototoxic effects of HAART in individuals living with HIV..

Matas et al. (2014) also noted that individuals who were on ART presented with poor hearing than those who were not on ART. Because one of the effects of ototoxic drugs is outer hair cells damage in the cochlear (Geyer, Barreto, Weigert & Teixeira, 2015), the prolongation of these drugs may results in sensory type of hearing loss (Appana, Joseph, & Paken, 2016; Rachana & Shabnam, 2017).

While SNHL is reported to be common in adults with HIV; this does not seem to be the case in the paediatric population. Chao et al. (2012) studied 139 children living with HIV. Of the total sample, 38.8% of the children presented with hearing loss, with conductive hearing loss being more prevalent than other types of hearing loss. A recent study by Hrapcak et al. (2016) found an even higher prevalence of conductive hearing loss in children. In this study, conductive hearing loss was reported to be present in 82% of children living with HIV. The only variation between these two studies was primarily the sample sizes. While Chao et al. (2012) had a sample of 139 children; the study by Hrapcak included a total of 380 children living with HIV.

2.5.3 HIV and vestibular disorders

Although hearing loss has been the central focus in individuals living with HIV, perhaps because of the added ototoxic effect of the treatments, literature has also reported the association between HIV and vestibular pathologies (Araújo et al., 2012; Heinze, Vinck, Hofmeyr & Swanepoel, 2014; Khoza-Shangase & Van Rie, 2017). Khoza-Shangase and Van Rie (2017) studied 96 adults diagnosed with HIV. The results revealed that 17% of the participants experienced vertigo. Although there are conflicting results on the contributing factors of vestibular pathologies; recent evidence suggests that HAART contributes to the development of vestibular pathologies, especially vertigo, in the initial stages of the treatment (Khoza-Shangase, 2017).

2.5.4 HIV and middle ear pathologies

The middle ear system plays a significant role in converting acoustic sound into neural waves in the fluid filled inner ear (Bess & Humes, 2003; MØller, 2006). Pathologies resulting from a dysfunction in one or more anatomical parts within the middle ear system may disrupt the conversion process, resulting in a conductive hearing loss (Martin & Clark, 2015). World Health Organisation (2011) has reported that the highest prevalence of middle ear pathologies is found in developing countries, and that this is the major contributing factor to disabling hearing loss. Recent studies conducted in developing countries have reported middle ear pathologies to range from 3.4% to 5.8% in children (Mukara, Lilford, Tucci & Waiswa, 2017); and 14.3% in adults (Ramma & Sebothoma, 2016).

Since middle ear pathologies can be assessed by both physicians, using clinical examination methods, and audiologists, using immittance techniques; the discussion below explores middle ear pathologies in individuals with HIV in accordance with these measures.

2.6 Middle ear pathologies and HIV according to clinical examination methods

Studies that have used clinical examination methods in individuals living with HIV have reported middle ear pathologies to be common and high in prevalence in this population. Sulyman et al., (2010) reported 65% of serous otitis media in individuals living with HIV. Another study, conducted in South Africa, by Tshifularo et al. (2013) reported the prevalence of middle ear pathologies to be 43% in individuals living with HIV, with chronic suppurative otitis media (CSOM) being the most predominant when compared to otitis media with effusion.

2.7 Middle ear pathology and HIV according to immittance measures

Studies that used immittance measures to investigate middle ear function have also indicated that middle ear pathologies are common in this population. Obasineke et al. (2014) noted that all types of abnormal tympanograms were present in adults living with HIV; however, type B tympanogram was more prevalent than other types in tympanometry. In a study conducted in South Africa by Van der Westhuizen et al (2013), the prevalence of abnormal tympanometry was reported to be 41% in adults living with HIV. Type B was also noted to be more prevalent (33%) than other types of tympanogram.

Although it is clear that middle ear pathologies are common in various forms and degrees, there appears to exist considerable differences in the prevalence of middle ear pathologies in this population. For example, while Van Weshuizen et al (2013) reported the prevalence of middle ear pathologies to be 41%, Sulyman et al., (2010) reported this to be higher (65%). The differences can be attributed to methodologies used and sample sizes in these studies. Despite these differences, it is clear that middle ear pathologies are common in individuals living with HIV. This is concerning for hearing health professionals, given the limited resources to deal with these pathologies in developing countries such as South Africa (Fagan & Jacobs, 2007). Additionally, the potential complications associated with untreated middle ear pathologies can have a significant impact on individuals, family, society and the country's economy as a whole.

2.8 The effects of middle ear pathologies

The association between middle ear pathologies and hearing loss has been reported in the literature. The World Health Organisation states that if ear infections are not prevented or treated early, they can lead to hearing loss (WHO, 2013). In a systematic review based on

studies conducted in Africa, middle ear diseases were among the common causes (36%) of hearing loss (Mulwafu, Kuper, & Ensink, 2016). Olusanya, Okolo and Adeosun (2004) in a study conducted in Nigeria, also noted that otitis media with effusion was one of the predictors for hearing loss in school going children.

Research reporting the prevalence of hearing loss in individuals with middle ear pathologies is lacking, especially in adult population. However, available evidence, primarily on the paediatric population, sheds some light on the prevalence of hearing loss. Muftah, Mackenzie, Faragher and Brabin (2015) found that 66.7% of school aged children with chronic otitis media were likely to develop disabling hearing loss. The community-based cross sectional study conducted by Hunt et al. (2017) on 281 children noted that 46.9% of children with hearing impairment presented with middle ear pathologies. The presence of hearing loss in conjunction with middle ear pathologies highlights the need to use measures that have high sensitivity and specificity in detecting middle ear pathologies.

An association between middle ear pathologies and auditory processing difficulties has been reported (Borges, Paschoal & Colella-Santos, 2013; Khavarghazalani, Farahani, Emadi & Dastgerdi, 2016). Haapala et al. (2013) indicated that recurrent otitis media has an effect on consonant discrimination and timing of pre-attentive auditory discrimination. Another study conducted by Villa and Zanchetta (2014) noted that children with a history of otitis media have difficulties with temporal ordering and resolution. These studies have noted that auditory processing skills in individuals with middle ear pathologies exist despite normal hearing sensitivity. These skills are necessary for the comprehension of speech and language (Bellis, 2012).

Further prolongation of middle ear pathologies within the middle ear system can permeate the neural system and alter the structure of the brain (Hafidh, Keogh, Walsh, Walsh, & Rawluk, 2006). A case report conducted by Ciorba et al. (2007) found that the prolongation of middle ear pathology leads to intra-cranial complications. This is characterised by the erosion of the bony anatomical barrier along the sigmoid sinus (Nivsarkar, Agrawal, Sikdar, Bhagat & Phatak, 2017). These studies have indicated that the intra-cranial complications results from delay of identification of middle ear pathologies (Nivsarkar et al., 2017). It is therefore crucial that early identification of middle ear pathologies occurs in order to reduce the potential long term effects.

2.9 Summary

It is clear from the literature review that HIV is still a major public health problem, particularly in developing countries such as South Africa. Although the current treatment regimen is shown to be effective in improving the immune system, thus improving the quality of life, middle ear pathologies seem to persist. These pathologies exists in various forms and degrees, and if left untreated or/and undetected, may cause further damage in the auditory system. Middle ear measures that have high sensitivity and specificity in identifying middle ear pathologies (even the subtle ones) are needed to prevent the potential long term impacts of untreated middle ear pathologies.

CHAPTER 3: MIDDLE EAR MEASURES

3.1. Clinical utility

Defining clinical utility

Clinical utility remains the most crucial tool for evaluating the accuracy of any diagnostic measures in health professions (Bossuyt, Reitsma, Linnet, & Moons, 2012). Grosse and Khoury (2006) defines clinical utility as the ability of a diagnostic measure to prevent the development of a disease and improves the clinical outcome of a patients based on the findings. Farkas (2016) also pointed out that clinical utility facilitates a clinical decision making process for administering treatment (or intervention) to a patient. This decision-making process for administering a treatment or intervention is ultimately linked to the health outcome of the patient (Bossuyt et al., (2012). The ultimate purpose of clinical utility is therefore to determine the clinical usefulness or the clinical value of a diagnostic or screening test (Lesko, Zineh & Huang, 2010), and thus improves the reliability and validity of the measure (Henstchel, Kreis, Damian, Krumm & Frölich, 2005).

In audiology, a number of diagnostic measures have demonstrated clinical utility in diagnosing various auditory pathologies. For example, disrtotion product otoacoustic emission and high frequency pure tone audiometry have demonstrated the ability to detect outer hair cell damage due to ototoxic effects of drugs (Al-Malky, Dawson, Sirimanna, Bagkeris & Suri, 2015; Reavis et al., 2011). As a result, guidelines are developed to guide audiologists on measures to use in order to identify early signs of ototoxicity (American Academy of Audiology [AAA], 2009; Health Professional Council of South Africa [HPCSA], 2018). If the clinical utility of DPOAE and high frequency pure tone audiometry had not been established, this could have serious implications for patients on treatment with ototoxic drugs (Roeser, Valente & Hosford-Dunn, 2007).

Lesko et al (2010) argues that the concept of clinical utility is also important for ethical reasons. For example, Lesko et al (2010) state that clinical utility measure the personal benefit that the patient receives from an intervention. These benefits depends on the decision making process that began with the accuracy of the diagnostic measure (Farkas, 2016). It is therefore important that the accuracy of a diagnostic measure be measured in order to correctly identify pathologies for the benefits of the patients (Bossuyt et al. 2012), hence the value of the current study.

Lesko and colleagues (2010) argue that the clinical utility of a diagnostic measure or intervention can contribute to the reduction of health related costs. In developing countries where resources are scarce and poverty is high (Mayosi & Benater, 2014), the clinical utility of a diagnostic measure is of utmost importance. For example, Fagan and Jacobs (2009) reported that the Ear, Nose and Throat (ENT) specialists are very scarce in South Africa, and that those available, are only located in big cities or in private practices. Therefore, patients requiring ENT services would have to travel long distances to receive this kind of service. However, early identification; with the use of accurate diagnostic measure, may reduce the costs associated with travelling long distances to specialised health facilities (Fagan & Jacobs, 2009). Early identification would also lead to positive ear health outcomes for these patients if early intervention is provided.

In the current study, the clinical utility of various middle ear measures is discussed.Middle ear measures are divided into objective and subjective measures. Objective measures of middle ear pathologies denote measures that are used by audiologists in their clinical settings which objectively provide immediate results about the middle ear status.

These include tympanometry with single probe tone such as 226Hz. 678Hz or 1000Hz, acoustic reflex threshold, multifrequency tympanometry, and WAI. Subjective measures of middle ear pathologies, in this thesis, denote measures that are commonly used by the ENT specialists and require expert personal judgement to perform and interpret. These include pneumatic otoscope, video otoscopy, otomicroscopy and radiological imaging techniques such as MRI and CT scans. This chapter presents a discussion of all these measures, focusing primarily on their clinical utility when assessing middle ear pathologies. Commentary on whether these measures can be used in adults living with HIV, and in developing countries is provided.

3.2 Clinical utility of objective measures

Objective measures refer to measures that do not require any participation and response from the patient (Bess & Humes, 2003). These measures are often quick and easy to conduct, and are not affected by personal factors.

3.2.1 Tympanometry with 226Hz

Tympanometry was first established approximately five decades ago (Jerger, 1970). Tympanometry is a measure that is used to determine the absence or/and presence of middle ear pathologies (Margolis & Hunter, 1999). The measure is completed by inserted a nub into the EAM in order to obtain a hermetic seal (Martin & Clark, 2015). The measure provides immediate acoustic admittance information about the status of the middle ear in a form of a graphical representation (BSA, 2013). Using clinical parameters, including the ear canal volume (V_{ea}), static compliance (Y_{tm}), tympanometric peak pressure (TPP), and tympanometric width (TW); Jerger (1970) classified the graphs into different types of

tympanograms. These types of tympanograms include those that indicate the presence of middle ear pathology (type As, type Ad, type B & type C), and the one indicating the absence of middle ear pathologies (type A) (BSA, 2013). As a result, normative values that can be used were established (ASHA, 1990; Margolis & Heller, 1987; Wiley et al., 1996).

The sensitivity and specificity of tympanometry has been reported in various studies. Harries et al. (2005) reported the sensitivity and specificity of tympanometry with 226Hz to be 80% and 100% respectively in identifying the presence of middle ear effusion. A recent study by Anwar, Khan, Rehman, Javaid, and Shahabi (2016) found sensitivity of tympanometry with 226Hz to be 85, 85% and specificity to be 72.22% in identifying otitis media with effusion. An even higher sensitivity (100%) of tympanometry with 226Hz was reported by Ozturk, Gode, Ogut, Bilgen and Kirazli (2011).

Although sensitivity and specificity of tympanometry with 226Hz has been established, studies mentioned above have focused primarily on otitis media with effusion, using type B tympanogram as a primary indicator for determining the presence of otitis media with effusion. Resonant frequency of the tympanometry with multiple frequencies was also specific in identifying otitis media with effusion below the frequency of 650Hz in a study conducted by (Ozturk et al., 2011). It is therefore not surprising that tympanometry with single probe tone; especially low frequency, is able to accurately identify middle ear effusion.

Published studies have indicated that tympanometry with 226Hz often fails to accurately identify subtle middle ear pathologies and pathologies affecting the stiffness of the middle ear system (Browning, Swan, & Gatehouse, 1985; Colleti, 1975, Kaf, 2011; Shahnaz & Polka, 1997). Bhatta and Adhikari (2008) noted that type As and type Ad has poor sensitivity and specificity in identifying middle ear pathologies. Kaf (2011) noted that over 60% of the individuals with confirmed otitis media, tympanometry with single probe tone presented with normal tympanograms. Hunter et al. (2017) also noted that 20% of

participants in their study presented with normal tympanometry despite the presence of conductive hearing loss. It is clear that tympanometry inaccurately identifies some middle ear pathologies (Shahnaz et al., 2009), especially if the tympanic membrane is still intact and mobile (Hunters et al., 2017).

The inability of the tympanometry with single probe tone to accurately identify subtle middle ear pathologies is concerning, given that individuals living with HIV present with a variety of middle ear pathologies that vary with regards severity or degree (Van der Westhuizen et al. 2013). Chandrasekhar et al (2000) has indicated that individuals living with HIV can present with subtle middle ear pathologies such as acute otitis media (AOM). Obasineke et al. (2014) also noted that, though type B tympanogram is the predominant type in individuals living with HIV, other types of tympanograms associated with Eustachian dysfunction (type C), ossicular chain disorders (type Ad), and stiffness (type As) are also evident in this population. Therefore, the continuous use of tympanometry with single probe may miss some of these pathologies, rendering early identification impossible.

3.2.2 Tympanometry with multiple frequencies

Tympanometry with multiple frequencies emerged as an alternative measure of middle ear function that aims to overcome the limitations of the standard tympanometry with single probe tone. Firstly, unlike the standard tympanometry with single probe tone, tympanometry with multiple frequencies uses a wide range of frequencies from 220Hz to 11000Hz (Iacovou et al., 2013). Secondly, tympanometry with wide range of frequencies are able to measure the resonant frequency of the middle ear system (Shahnaz, 2008). Two of these will be covered below: Multifrequency tympanometry, and Wideband Acoustic Immittance.

3.2.2.1 Multifrequency tympanometry

Although multifrequency tympanometry has not been a common measure of middle ear function in the clinical setting, research on multifrequency tympanometry emerged over four decades ago (Vanhuyse, Creeten & Camp, 1975), indicating its potential usefulness as a measure of middle ear pathologies. Similar to the tympanometry with single probe tone, multifrequency tympanometry is measured by inserting a nub into the external auditory meatus to obtain a seal. However, instead of a single peak pattern produced during measurement of tympanometry with single probe tone (BSA, 2013); multifrequency tympanometry produces multiple peaks pattern of susceptance and conductance (Hunter & Shahnaz, 2014). Multifrequency tympanometry uses various clinical parameters such as tympanometric configuration, Vanhuyse pattern, resonant frequency, frequency corresponding to admittance phase angle of 45 degrees, and static admittance at multiple frequencies (Iacovou et al., 2013; Shahnaz, 2008).

Due to the multiple peaks produced by the multifrequency tympanometry, Vanhuyse model was used to categorise tympanograms based on the susceptance (B_a) and conductance (G_a), and use these to predict the four tympanometric patterns which are used to distinguish between normal and abnormal middle ear function (Shahnaz, 2008). As a result, multifrequency tympanometry has been reported to be an accurate measure of middle ear pathologies (de Moraes, Macedo, & Feniman, 2012; Harris et al., 2005; Shahnaz & Polka, 1997). The sensitivity and specificity of multifrequency tympanometry was reported to be 63.5% and 100% respectively in identifying otitis media with effusion (Ozturk et al., 2011).

3.2.2.2 Wideband Acoustic Immittance (WAI)

WAI emerged in the literature as the potential measure to overcome the limitations of the tympanometry with single probe tone and multifrequency tympanometry (Hunter &

Shahnaz, 2014). Although WAI is measured by inserting the nub in the EAM, unlike the tympanometry with single probe tone, Hunter and Sanford (2015) reported that WAI is independent of the location of the nub. Studies have reported that unlike the tympanometry with single probe tone, WAI can overcome the effects of the standing waves in the EAM, which often limit the measurements at frequencies higher than 1.5 kHz (Allen, Miller, Jeng & Levitt, 2015; Huang Rosowski & Peake, 2000; Keefe & Feeney, 2009; Margolis et al., 1999). Furthermore, WAI uses broadband stimulus such as a click over a wide range of frequencies (Hunter & Shahnaz, 2014). This allows the measure to provide a comprehensive view of middle ear function (Sanford et al., 2013).

Feeney et al (2013) reported that WAI consists of two types of measures, namely, absorbance and reflectance. These two measures represent how the measurement is conducted. For example, wideband absorbance tympanometry represents the amount of sound energy absorbed by the middle ear system; while wideband reflectance represents the amount of sound energy reflected back into the middle ear system (Hunter & Sanford, 2015). Both types of WAI can be measured through pressurization or through ambient pressure (Liu et al., 2008).

Several studies have reported that WAI can accurately identify middle ear pathologies in both children and adults (Aithal et al., 2015; Ibraheem; 2014). Unlike the tympanometry with single probe tone, WAI has been shown to accurately identify various middle ear pathologies that affect both the mass and stiffness of the middle ear system (Nakajima, Rosowski, Shahnaz & Voss, 2013). These pathologies include tympanic membrane perforations, otitis media with effusion (Beers et al., 2010), and ossicular chain disorders (Shahnaz & Bell, 2009; Shahnaz & Bork, 2005). Furthermore, studies have shown that WAI can also predict conductive hearing loss (Keefe & Simmons, 2003; Keefe et al., 2012). Given that people living with HIV present with different types of middle ear pathologies including

the subtle ones that are difficult to identify with tympanometry with single probe tone (Obasineke et al., 2014), Kaf (2011) states that WAI can identify such pathologies. The sensitivity and specificity of WAI is also established in the literature.

Hunter et al (2008) compared the test performance of WAI (reflectance) with tympanometry with single probe tone in 17 children aged nine weeks to two years diagnosed with cleft palate. Findings of this study indicated that there was statistically significant difference between the tympanometry with single probe tone (67% & 73%) and wideband acoustic immittance (82%) in identifying middle ear pathologies. Shahnaz et al. (2009) compared the test performance of tympanometry with 226Hz, multifrequency tympanometry and energy reflectance (ER) in differentiating normal middle ear from otosclerotic ears. Their findings revealed that ER can accurately identify otosclerosis far better than tympanometry with 226Hz. Terzi et al (2015) examined 44 paediatric patients diagnosed with otitis media with effusion, 28 patients with otitis media (without effusion) and 34 control group using WAI. This study obtained a sensitivity of 100% in identifying otitis media with effusion when using wideband tympanometry average.

3.3 Clinical utility of subjective measures (clinical examination)

Clinical examination in this study refers to evaluation techniques used by physicians such as ENT specialists to identify middle ear pathologies. This involves the visual analysis of the anatomical structures of the middle ear system (Biagio et al., 2013). The most commonly used clinical examination techniques in clinical practice to identify middle ear pathologies include pneumatic otoscopy, video otoscopy, otomicroscopy, and radiological imaging techniques such as computed tomography (CT) scan and magnetic resonance imaging (MRI) (Trojanowska et al., 2012; Veillon et al., 2000).

3.3.1 Pneumatic Otoscopy

Pneumatic otoscopy is a technique that is based on the assumption that middle ear pathologies impede the normal mobility of the tympanic membrane (Ponka & Baddar, 2013). It involves the use of a bulb and air transmitted into the ear to cause the tympanic membrane to vibrate (Ponka & Baddar, 2013). The primary goal of pneumatic otoscopy is to determine the presence or absence of middle ear pathologies by measuring the mobility of the tympanic membrane.

The sensitivity and specificity of pneumatic otoscopy is reported to be 87% and 89% respectively in identifying middle ear pathologies (Toner & Mains, 1990). Although the sensitivity and specificity of pneumatic otoscopy is high and can be used effectively to identify middle ear pathologies, this measure has been shown to be more accurate in identifying middle ear effusion (De Melker, 1993). This could be problematic in clinical settings given that not all middle ear pathologies affect the mobility of the tympanic membrane (Hunters et al., 2017). In a study conducted by Takahashi, Honjo, Hasebe, Sudo and Tanabe (1999), involving 56 ears with middle ear pathologies, half of the ears were found to have intact mobility of the tympanic membrane. Furthermore, although pneumatic otoscopy may be cost effective; this measure requires extensive training and expertise on the part of the examiner (Abbott et al., 2014).

3.3.2 Video otoscopy

Video otoscopy is based on the notion that middle ear pathologies can be diagnosed by analysing the colour and structural changes of the tympanic membrane (Jaisinghani et al., 1999). Video otoscopy produces clearer images of the tympanic membrane, which allows the physician to clearly visualise the tympanic membrane in order to make the diagnosis (Myburgh et al., 2016; Ting et al., 2016). A video clip or an image of the tympanic membrane

can be captured by projecting the results onto the computer screen (Sullivan, 1997). Studies conducted in South Africa showed that video otoscopy is an easy and quick measure to use and it can be operated by non-health professionals following sufficient training (Biagio et al., 2013).

While video otoscopy can be classified as a type of otoscopy that is used to assess the integrity of EAM and tympanic membrane (Martin & Clark, 2015), literature continues to indicate that video otoscopy can also be used to assess middle ear status. For example, a study conducted by Ting et al (2016) indicated that video otoscopic image findings correlated with the tympanograms. Biagio and colleagues (2014) found that the diagnoses made through the use of video otoscopy were similar (k=0.70) to those made from the onsite otomicroscopy. The sensitivity of video otoscopic images was reported to be 80% and 91%, while the specificity of video otoscopy was 85% and 89% (Biagio et al., 2014). These findings therefore indicate that video otoscopy can be used to assess the presence of middle ear pathologies.

While it is easy to operate the video otoscopic measure and capture reliable images (Biagio et al., 2013); the diagnosis of middle ear pathologies can be difficult, requiring trained physicians with sufficient knowledge of the anatomy and physiology of the tympanic membrane and other parts of the middle ear system (Biagio et al., 2014). Further research in this area is warranted to determine whether other health professionals can identify middle ear pathologies using video otoscopic images.

3.3.3 Otomicroscopy

Otomicroscopy is another common measure used to identify middle ear pathologies (Lundberg, 2014). This technique involves the use of a binocular microscope (3-D vision)

that magnifies the image of the tympanic membrane (Biagio et al., 2014). This allows the assessor, typically the physician (e.g. ENT) to clearly visualise the tympanic membrane and its components and make the diagnosis. Higher magnification and a bifocal image allows for the depth perception of the tympanic membrane (Lundberg, 2014). Otomicroscopy is built on the notion that middle ear pathologies change the colour and structure of the tympanic membrane.

Considerable literature (Lee & Yeo, 2004; Rogers et al., 2010; Young et al., 2009) has reported that the sensitivity and specificity of otomicroscopy in identifying middle ear pathologies is high, often reaching approximately 100% and 94% respectively. Although the sensitivity and specificity of otomicroscopy are reportedly high in identifying middle ear pathologies, this test requires specialised skills. These skills are necessary to operate and interpret whether a pathology is present or not. Thus, physicians, especially ENT specialists, are specially trained to operate and interpret its results. Unfortunately, due to shortages of ENT specialists and basic resources in developing countries (Fagan & Jacobs, 2009), the use of otomicroscopy is not feasible to accommodate the vast majority of individuals in communities. This will also mean that individuals suspected of middle ear pathologies should travel long distances to see trained ENT specialists for the diagnoses.

3.3.4 Radiological imaging

Radiological imaging techniques play an important role in the diagnosis of various middle pathologies. Radiological imaging involves the use of X-rays such as computed tomography (CT) and magnetic resonance imaging (MRI) to identify the specific pathologies (Trojanowska et al., 2012). Unlike other measures of middle ear pathologies, radiological imaging techniques can provide additional information about the pathologies that includes the extent of the pathology, the exact location of the middle ear pathologies within the middle ear

system, as well as indicate the bony structures that are involved (Khater, Fahmy, El Shahat, & Khater, 2015; Trojanowska et al., 2012; Veillon et al., 2000). This additional information about the pathology can facilitate appropriate intervention such as surgery and/or prescription of medication.

Studies have compared the sensitivity and specificity of high resolution CT scan and MRI in diagnosing middle ear pathologies. Khater et al. (2015) compared the CT and MRI in 50 patients who had a history of chronic otitis media (COM). The sensitivity and specificity of CT scan in diagnosing cholesteatoma was 100% and 53.8% respectively, while the sensitivity and specificity of MRI in the diagnosis cholesteatoma was 92.8% and 100% respectively. However, MRI displayed a high sensitivity and specificity in diagnosing pathologies of the soft tissues such as granulation tissue where the score was 100% and 95.8% respectively.

3.4 Summary

The literature reviewed illustrates that there are several middle ear measures used in clinical settings. However, these measures have limitations and also provide a poor balance between high sensitivity in identifying middle ear pathologies and usability. For example, while clinical examinations have been shown to have high sensitivity and specificity in identifying middle ear pathologies (Khater et al., 2015), clinical examination techniques require subjective judgement from a qualified physician such as an ENT specialist. Secondly, the costs of these measures are also high (Rehana, Tabish, Gojwari, Ahmad & Abdul, 2013), making it difficult for health facilities in resource constrained contexts to buy their own. Health facilities that afford to buy these measures may be located in big cities and private medical facilities where sufficient resources are available (Fagan & Jacobs, 2009), however access to the majority of populations is limited due to costs involved. Accessibility to these healthcare facilities may be difficult for individuals living in rural and township areas

(Ibekwe & Nwaorgu, 2011); which is over 70% of the South African population that obtains its health care from the poorly resourced public healthcare sector.

WAI appears to create a balance between high sensitivity and specificity and usability (Sanford et al., 2013; Liu et al., 2008). However, there is limited evidence-base on WAI on adults living with HIV. This study therefore aimed to evaluate the clinical utility of wideband absorbance tympanometry when assessing the middle ear function in this population.

EMPIRICAL RESEARCH

CHAPTER 4: METHODOLOGY

4.1 Primary objective of the study

- The primary aim of the study was to evaluate the clinical utility of wideband absorbance tympanometry when assessing the middle ear function in adults living with HIV

Secondary objectives

- To determine the sensitivity and specificity of wideband absorbance tympanometry when assessing middle ear function in adults living with HIV by comparing the results with the gold standard (ENT diagnosis)
- To determine the sensitivity and specificity of tympanometry with a 226Hz probe tone when assessing middle ear function in adults living with HIV by comparing the result with the gold standard (ENT diagnosis)
- To compare the sensitivity and specificity of wideband absorbance tympanometry to tympanometry with a 226Hz probe tone

4.2. Research questions

- What is the sensitivity and specificity of WBA when assessing middle ear function in adults living with HIV?
- What is the sensitivity and specificity of tympanometry with a 226Hz probe tone when assessing middle ear function in adults living with HIV?
- How do these results compare with the gold standard (ENT diagnosis)?
- How does WBA compare with tympanometry with a 226Hz probe tone in terms of sensitivity and specificity?

4.3. Research hypotheses

- *Null hypotheses H_0*:
    - Wideband absorbance tympanometry has no clinical utility when assessing middle ear function in adults living with HIV when compared with the gold standard (ENT diagnosis)**.**
    - Tympanometry with 226Hz has no clinical utility when assessing middle ear function in adults living with HIV when compared with the gold standard (ENT analysis)
    - There is no statistically significant difference between the clinical utility of the wideband absorbance tympanometry and tympanometry with 226Hz when assessing middle ear function in adults living with HIV

- *Alternative hypothesis H_1*:
    - Wideband absorbance tympanometry has clinical utility in assessing middle ear pathologies in adults living with HIV
    - Tympanometry with 226Hz has clinical utility when assessing middle ear function in adults living with HIV
    - There is statistically significant difference between the clinical utility of wideband absorbance tympanometry and tympanometry with 226Hz when assessing middle ear function in adults living with HIV

4.4 Research design

Typically the clinical utility of a diagnostic measure is evaluated by the Randomised Control Clinical Trial design (RCT) (Ashcroft, 2002). However, in this study, RCT could not be conducted because RCT requires a control group, whereas in this study there was no control group. Therefore, due to the practical and ethical barriers to conducting RCT in this

study, an alternative design was chosen. Consequently, this study utilised a prospective quantitative, non-experimental, correlational design (Leedy & Ormrod, 2010), that involved blinding. A quantitative approach was adopted because it uses numeric data obtained from middle ear measures to analyse. The study was non-experimental because all variables of interests were included and described without manipulation (Irwin, Pannbacker & Lass, 2014). The patterns and frequencies of these variables are described. The study employed a correlational design because it aimed at determining the relationship between variables of interest. For example, the researcher determined whether there was a relationship between ENT diagnoses and tympanometric measures (wideband absorbance tympanometry and tympanometry with 226Hz (Leedy & Ormrod, 2010). Finally, the study is exploratory because the ultimate goal of the study was to evaluate whether wideband absorbance has high sensitivity and specificity, and is feasible in a South African context.

The method of blinding was also important in this study because of the potential bias that could have arisen (Altman & Schulz, 2001) due to the association between HIV and middle ear pathologies (Tshifularo et al., 2013). Blinding in research refers to withholding some of the information from individuals who participate in the study (Polit, 2011).. According to Polit (2011), blinding of participants can occur at any stage of the research. In this study, blinding was employed at the data analysis stage where the two ENT specialists who analysed and made the diagnosis of the middle ear pathologies via the video otoscopic images did not have the demographic characteristics and medical histories of the participants. Only video otoscopic images with assigned numbers were provided to the ENT specialists.

4.5 Description of Participants

4.5.1 Participant Inclusion Criteria – Participant inclusion Criteria

Participants needed to meet the following criteria before being included in the study:

- All participants had to be aged 18 years or older
- All participants had to have a confirmed diagnosis of HIV
- All participants had to be living in one of the villages within EMLM
- All participants must have signed the consent form (Appendix A)

4.5.2 Participant Exclusion criteria

Participants were excluded from the study if they:

- Presented with ear discharge on the day of testing. Otorrhea has been documented to be the contraindication of tympanometric testing due to possible infection control issues (BSA, 2013; Hunter & Sanford, 2015)

4.5.3 Recruitment and sampling procedure

A non-probability purposive sampling technique was used in this study. Purposive sampling was deemed appropriate as it allows the researcher to carefully select participants who exhibit the characteristics that are important and useful for the study (Leedy & Ormrod, 2010). In this study, for example, participants had to have been diagnosed with HIV. Several advantages of purposive sampling are documented in the literature. Brink (1996) asserted that purposive sampling is a more convenient and cheap method to use than other sampling methods. Participants are available in the clinic and could be invited easily to participate in the study. However, non-probability sampling methods do not allow the researcher to generalise the findings to a large population (Leedy & Ormrod, 2010).

4.5.4 Research context

This study was conducted at Ndlovu Medical Centre in Limpopo province. Ndlovu medical centre is situated in Elandsdoorn, Elias Motsoaledi Local Municipality (EMLM), and Sekhukhune district in Limpopo Province. This clinic was started in 1994 as a non-profit organisation (NPO) offering various health related services for a number of villages within EMLM (www.ndlovucaregroup.co.za). The clinic has created a research consortium in collaboration with the University of the Witwatersrand, South Africa and Utrecht University, Netherlands. The collaborative work is aimed at investigate HIV in rural communities. In 2014, the clinic established an audiology clinic with the financial assistance from Oticon Foundation. As a result, Ndlovu Wits Audiology (NWA) became one of the few clinics in South Africa to have wideband absorbance tympanometry machine. Therefore, the choice of the study site was based on the availability of equipment and population being served in the clinic

4.5.5 The study population

The target population for the study was adults living with HIV living in Limpopo Province, South Africa

4.5.6 The study sample

A sample is a representation of a population in which it was drawn. According to Kumar (2011) the purpose of sampling is to make an inference about a population from where the sample was drawn**.** All participants selected for the purpose of this study were recruited from Ndlovu medical centre (NMC). Although the clinic does not cater for HIV infected individuals alone, the clinic has an established research centre that deals with individuals with HIV (Vos et al., 2017). Participants who are enrolled at the Ndlovu research unit have already been diagnosed with HIV and most are currently taking antiretroviral therapy. Therefore, the researcher was able to identify these patients through the help of Ndlovu research staff assistance. The sample of this study comprised of 99 adults (198 ears). The sample included 27 males (27%) and 72 females (73%), (M=46, SD, 9.483). All participants were diagnosed with HIV. A total of 98 (99%) adults were taking ART as part of their treatment, while only 1 (1%) participant was ART naïve.

4.5.7 Sample size and distribution of participants

Sample size estimation was based on the determination of 95% sensitivity and specificity, with 5% precision, given the prevalence of ear pathology of 35% (Van Westhuizen et al., 2013) and the 95% confidence level. This required a sample of 209 ears. The actual sample size of 198 ears was thus adequate for the objective of the study. Sample size calculations were carried out in G*Power (Buchner, 2007).

4.8Test Protocol

4.8.1 Research Process

The current study was submitted for ethical approval from the human research ethics committee (HREC) (medical) of the University of the Witwatersrand, Johannesburg (see Appendix B). Following ethical clearance (M160663), permission was obtained from the chief executive officer of Ndlovu medical centre (see Appendix C) and the Limpopo department of Health (see appendix D). After all relevant permissions were obtained; advertisement posters (see Appendix E) were placed on the walls in the waiting area and at Ndlovu Wits Audiology clinic.

Once the ethical clearance and permission were obtained, a pilot study was conducted on a small sample (n=5). The purpose of the pilot study was to determine the feasibility, process, and time that will be taken to complete all procedures on one participant (Van Teijlingen & Hundley, 2001). Given the multiple research projects that are underway at NCG at any given point in time, a pilot study was also important to plan the number of participants that can be assessed in a day, taking into consideration the scheduled patients of the audiology clinic. The results of the pilot study indicated that the research process was feasible and appropriate. All the results of the pilot study were excluded from the main study.

4.8.2 Measures/ Materials

- Self-developed case history form (see Appendix F)
- Video otoscope using Aurical otocam 300 (with sensor resolution of 752 (H) x 582 (V) pixel)
- Tympanometry with 226Hz using Interacoustics Titan 3.3 version
- Wideband absorbance tympanometry using Interacoustics Titan 3.3 version
- Pure tone audiometry using AD 629 diagnostic audiometer with Sennheiser HA200 supra-aural headphones and Radio Ear B-71 bone conductor

- Speech reception threshold using The South African Spondaic (SAS) wordlist (Hanekom et al., 2015)
- Acer laptop with Windows 10
- Otosuite and Otoaccess version 1.4 softwares installed into the acer laptop
- Infection control using Chlorhexidine gluconate and alcohol hand rub (Ehlert & Naude, 2014).
- Recording forms to record audiological results (see Appendix F)

4.9 Data Collection Procedure

Case history interviews were conducted with all participants prior to the testing. The researcher reviewed the medical files to confirm the the medical history of each participant obtained during case history interviews, as part of standard audiological practice in the clinic. All potential participants who came to the audiology clinic brought their clinic files. The perusal of the clinic file was completed to confirm the diagnosis of HIV and other medical diagnoses. The self-developed case history form (Appendix F) was utilised to gather pertinent information for the study. This information included the demographic information, clinical information, head and neck trauma, as well as history and current auditory related symptoms. The self-developed case history form was developed based on existing literature in the area of HIV and audiology (Chandrasekhar et al., 2000; Khoza & Ross, 2002; Khoza-Shangase, 2011; Van der Westhuizen et al., 2013) with addition of other elements to suit the current study

Once the case history information was completed, video otoscopic examination was conducted to examine the status of the EAM and the tympanic membrane (TM) (Martin & Clark, 2015). Each participant was seated comfortably on a chair in the booth. A physical inspection of the pinna was conducted to ensure that there were no abnormalities [British

Society of Audiology (BSA), 2010]. An appropriate speculum was attached to the video otoscope. The pinna of each participant was pulled back and up in order to widen the EAM (Martin & Clark, 2015). The speculum attached on the video otoscope was then inserted into the EAM while observing the computer screen. As soon as the tympanic membrane was visible on the screen, a video otoscopic image was captured. Where the first video otoscopic image was not clearly visible, the researcher repeated the procedure in order to capture the most clearly visible image. The video otoscopic images captured were saved onto the laptop in a folder created for this purpose. In participants whose EAM were occluded with wax, cerumen management was done by the audiologist at the site. Participants who presented with otorrhea on the day of testing were referred to the doctor at the clinic and excluded from the study (BSA, 2013).

4.10 Video otoscopy as a gold standard

The video otoscopic analysis and diagnosis of middle ear pathologies by the ENT specialists was considered a gold standard for the purpose of this study. The two ENT specialists were conveniently selected because of their close proximity to the University, and their collective experience of over 20 years working in clinical setting. The researcher also made sure that the two ENT specialists were registered with the Health Professions Council of South Africa.

Although otomicroscopy is often used as a gold standard and not video otoscopy, Biagio et al (2014) found that asynchronous video otoscopic analysis and diagnosis of middle ear pathologies were comparable with onsite otomicroscopy. An earlier study by Patricoski et al (2003) also noted that that there was a higher concordance between the asynchronous video otoscopic analysis and diagnosis of middle ear pathologies and in-person microscopic examination of the middle ear. Based on these findings, asynchronous video otoscopy was

chosen as a gold standard for this study, and video otoscopic images were sent to two ENT specialists. Furthermore, because the study was conducted in a rural area where ENT specialists are unavailable to make the diagnosis (Fagan & Jacobs, 2009), and it may have been impractical to transport each participant to see an ENT specialist, asynchronous video otoscopy was deemed contextually relevant and contextually responsive.

Tympanometry with 226Hz set at 85 dB SPL was used to determine the status of the middle ear on each participant (Hunters & Sanford, 2015). Appropriate nubs, depending on the size of the participants' EAM, were used to obtain hermetic seal. Clinical parameters of the tympanometry with 226Hz which included ear canal volume (ECV), static acoustic admittance and tympanometric peak pressure (TPP), were used to determine the presence/absence of middle ear pathology (Hunter & Sanford, 2015). The clinical parameters of tympanometry with 226Hz were also used to determine the type of tympanogram according to the Jerger classification system (Jerger, 1970). The results obtained from tympanometry with 226Hz were recorded on the recording form (see Appendix E).

Wideband absorbance tympanometry was conducted subsequent to the tympanometry with 226Hz. Wideband absorbance tympanometry using click stimulus over a wide frequency ranging from 226 Hz to 8000 Hz, was used to determine the status of the middle ear. The results obtained from wideband absorbance tympanometry were displayed graphically on the laptop screen. These results were saved using on the Acer laptop using Otoaccess software (Terzi et al., 2015).

Pure tone audiometry was conducted to determine the participants' hearing sensitivity (Martin & Clark, 2015). Air conduction was conducted at the conventional octave

frequencies from 250Hz to 8000Hz. Bone conduction was conducted at the octave frequencies from 250Hz to 4000Hz. Inter-octave frequencies were only conducted if the intensity difference between two subsequent octave frequencies equalled or exceeded 20dBHL (Martin & Clark, 2015; Wilson & McArdle, 2014). For both air and bone conduction thresholds, a 10dB/5dB steps for descending and ascending was used [American Speech-Language-Hearing Association (ASHA), 2005]. Speech reception threshold (SRT) was conducted to determine the participants' level of hearing speech and the reliability of pure tone thresholds (Bess & Humes, 2003). All participants were asked to repeat the SAS word list. SRT scores are also used to determine the consistency between pure tone thresholds. Results for both pure tones and SRT were recorded on the recoding form (see Appendix E).

For all participants who presented with either conductive hearing loss (CHL), mixed hearing loss (MHL) or asymmetrical sensory/neural hearing loss (SNHL), a referral for further evaluation and management was completed according to Ndlovu Wits Audiology protocol and procedures. However, for participants who presented with sensory/neural hearing loss (SNHL) that is symmetrical, counselling was provided and hearing aid evaluation was conducted. It is worth noting that the pure tone audiometric data was not included for the analysis as this was not part of the current study. The results of pure tone audiometry were used specifically to make appropriate referrals where participants presented with hearing loss.

Upon completion of audiological testing, all data were converted into Microsoft Excel Spreadsheet as numeric values. Data was saved on a password-protected computer in a folder created for the purpose of the study. Hard copies were kept in the patients' files in a locked cabinet at the audiology clinic. Video otoscopic images were sent to two ENT doctors using asynchronous (store and forward) telehealth technique (Biagio et al., 2013; Swanepoel, 2015)

for further analysis and to make the diagnoses (Hunter, Tubaugh, Jackson & Propes, 2008). The ENT doctors were blinded on the demographic characteristics and the medical diagnoses of the participants.

4.11 Validity and Reliability

Reliability means that the measure can consistently produce the same results if the aspects that is being measured has not changed (Polit & Beck, 2010). For the purpose of this study, reliability was ensured through test-retest reliability and interrater reliability (Satake, 2015). Test-retest reliability is a statistical measure that shows the degree to which two measurements are consistently related when performed between two points separately by an interval of time (Polit & Beck, 2010). A test-retest method is often recommended on small populations to assess the reliability of the instrument. In this study, although test-retest reliability of the instruments is already established (Sun, 2016), a pilot study was used to determine test-retest reliability. First, the researcher confirmed that tympanometry with 226Hz and wideband tympanometry were calibrated for their cycle before they were used (i.e. for the period 2016 – 2017). A biologic check was completed before the commencement of testing. Finally, the researcher performed the tympanometry and recorded the results, and repeated the measurements with the same participants. A total of 8 adults living with HIV were tested. The procedure was completed with both the tympanometry with 226Hz and wideband absorbance tympanometry

Validity looks at whether the instrument measures what is intended to measure and to what extent can the findings be generalized to populations, settings, treatment variables, and measurement variables (Polit & Beck, 2010; Leedy & Ormrod, 2010). First, the self-developed case history form was given to two qualified audiologists with a minimum clinical experience of five (5) years. The audiologists were requested to review the content (items) of the self-developed case history form and provide input on whether it will or will not yield

expected results. Subsequently, a pilot study was conducted to determine if participants understood the questions. Secondly, the researcher ensured that all audiological equipment were calibrated according to American National Standards Institute (ANSI) (HPCSA, 2002). Daily biologic calibration was also performed to ensure that all equipment functioned optimally before commencing with the study (Wilber & Burkard, 2015). Lastly, the sample was deemed representative of the adult population infected with HIV in the South African context.

4.12 Data Analysis and Statistical Procedure

The first part of the analysis was conducted by the two ENT specialists. The ENT specialists analysed the video otoscopic images and made the diagnoses. The diagnoses of middle ear pathologies was made based on the structural appearance and colour of the tympanic membranes of each participant. This method of analysis and diagnosis of the middle ear status was found to be consistent with the in-patient otomicroscopy (Biagio et al., 2014). Each ENT was given a form (Appendix H) on which to record the results. Each ENT specialist sent back the analysis and diagnoses of the middle ear pathologies made from the video otoscopic images. The results of each ENT specialist were entered on the Microsoft Excel Spreadsheet on the computer.

Descriptive statistics using IBM Statistical Package for Social Sciences (SPSS) version 24 was used to describe and summarise all the results (Ali & Bhaskar, 2016). A description of the demographic characteristics of the participants, middle ear pathologies made by each ENT specialist, tympanometry with 226Hz and wideband absorbance tympanometry was made. Cohen's kappa (Viera & Garrett 2005; McGinn et al., 2004) was used to evaluate the agreement of diagnoses between the two ENT specialists. These results served as the gold standard against which the tympanometry with 226Hz and wideband

absorbance tympanometry were measured (Hunter et al., 2017). Table 1 below is an illustration of the degree of the kappa values used.

Table 1: Interpretation of Kappa Statistics

Kappa value	Degree of agreement
< 0	Less than chance agreement
0.01 to 0.20	Slight agreement
0.21 to 0.40	Fair agreement
0.41 to 0.60	Moderate agreement
0.61 to 0.80	Substantial agreement
0.81 to 0.99	Almost perfect agreement

Receiver operating characteristics (ROC) curves were measured to evaluate the sensitivity and specificity of wideband absorbance tympanometry over a wide range of frequencies. ROC curves were used to determine the cut-off values for each frequency from 226Hz to 8000Hz on which to determine sensitivity and specificity of the wideband absorbance tympanometry (Kumar & Indrayan, 2011; Terzi et al., 2015). ROC curves were also used to determine the sensitivity and specificity of tympanometry with 226Hz. The area under the ROC (AUROC) curve and 95% confidence interval (CI) were calculated automatically on the SPSS version 24. A comparison of the sensitivity and specificity of wideband absorbance tympanometry and tympanometry with 226Hz probe tone was made based on the ROC curves. In response to the South African context where resources do not always allow for established gold standards to be utilised, additional analysis comparing wideband absorbance tympanometry to video otoscopiy (ENT analysis) using tympanometry as a gold standardwere also done.

4.13 Ethical considerations

All research procedures were followed in accordance with the World Medical Associations (WMA) Declaration of Helsinki (2013). The following ethical principles were applied throughout the study, namely: permission, informed consent, confidentiality, anonymity, autonomy, beneficence, non-maleficence, and justice

4. 13.1 Confidentiality

The researcher is responsible for ensuring confidentiality and privacy of research participants and the data obtained from them (Leedy & Ormrod, 2010). The researcher ensured confidentiality by not recording names of participants on the data collection forms. Furthermore, the researcher also ensured that data was stored on a password protected spreadsheet and computer.

4.13.2 Beneficence

Beneficence emphasizes the moral importance of doing well to others by minimizing risks and harm and maximize the benefits (Polit & Beck, 2010). All participants underwent an audiological test battery that is non-invasive and quick to complete. Participants whose audiological results were abnormal were managed accordingly. Management included referring the participants to a doctor for middle ear management or refer to NWA for further audiological and management of other auditory pathologies (e.g. fitting hearing aid).

4.13.3 Non-maleficence

The ethical principle of non-maleficence means to do no harm to participants (Parahoo, 2006). In this study, all audiological measures that were used are non-invasive and

would be operated by the researcher. Therefore, no harm to participants was anticipated by participating in the study

4.13.4 Justice

The ethical principle of justice is synonymous with fairness and equity (Polit & Beck, 2012). The researcher is obliged to treat participants fairly and equitably during the course of the study without discriminating the participants based on defining variables such as gender, language etc. The researcher ensured that participants have an equal chance of being included. The participants were provided with the same instructions and were tested using the same protocol described above

4.13.5 Referral

All participants who needed further management (e.g. presenting with middle ear pathologies or hearing loss) were referred accordingly to other health professionals (see Appendix F).

RESULTS OF THE STUDY

CHAPTER 5: RESULTS

The current chapter presents findings from this study**.** The first part of the findings will comprise of the descriptions of participants and the prevalence of middle ear pathologies in adults living with HIV. The second part presents the findings in accordance with the specific objectives of the study as presented in the methodology chapter.

5.1 Description of participants

The study comprised of 99 (198 ears) participants. The sample included 27 males (27%) and 72 females (73%), (M=46, SD, 9.483). All participants were diagnosed with HIV. A total of 98 (99%) adults were taking ART as part of their treatment, while only 1 (1%) participant was ART naïve. However, during the ENT analysis part of the study, a total of 25 ears (13%) were excluded because of poor visualisation quality of the video otoscopic images. Figure 1 below illustrates how many ears were included and excluded from the analysis by each ENT.

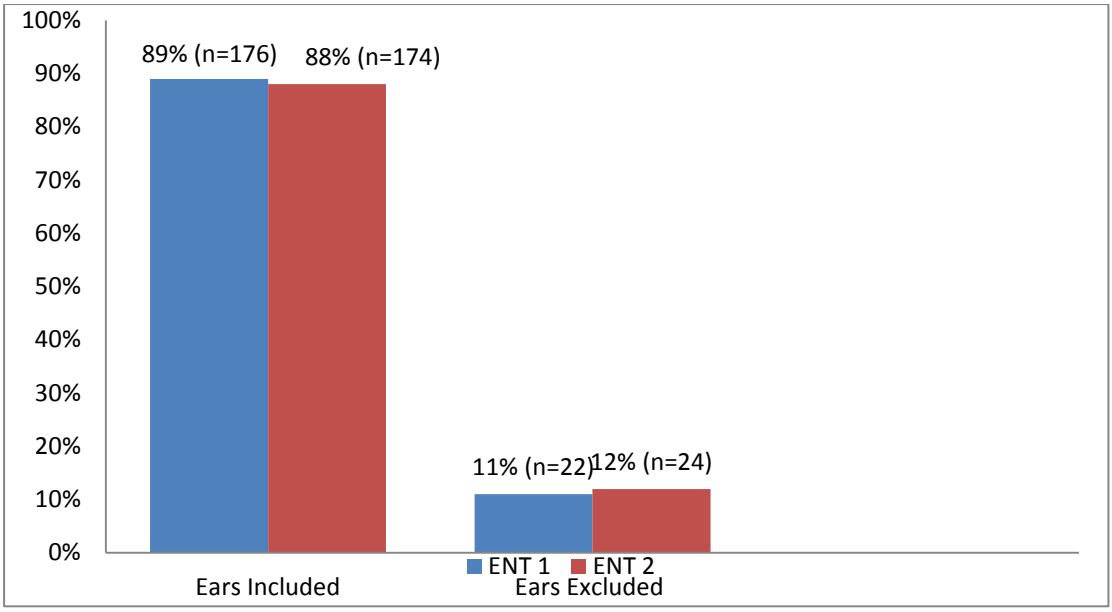


Figure 1: A comparison between ENTs with regards to exclusion and inclusion of ears (n=198)

Each ENT specialist was able to make the diagnosis on 173 ears of the sample. Of this, ENT specialists could not agree on the diagnoses of 12 ears (16%). Table 2 below indicates the number of ears diagnosed with normal middle ear function or abnormal middle ear by each ENT. Figure 2 below illustrates the diagnostic concordance (agreement and disagreement) between the two ENT specialists. Kappa value (k=0.7) indicated a substantial agreement between the diagnoses of two ENT doctors.

Table 2: Summary of the middle ear diagnoses from each ENT

ENT	Normal ears		Abnormal ears	
	n	%	n	%
ENT 1	158	91	15	9
ENT 2	150	87	23	13

Since ENT diagnoses served as the gold standard on which tympanometry with 226Hz and wideband absorbance tympanometry were measured, the 12 ears that the ENT specialist did not agree with, were not included when evaluating the sensitivity and specificity of these measures. Consequently, only 161 ears were included as the reference standard

5.2 The occurrence of middle ear pathology in this study

ENT diagnoses

Of the 161 ears analysed and diagnosed by the two ENT specialists, 17 of them (11%) had some form of middle ear pathologies (see Figure 2). Of the 17 ears with middle ear pathologies, 10 (59%) affected 5 individuals bilaterally, while 7 (41%) affected 7 individuals unilaterally. So, in a sample of 87 adults with HIV, 17 presented with middle ear pathologies.

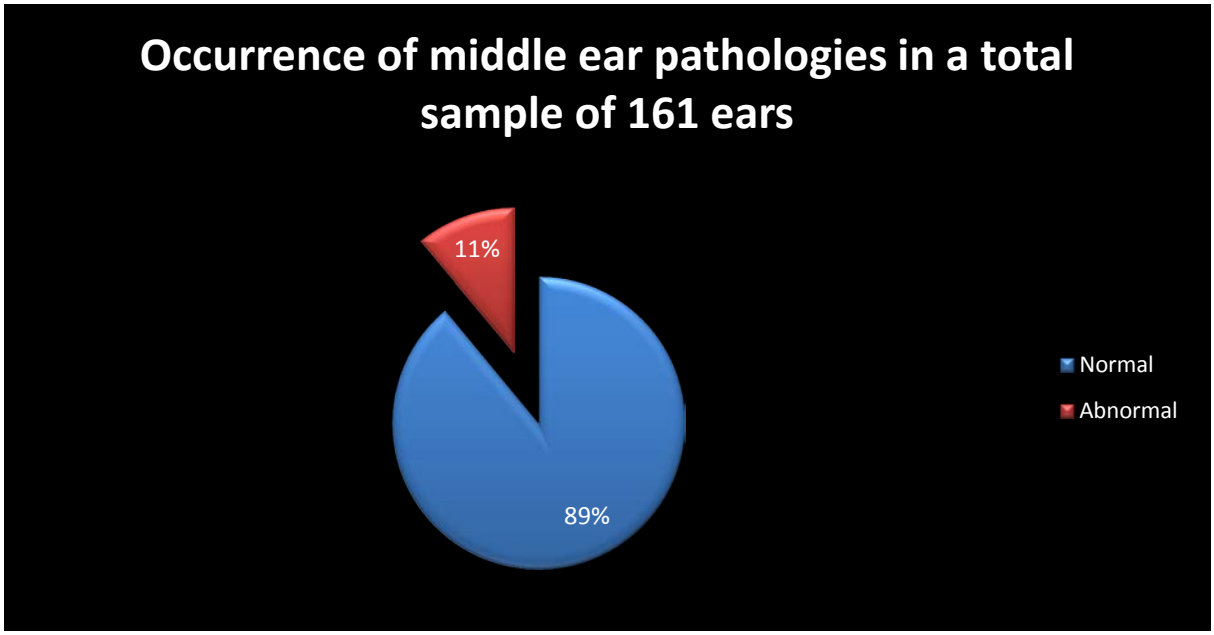


Figure 2: The occurrence of middle ear pathologies in 161 ears of adults living with HIV (N=161 ears)

Tympanometry with 226Hz

Tympanometry with 226Hz revealed 13 ears (8%) with abnormal tympanograms (see Figure 4). Type Ad tympanogram comprised the majority (70%) of the tympanograms, while type As and type B constituted 15% each (see Figure 5). There were no type C tympanograms in this data.

The difference between the numbers of ears with middle ear pathologies diagnosed via the clinical examination versus those diagnosed using tympanometry with 226Hz was statistically different ($P < 0.0001$)

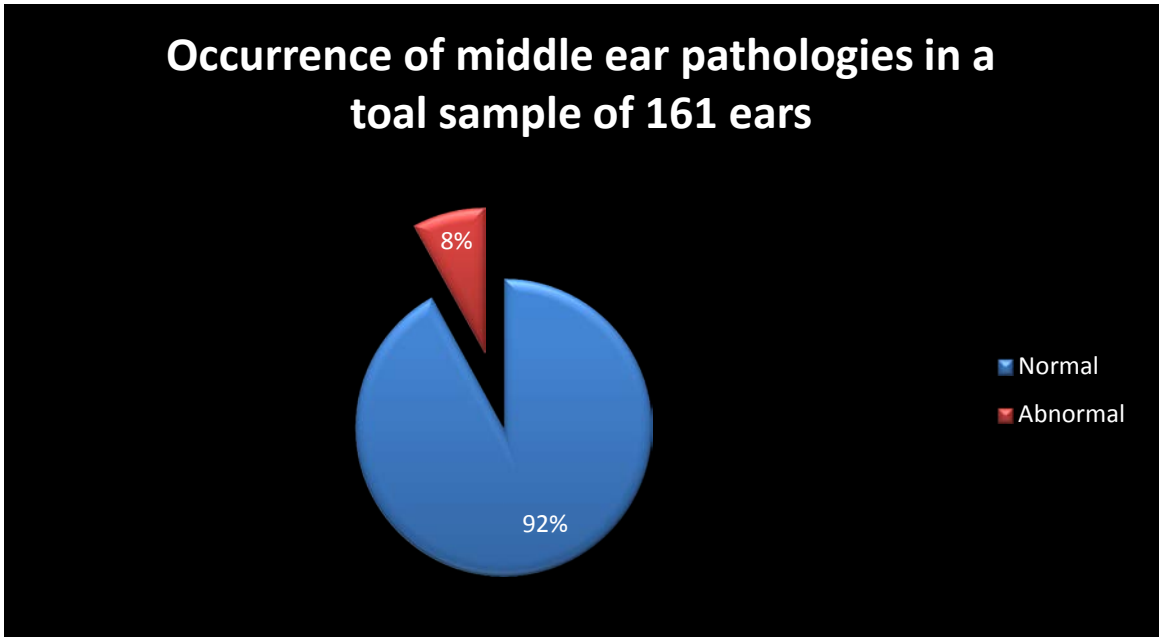


Figure 3: The occurrence of middle ear pathologies as determined by tympanometry with 226Hz probe tone (n=161)

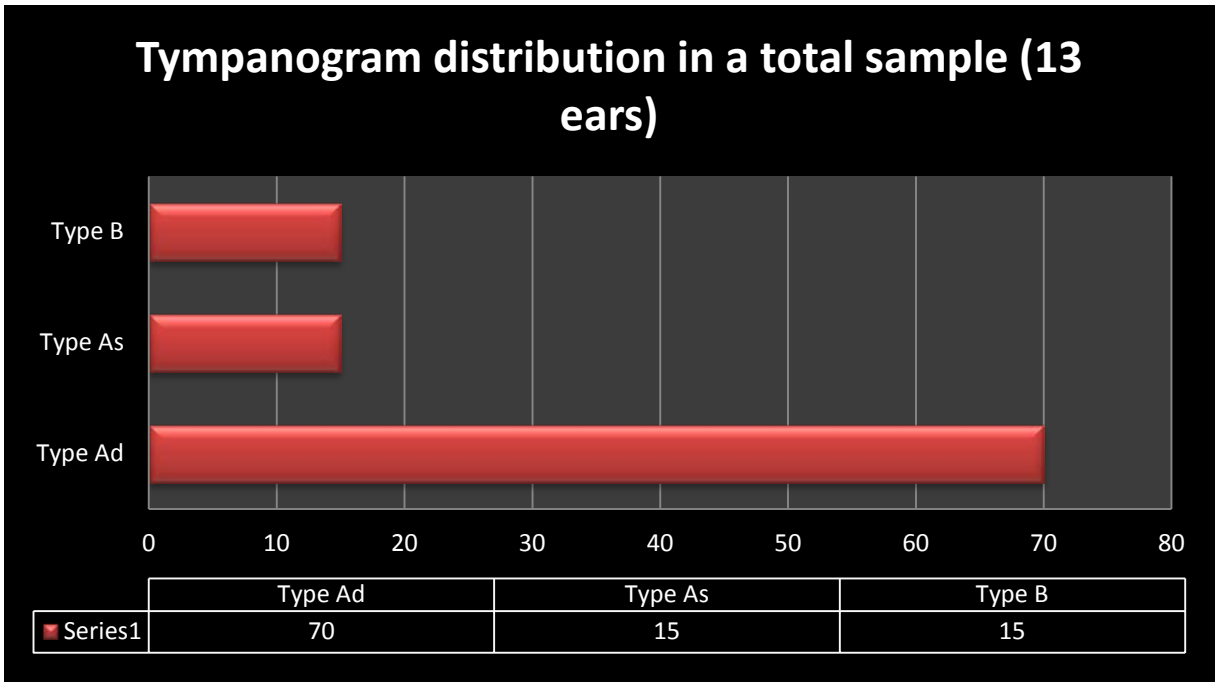


Figure 4: Types of abnormal tympanograms in 8% of the sample with middle ear pathologies (n=13)

5.3 Sensitivity and specificity of wideband absorbance tympanometry

5.3.1 Sensitivity and specificity of Wideband absorbance tympanometry when assessing middle ear function in adults living with HIV

Before the sensitivity and specificity of wideband absorbance tympanometry was calculated, the area under the curve (AUROC) was determined. Table 3 indicates specific AUROC that were automatically determined. When using AUROC, one looks at the sensitivity and specificity measure. For values 0, AUROC indicates that a diagnostic measure incorrectly identifies all pathologies, while a value of 1 indicates that a diagnostic measure can correctly identifies all pathologies (Kumar & Indrayan, 2011). The value of 0.5 is considered a minimum for classifying whether a diagnostic measure can be used practically to identify pathologies (Park, Goo & Jo, 2004). Table 3 therefore shows that AUROC values were above the minimum value of 0.5 at low to mid frequencies (226Hz to 971.53Hz), with the rest frequencies below the minimum 0.5.

Table 3: An illustration of area under the curve for wideband absorbance tympanometry

Frequency	AUROC	95% CI	
226	0.591	0.452	0.731
363.91	0.600	0.473	0.726
514.65	0.629	0.512	0.747
667.42	0.641	0.520	0.761
793.7	0.631	0.502	0.759
971.53	0.581	0.432	0.730
1155.35	0.452	0.288	0.616
1414.21	0.446	0.293	0.599
1781.8	0.493	0.339	0.647
2058.6	0.448	0.284	0.612
2519.84	0.441	0.282	0.599
3084.42	0.465	0.305	0.625
3775.5	0.416	0.271	0.560
4495.8	0.438	0.309	0.567
5495.8	0.417	0.251	0.584
6535.6	0.346	0.211	0.481

After determining AUROC, specific cut-off values at each frequency were determined to calculate sensitivity and specificity of wideband absorbance tympanometry (see Table 4). The sensitivity of wideband absorbance tympanometry was higher (88%) at higher frequency (4495.8 Hz), with a specificity of 20%. The sensitivity of wideband absorbance tympanometry was also slightly higher (82%) at 667.42 Hz with a specificity of 39% in the same frequency. Table 4 below summarises the AUROC for wideband absorbance tympanometry with specific cut-off values for each frequency. These results do not support the rejection of null hypothesis, which states that wideband absorbance tympanometry does not have clinical utility in assessing middle ear pathologies in adults living with HIV.

Table 4*:* The sensitivity and specificity of wideband absorbance tympanometry in identifying middle ear pathologies in adults living with HIV

Frequency	Cut-off value	Sensitivity (%)	Specificity (%)
226	0.135	59	65
363.91	0.280	77	41
514.65	0.435	71	46
667.42	0.704	82	39
793.7	0.641	65	60
971.53	0.727	71	53
1155.35	0.614	30	F
1414.21	0.592	23.5	85
1781.8	0.556	23.5	81
2058.6	0.497	23.5	87
2519.84	0.541	23.5	82
3084.42	0.346	23.5	90
3775.5	0.249	18	83
4495.8	0.524	88	20
5495.8	0.139	23.5	88
6535.6	0.079	12	90

5.3.2 Sensitivity and specificity of tympanometry with a 226Hz probe tone when assessing middle ear function in adults living with HIV

The sensitivity of tympanometry with 226Hz probe tone was found to be 23.5%, while the specificity was 93.8%. The positive and negative predictive values were found to be 30.8% and 91.2% respectively. The AUROC that approaches the value of 1 indicates a better performance (sensitivity and specificity) for a diagnostic measure to identify pathology. As depicted in figure 6 below, the value of AUROC is approximately 0.3, which indicates low sensitivity and high specificity. These results accept the null hypothesis, which states that tympanometry with 226Hz has no clinical utility when assessing middle ear function in adults living with HIV. High specificity leads to the probability of accepting true null hypothesis (Owusu-Ansah, Sampson, Samuel & Robert, 2016).

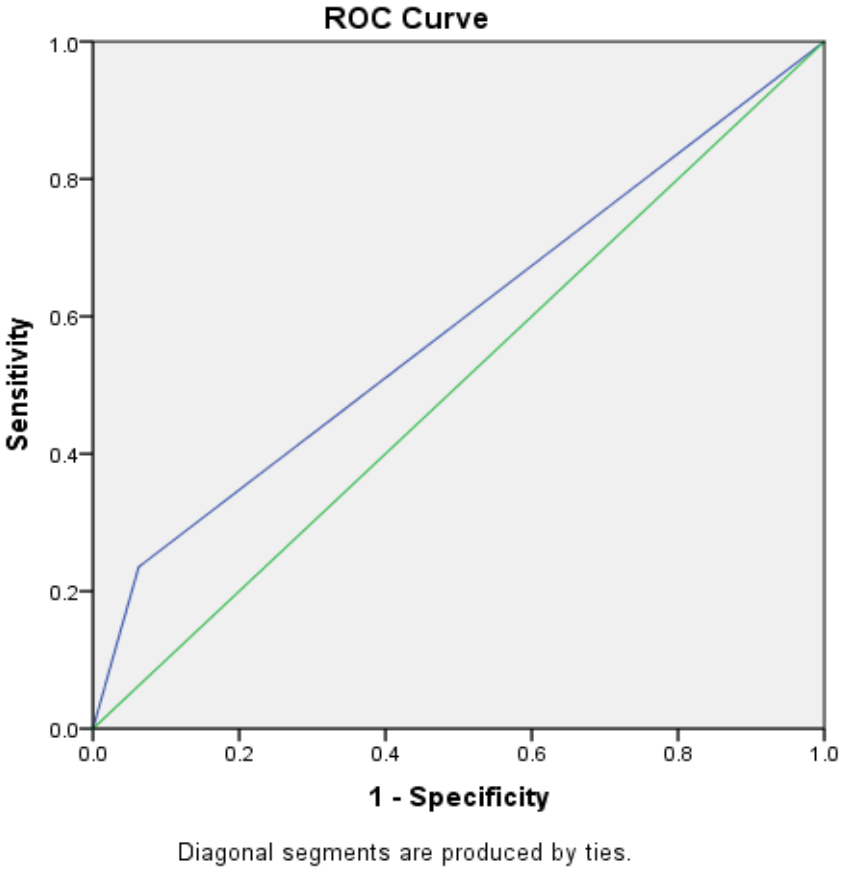


Figure 5: ROC curve showing the area under the curve for tympanometry with 226Hz

5.3.3 Comparison of the sensitivity and specificity of WBA to tympanometry with a 226Hz probe tone

When comparing the sensitivity and specificity of tympanometry with 226Hz probe tone and wideband absorbance tympanometry, it was clear that there was a statistically significant difference ($p< 0.001$) between the sensitivity and specificity of the two measures. While the sensitivity of tympanometry with 226Hz probe tone was 23.5%, the sensitivity of wideband absorbance tympanometry reached as high as 88%. However, the specificity of tympanometry with 226Hz probe tone and wideband absorbance tympanometry were comparable ($p=1.00$). These findings showed that the sensitivity of tympanometry with 226Hz probe tone and wideband absorbance tympanometry are statistically significant different in assessing middle ear pathologies in adults living with HIV. However, the specificity of wideband absorbance tympanometry and tympanometry with 226Hz probe tone were comparable These findings reject the null hypothesis, which states that there is no statistical significant difference between the clinical utility of the wideband absorbance tympanometry and tympanometry with 226Hz in assessing middle ear pathologies in adults living with HIV.

5.3.4 ADDITIONAL ANALYSIS using tympanometry with 226Hz as a gold standard

5.3.4.1 Sensitivity and specificity of wideband absorbance tympanometry

An additional analysis was conducted using tympanometry with 226Hz probe tone as a gold standard. The primary purpose of this additional analysis is to determine whether wideband absorbance tympanometry show high sensitivity and specificity in identifying middle ear pathologies when compared with various measures of middle ear as gold standards. When tympanometry with 226Hz was considered a gold standard, the AUROC values for wideband absorbance tympanometry were higher than the minimum (0.5) in the mid to high frequencies

(971.53Hz to 1781.8Hz, and 3084.42Hz to 6535.6Hz), with majority of low frequencies falling below the minimum. Table 7 below therefore shows different AUROC values in frequencies from 226Hz to 6535Hz; while Table 8 shows the sensitivity and specificity of wideband absorbance tympanometry in different frequencies based on various cut-off values

Table 5: An illustration of area under the curve for wideband absorbance tympanometry

Frequency	AUROC	95% CI	
226	0.361	0.145	0.577
363.91	0.344	0.138	0.550
514.65	0.336	0.126	0.546
667.42	0.398	0.196	0.607
793.7	0.423	0.212	0.635
971.53	0.493	0.276	0.710
1155.35	0.600	0.387	0.813
1414.21	0.608	0.425	0.792
1781.8	0.524	0.356	0.692
2058.6	0.494	0.305	0.683
2519.84	0.472	0.287	0.656
3084.42	0.505	0.328	0.683
3775.5	0.530	0.357	0.702
4495.8	0.584	0.449	0.719
5495.8	0.666	0.512	0.820
6535.6	0.543	0.387	0.699

Table 6: The sensitivity and specificity of wideband absorbance tympanometry in identifying middle ear pathologies in adults living with HIV

Frequency	Cut-off value	Sensitivity (%)	Specificity (%)
226	0.10	23.3	82
363.91	0.143	18.2	86
514.65	0.216	18.2	86
667.42	0.296	27.3	90
793.7	0.384	27.3	89
971.53	0.574	36	83
1155.35	0.6559	55	76
1414.21	0.652	55	73

1781.8	0.664	46	61
2058.6	0.660	46	61
2519.84	0.708	73	39
3084.42	0.752	82	25
3775.5	0.269	36	80
4495.8	0.348	64	50
5495.8	0.227	73	63
6535.6	0.270	91	27

Based on table above, the sensitivity of wideband absorbance tympanometry were higher in high frequencies (2519.6Hz to 6535.6Hz) with low sensitivity in low to mid frequencies (226Hz to 2058.6Hz). However, the specificity of wideband tympanometry was fairly high across frequencies.

5.3.4.2 Sensitivity and specificity of video otoscopy (ENT diagnosis)

When tympanometry with 226Hz was used as a gold standard, the sensitivity and specificity of video otoscopy was 30.8% and 91.2% respectively. As depicted in figure 6, AUROC curve was 0.3, indicating low sensitivity but high specificity in identifying middle ear pathologies. These results accept the null hypothesis, which states that clinical examination has no clinical utility when assessing middle ear function in adults living with HIV. High specificity leads to the probability of accepting true null hypothesis (Owusu-Ansah, et al., 2016)

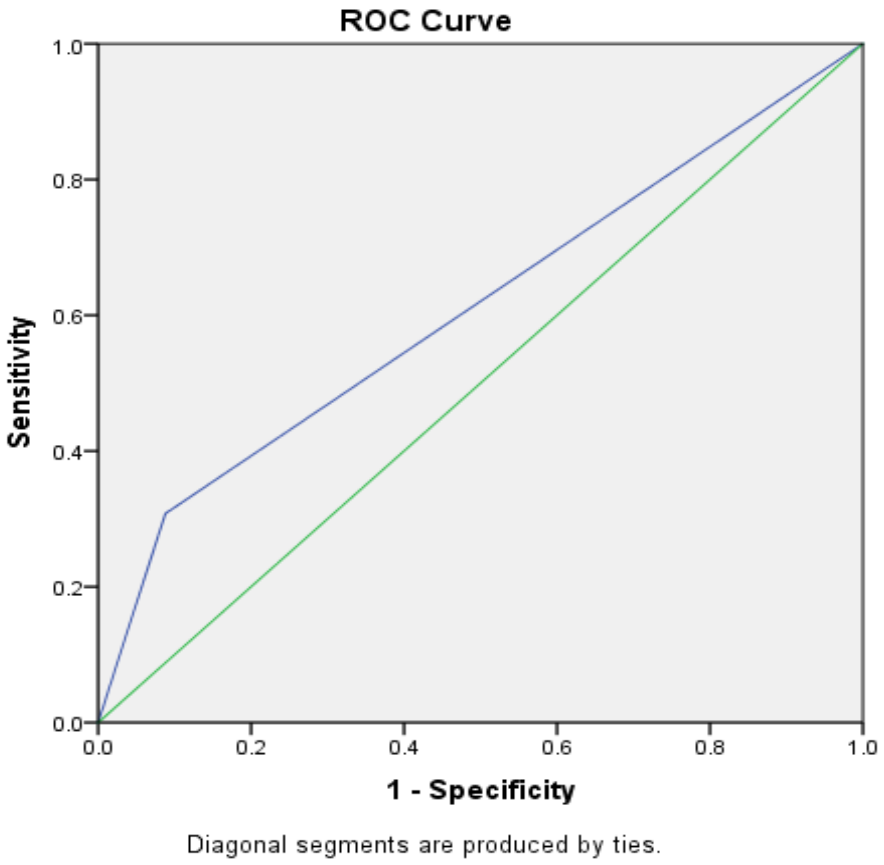


Figure 6: ROC curve showing the area under the curve for video otoscopy (ENT diagnosis)

5.3.4.4 Comparison of the sensitivity and specificity of wideband absorbance tympanometry and video otoscopy (ENT diagnosis)

When comparing the sensitivity and specificity of wideband absorbance tympanometry with video otoscopy (ENT diagnosis), there was a statistically significant difference ($p< 0.001$) between the sensitivity and specificity of the two measures. While the sensitivity of video otoscopy (ENT diagnosis) was 30.8%, the sensitivity of wideband absorbance tympanometry reached as high as 91%. However, there was no statistical significant difference between the specificity of wideband absorbance tympanometry and video otoscopy. These findings showed

that the sensitivity of wideband absorbance tympanometry and video otoscopy are statistically significant different in assessing middle ear pathologies in adults living with HIV when tympanometry with 226Hz probe is used as a reference standard. However, the specificity of wideband absorbance tympanometry and tympanometry with 226Hz probe tone were comparable.

CHAPTER 6: DISCUSSION OF THE RESULTS

The purpose of the current study was to evaluate the clinical utility (sensitivity and specificity) of wideband absorbance tympanometry when assessing the middle ear function in adults living with HIV, and compare it with the sensitivity and specificity of tympanometry with 226Hz probe tone. The sensitivity and specificity of wideband absorbance tympanometry and tympanometry with 226Hz probe tone were determined by using ENT diagnosis through the use of video otoscopic images as the gold standard. Overall, the study demonstrated that wideband absorbance tympanometry has high sensitivity when assessing middle ear pathologies.

The initial sample size of the current study was a total of 99 adults (198 ears) who were diagnosed with HIV. However, 25 ears (13%) were excluded from the analysis because of poor visualisation due to lack of focus of the picture and/or wax occlusion. The exclusion of video otoscopic images from the present study is consistent with findings from previous studies on video otoscopy. Mbao, Eikelboom, Atlas and Gallop (2003), for example, found that less than 16% of video otoscopic images in their study could not be analysed due to poor quality. The number of acceptable video otoscopic images in the current study for analysis was similar to those reported in the study conducted by Biagio et al. (2013). The occurrence of poor quality video otoscopy images raises concerns where diagnosis of middle ear pathologies may be inaccurate when video otoscopy is used in adults living with HIV. Current findings bring forth implications for audiologists and other hearing health professionals with regards to the use of video otoscopy as a measure of middle ear function

Although 99 adults who were diagnosed with HIV participated in this study, 87 adults were finally included in the study for further analysis. This sample size was smaller

compared to other previously published studies (Tshifularo et al., 2013; Van der Westhuizen et al., 2013). Despite the different sample size between the present study and previously published studies, the demographic characteristics of the participants in this study represent that of South Africa population, in that a higher proportion of women in South Africa have high prevalence of HIV (SSA, 2017). However, the fact that participants were selected from a single province which only represent 9.2% of the population living with HIV in South Africa (Human Science Research Council [HSRC], 2014), threatens the generalizability of the study to the population. Therefore, caution must be exercised when interpreting the findings of the present study.

Furthermore, 99% of the participants in the present study were on HAART regimen. The findings of the present study were not consistent with other published studies. For example, in a study conducted by Van der Westhuizen and colleagues (2013), only participants with CD4 count cells lower than 200 cells/uL (category 3 according to CDC classification) received HAART treatment. However, participants in category 1 and 2 whose CD4 cell counts were higher than 200 cells/uL did not receive any HAART treatment. Tshifularo and colleagues (2013) also indicated that some participants diagnosed with HIV were treated with ARV while others were not on treatment. The implications of these findings may be that in the present study the use of HAART in nearly all participants may have reduced the development of middle ear pathologies. It is well known that the use of HAART improves the immune system of individuals with HIV (Misker, et al., 2014; Morsheimer, et al., 2014).

The occurrence of middle ear pathologies in adults living with HIV was 11% (n=17) in this study as diagnosed by ENT specialists and 8% (n=13) as diagnosed by tympanometry

with 226Hz. As far as the occurrence of middle ear pathologies in this population was concerned, current findings are not consistent with available evidence which indicates that the occurrence of middle ear pathologies in adults living with HIV is higher. Van der Westhuizen et al. (2013), using tympanometry with 226Hz reported an occurrence of middle ear pathologies in adults living with HIV to be 41%; while Tshifularo et al. (2013), using clinical examination methods, reported the occurrence at 42%. Sample size and methodological difference may have contributed to the difference in the occurrence of middle ear pathologies in the present study and other published research. Despite this difference, these findings have implications for audiologists and other hearing health professionals regarding the existence of middle ear pathologies in individuals living with HIV. The occurrence of middle ear pathologies in individuals living with HIV highlights the need for monitoring of these individuals through early identification and intervention.

The sensitivity and specificity of wideband absorbance tympanometry

In this study, there was a balance between the sensitivity and specificity of wideband absorbance tympanometry in frequencies between 226Hz to 971.53Hz. This means, there was a fairly high sensitivity and high specificity of wideband absorbance tympanometry across those frequencies. However, as the frequencies increases from 1155.35 Hz to 6535.6Hz, there was poor sensitivity of wideband absorbance tympanometry but high specificity. While the findings confirm previous studies that wideband absorbance tympanometry can provide an accurate diagnosis of middle ear pathologies (Kaf, 2011; Ibraheem, 2011); the findings of this study are inconsistent with previous research. The sensitivity and specificity of wideband tympanometry was balanced, meaning that the sensitivity and specificity were both high across wide range of frequencies. For example, the sensitivity and specificity of wideband

tympanometry ranged from 61% to 100%. Beers et al. (2010) reported a much higher sensitivity of 96% when assessing middle ear pathologies.

The variations between the sensitivity and specificity of wideband absorbance tympanometry in the current study and previously published studies can be attributed to several factors. Firstly, the cut –off values used in the current study for different frequencies were different to previously published studies. Terzi and colleagues (2015) used a cut off of 32.0 and 54.0 at 1 kHz and 1.5 Hz respectively, while the current study used 72.7 and 61.4 at 971.53Hz and 1414.21Hz respectively. Secondly, this study used ENT diagnosis through the use of video otoscopy as a gold standard. The use of ENT diagnosis using video otoscopic images as a gold standard has been proven to be the stringent way because the diagnosis is primarily made based on structural and colour changes of the tympanic membrane (Jaisinghani et al., 1999) rather than the mechanical change of the tympanic membrane.

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The sensitivity and specificity of tympanometry with 226Hz probe tone

The sensitivity of tympanometry with 226Hz probe was 23.5% while the specificity was 93.8%. The findings of the current study confirm existing literature indicating that tympanometry with single probe tone has low sensitivity when assessing middle ear pathologies (Kaf, 2011; Shahnaz & Polka, 1997; Hunters et al., 2017). However, the sensitivity of the current study was significantly lower when compared to sensitivity of the tympanometry with 226Hz reported in previous reports. Terzi et al. (2015) reported the sensitivity and specificity of tympanometry with 226Hz to be 88.2% and 84% respectively when identifying OME. Other studies have obtained an even higher sensitivity when assessing middle ear pathologies. Finitzo et al., (1992) based the sensitivity of tympanometry with single probe on type B tympanograms when assessing middle ear pathologies. In their study, type B tympanograms revealed a higher sensitivity of 96% when assessing OME.

Bhatta and Adhikari (2008) also found type B tympanograms to have a higher sensitivity when assessing middle ear fluid.

Several published studies have shown that some middle ear pathologies, especially subtle middle ear pathologies such as acute otitis media or/and those affecting the ossicular chain such as otosclerosis, may not change the mechanical aspect of the tympanic membrane, but may perhaps shift the resonant frequency of the middle ear slightly to the right or left (Kaf, 2011; Margolis & Goycoolea, 1993; Shahnaz, 2007; Shahnaz & Polka, 1997). In these situations, the mobility of the tympanic membrane may still be intact (Hunter et al., 2017). These are the pathologies that may manifest on the tympanic membrane without affecting the mechanical aspect of the tympanic membrane (Hunters et al., 2017). Therefore, a sensitive measure is required to identify these middle ear pathologies. If these pathologies are not identified, they may progress into the middle ear cavity and become chronic, causing other complications

There are several reasons for the significant difference between the sensitivity of the tympanometry with 226Hz in the current study and previously published studies. Firstly, the high sensitivity of tympanometry with single probe tone in previous studies was based primarily on identifying the presence of middle ear effusion (OME) (Finitzo et al., 1992; Harris et al., 2005; Terzi et al., 2015). Unlike other forms of middle ear pathologies, the presence of middle ear effusion affects the mechanical aspect of the tympanic membrane (Harries et al., 2005; Martin & Clark, 2015). Therefore, it can be argued that type B tympanogram represents an advanced form of middle ear pathologies which completely impedes the mobility of the tympanic membrane. It is often associated with chronic type of middle ear pathologies (Hall-Stoodley et al., 2006). However, when other forms of middle ear pathologies are considered and evaluated, low sensitivity is indicated by tympanometry

with single probe tone (Shahnaz & Polka, 1997). For example, Ogut et al. (2008) found the sensitivity of type As to be 40% and specificity to be 98% when assessing middle pathologies in the adult population.

Secondly, the present study measured the sensitivity and specificity of tympanometry with 226Hz probe tone against the diagnosis of ENT through the use of video otoscopic examination (clinical examination) which reported middle ear pathologies that did not affect necessarily affected the mechanical aspect of the tympanic membrane (Jaisinghani et al., 1999). These findings have important clinical implications indicating that tympanometry with single probe tone inaccurately identifies middle ear pathologies that do not affect the mechanical aspect of the tympanic membrane. Given that individuals living with HIV present with a number of middle ear pathologies varying in severity (Obasineke et al., 2014; Van der Westhuizen et al., 2013), it is crucial that accurate measures of middle ear function with high sensitivity and specificity be used in this population.

Wideband absorbance tympanometry versus tympanometry with a 226Hz probe tone

There was a statistical significant different between the sensitivity of wideband absorbance tympanometry and tympanometry with 226Hz probe tone when assessing middle ear pathologies in adults living with HIV. While the wideband absorbance tympanometry could reach a sensitivity of 82%, the sensitivity of tympanometry with 226Hz probe tone was 23.5%. However, the specificity of wideband absorbance tympanometry was generally comparable to the specificity of tympanometry with 226Hz probe tone. These findings demonstrate that wideband absorbance tympanometry could accurately identify middle ear pathologies in relation to the tympanometry with 226Hz probe tone in this study. The findings of the current study confirms previous research indicating that wideband absorbance

tympanometry can accurately identifies middle ear pathologies than the tympanometry with 226Hz probe tone (Harris et al. 2005; Kaf, 2011; Terzi et al., 2015). However, it must be cautioned that the sensitivity of wideband absorbance tympanometry in this study was variable, with low sensitivity in the high frequencies. Nevertheless, the null hypothesis stating that there is no statistical significant difference between wideband absorbance tympanometry and tympanometry with 226Hz probe tone is rejected.

Sensitivity and specificity of wideband absorbance tympanometry (based on additional analysis)

The sensitivity of wideband absorbance tympanometry was higher in high frequencies (2519.6Hz to 6535.6Hz) with poor sensitivity in low to mid frequencies (226Hz to 2058.6Hz). However, the specificity of wideband tympanometry was fairly high across frequencies. These findings also confirmed previous research, indicating that the sensitivity and specificity of wideband absorbance tympanometry is high in identifying middle ear pathologies (Kaf, 2011; Terzi et al., 2015). While the pattern of sensitivity changed when compared with the previous (i.e. when video otoscopy was considered a gold standard), it appears that the sensitivity of wideband absorbance tympanometry differs with previously published studies. In previous studies, the sensitivity of wideband absorbance tympanometry was high across frequencies (i.e. from low to high frequencies) (Beers et al., 2010; Terzi et al., 2015).

The variation can also be attributed to different cut-off values used, and the use of different gold standard. For example, Hunter et al (2017) used pneumatic otomicroscopy or pneumatic otoscopy as gold standard to measure the sensitivity and specificity of wideband absorbance tympanometry. Because Otomicroscopy has been established as a gold standard, various studies have used it to determine the sensitivity and specificity of other measures

(Baigio et al. 2013; Biagio et al., 2013). In addition, some studies have used a combination of measures to identity the presence of middle ear pathologies. For example, Terzi et al (2015) used transient evoked otoacoustic emission, tympanometry and otoscopic examination analysed by trained ENT specialists to determine the presence or absence of middle ear pathologies. These differences could have contributed to the different results obtained in the current study and previous studies.

When tympanometry with 226Hz was used as a gold standard in this study, there was a statistical significant difference between the sensitivity of wideband absorbance tympanometry and video otoscopy. These findings are difficult to compare with published studies due to lack of available research that used tympanometry as a gold standard. When sensitivity and specificity of measures of middle ear function are evaluated, some clinical examination procedures such as otomicroscopy, pneumatic otoscopy and myringotomy (a form of clinical examination) becomes the common measure used as a gold standards (Harris et al., 2005; Rogers et al., 2010). Al-Khalib (2010) reported that myringotomy is regarded as the ultimate diagnostic indicator for identifying the presence or absence of middle ear pathologies. Therefore, further research is required in this area investigating the sensitivity and specificity of clinical examination techniques such as video otoscopic analysis made by ENT specialists

There is evidence indicating that middle ear pathologies exists in adults living with HIV (Araújo et al., 2012; Khoza & Ross, 2002; Obasineke et al., 2014; Tshifularo et al., 2013). These pathologies persist despite the efficacy of highly active antiretroviral therapy (HAART) (Khoza-Shangase, 2011, 2017; Khoza-Shangase & Van Rie, 2017; Matas et al., 2014; Torre et al., 2015). The presence and persistence of middle ear pathologies in this population, current findings suggest a need for early identification of these pathologies to

reduce the potential long term impacts associated with untreated middle ear pathologies. For example, published studies have indicated that undetected and untreated middle ear pathologies can contribute to the burden of hearing loss (Mulwafu et al., 2016; Olusanya et al., 2004). The World Health Organisation (2011) reported that majority of the existing hearing loss, especially in developing countries results from middle ear pathologies that are not treated early; and since majority of HIV infected individuals reside in developing countries such as those in Sub-Saharan Africa; current findings have important implications for such contexts.

Assessing middle ear pathologies using wideband absorbance tympanometry in adults living with HIV may increase the chance for early identification of middle ear pathologies and improve patients' health outcomes. Patients' identified early may be treated in primary health clinics with medications. However, if patients are diagnosed late with middle ear pathologies, further complications may occur requiring specialised services such as ENT (Fagan & Jacobs, 2009). Because of the lack of resources and the pandemic of HIV in countries such as South Africa (UNAIDS, 2016), a measure that has high sensitivity and specificity in identifying middle ear pathologies can contribute to early detection and management of hearing loss related to middle ear disorders. With the technological advancements that continue to grow rapidly in the field of hearing health (Clark & Swanepoel, 2014); wideband absorbance tympanometry can be imbedded within the early identification and management programmes to ensure its widespread utility.

CHAPTER 6: CONCLUSIONS, STRENGTHS, LIMITATIONS AND RECOMMENDATIONS

CONCLUSIONS

The results of the current study revealed that wideband absorbance tympanometry has high sensitivity than the tympanometry with 226Hz probe tone when these measures are compared with clinical examination (video otoscopy). Wideband absorbance tympanometry also has higher sensitivity than video otoscopy when additional analysis was used (tympanometry with 226Hz as gold standard) However, the sensitivity of wideband absorbance tympanometry were variable in this study, with high sensitivity in the low to mid frequencies but low sensitivities in high frequencies. When tympanometry with 226Hz was used, wideband absorbance tympanometry showed variable results with high sensitivity in high frequencies and poor sensitivity in low to mid frequencies.

The variabilities of sensitivity in this study can be attributed to the methodology used. For example, in this study video otoscopic analysis of the tympanic membrane by the two ENT specialists was considered a gold standard on which to measure the sensitivity and specificity of wideband absorbance tympanometry. Despite these challenges, wideband absorbance tympanometry might be an appropriate measure for identifying middle ear pathologies in adults living with HIV. This measure can be used to assess middle ear pathologies where other measures (e.g. tympanometry) are unable to detect those pathologies.

STUDY STRENGTHS

While previous studies utilised wideband acoustic immittance (absorbance or reflectance) to evaluate its clinical utility in identifying middle ear pathologies in various populations, none of the studies have used wideband acoustic immittance in adults living with HIV. Therefore, the strength of this study was the selection of a population that is known to

be prone to middle ear pathologies due to their immunocompromised systems. Current findings therefore contribute to existing literature about the clinical utility of wideband acoustic immittance as a measure of middle ear pathologies. Unlike previously published studies that used a combination of tests as gold standard (Hunter et al., 2016) to measure the clinical utility of wideband acoustic immittance, the current study has included ENT diagnosis through the use of video otoscopic examination (Biagio et al., 2014) as a gold standard to measure the sensitivity and specificity of wideband absorbance tympanometry. Published studies have shown that ENT diagnosis of middle ear pathologies using video otoscopic images is always superior to tympanometry with single prone tone (Ting et al., 2016. Blinding of ENT specialists on the demographic characteristics of the participants allowed for the objective assessment of the tympanic membrane and making sound decision.

STUDY WEAKNESSES

Although the current study has reported on the clinical utility in a population that has not been studied before, the sample size was small. Poor visualisation of other tympanic membranes and disagreement about the diagnoses between ENTs further decreased the sample size. This study also has a methodological weakness. For instance, there was no control group on which to make a comparison. This weakness has made it difficult to use the most appropriate design for evaluating clinical utility. In addition, the current study was confined to one municipality, which reduces generalizability to the broader South African HIV infected population. This localised sample limited diversity in terms of race and socioeconomic backgrounds. Emerging literature in the area of wideband acoustic immittance has indicated that different ethnicities may yield different wideband acoustic immittance results (Wali & Mazlan, 2018). Therefore, because of this limitation, the findings of the current study cannot be generalised to a larger South African population living with HIV.

RECOMMENDATIONS FOR FUTURE RESEARCH

Similar studies should be conducted to replicate the current study. These studies must be conducted on larger sample sizes so that generalisation can be drawn from the findings. Furthermore, follow up studies on wideband acoustic immittance on individuals living with HIV should include a control group [e.g. age matched control group (HIV negative) or individuals who are diagnosed with HIV but not on treatment]. Although it may be difficult to find the latter group because of the current wave of ART rollout; findings from these individuals will provide more information about the effects of ART on the middle ear system. Due to the known effects of various factors such as ethnicity and socioeconomic background on wideband acoustic immittance, subsequent studies should include individuals living with HIV from different ethnic and socio economic backgrounds. Another possibility is to compare the wideband acoustic immittance with pure tone audiometry (ABG) in this population. Lastly, determining the clinical utility of wideband acoustic immittance in children living with HIV would provide more information about whether HIV affects children and adults middle ear system differently or not.

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Appendices

Appendix A – Consent form

Study title: The Clinical Utility of Wideband Acoustic Immittance in Adults living with HIV

I hereby agree to participate in this study on the effects of HIV on the middle ear system. The purpose and procedures have been explained to me. I understand that:

- My medical records will be reviewed
- 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.

Full name/s and surname of participant: _____

Participant signature: _____ Date: _____

Researcher signature: _____Date: _____

Appendix B: Ethics certificate

R14/49 Mr Ben Sebothoma

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M160663

NAME: (Principal Investigator)	Mr Ben Sebothoma
DEPARTMENT:	Speech Pathology and Audiology Ndlovu Wits Audiology Clinic, Elandsdoorin, Limpopo
PROJECT TITLE:	Use of Wideband Absorbance Tympanometry in Individuals Living with HIV
DATE CONSIDERED:	24/06/2016
DECISION:	Approved uncondionally
CONDITIONS:	
SUPERVISOR:	Dr Karin Joubert
APPROVED BY:	Professor P Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	01/07/2016

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 conditions under which I am/we are authorized 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 the application 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 reviewed in June and will therefore be due in the month of June each year.

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix C: Permission letter from the CEO

NDLOVU MEDICAL TRUST
NDLOVU CARE GROUP
Community Program with a Difference
P.O. Box 14, Groblersdal, 0470
Republic of South Africa

To whom it may concern,

Permission to conduct research: Ndlovu Care Group

This serves to grant permission to **Ben Sebothoma,** a Masters student at the University of the Witwatersrand to conduct her research titled:

Use of wideband absorbance tympanometry in individuals living with HIV

at the Ndlovu Medical Centre and Audiology Department, Elandsdoorn Limpopo.
Please do not hesitate to contact me should you need any further information.

Yours Sincerely,



Dr HA Tempelman
CEO Ndlovu Care Group
31 March 2016

Tel: +27 (0) 13 262 9000 • Fax: +27 (0) 13 262 3498 • info@ndlovu.com • www.ndlovucaregroup.com
NPO: 019-524-NPO • PBO: 930002417 • Reg no: IT 10961/99 • Vat Reg No 4300226059
Ndlovu Care Group: CEO Hugo Tempelman • FM Lourens Duvenhage
Board of Trustees:
Chairperson: Prof Geert H Bijlsma **Non Executive Members:** Ronald Vlies, Lynn van der Elst, Sagie Pillay, Dr Eugene Sickle **Executive Member:** Dr Hugo Tempelman

Appendix D: Permission letter from Limpopo Department of Health

LIMPOPO
PROVINCIAL GOVERNMENT
REPUBLIC OF SOUTH AFRICA

DEPARTMENT OF HEALTH

Enquiries: Stander SS (015 293 6650) Ref:LP_

Sebothoma B

Human Research Ethics Committee

Greetings,

RE: Use of Wideband Absorbance Tympanometry in Individuals Living with HIV

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.I
    - In the course of your study there should be no action that disrupts the services, or incur any cost on the Department
    - 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

02/03/2018
Date

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

The heartland of Southern Africa - development is about people

Appendix E: advertisement poster

VOLUNTEEERS NEEDED FOR A RESEARCH STUDY at Ndlovu Wits Audiology

Study title: The clinical utility of wideband absorbance tympanometry in adults living with HIV

We are conducting a research study to evaluate whether wideband absorbance tympanometry (a test of middle ear diseases) can accurately identify middle ear pathologies in adults living with HIV.

Eligibility criteria:

- Males and females
- Aged 18 years and above
- Diagnosed with HIV

Participants' hearing will be tested with otoscope, tympanometry and pure tone audiometry. Hearing tests will take approximately **20 minutes** to complete and are **free** of charge. None of the tests are harmful

If you are willing take part in this study, please visit Ndlovu wits audiology from Monday to Friday at 08h00 to 17h00 or consult me on **0730847463** for further information. Remember that your name will **NOT** be identified in the research study.

Appendix F: Self-developed case history form

Demographic information					
Age					
Gender					
Highest level of education					
Home language					
Clinical Information					
Date of HIV diagnosis					
Treatment					
Duration of treatment					
Head trauma					
Yes					
No					
History of auditoy symptoms	Onset	duration	frequency	treatment	treatment method
Ear pain					
Itchiness					
Discharge					
Other					
Current auditory symptoms	onset	duration	frequency	treatment	treatment method
Ear pain					
Itchiness					
Discharge					
Other					

Audiological Assessment							
Otoscopy							
Ear	Normal	Partial wax	mplete occlusio	Peforation	foreign object	discharge	Other
Right							
Left							

Tympanometry				
Ear	ECV	Pressure	compliance	Type
Right				
Left				

Recommendations:

Normal hearing: No referral required	
Refer to hospital for medical management	
Refer to clinic for medical management	
Comments:	
Other	

Appendix G: Information sheet for ENT specialists

Study Title: The clinical utility of wideband absorbance tympanometry in adults living with HIV

Good day,

My name is Ben Sebothoma and I am an Audiologist working at the University of Witwatersrand in Johannesburg. I am currently studying toward my postgraduate degree through the University of the Witwatersrand. As part of my research work, my study aims to investigate the effects of HIV/AIDS on middle ear system using wideband absorbance (WBA) tympanometry.

The aim of the study is to evaluate the clinical utility of wideband absorbance tympanometry in identifying middle ear pathologies in adults living with HIV. The clinical utility of wideband absorbance tympanometry will be compared with the clinical utility of the tympanometry 226 Hz. However, in order to evaluate the clinical utility and make a comparison between the two tests, a gold standard measure is required to measure the two test against.

I would like to request your assistance with reviewing video otoscopy images that will be e-mailed to you. You will be required to analyse the video otoscopic images and comment on whether there is a presence or absence of middle ear pathology. Where possible, you can also provide the diagnosis of the middle ear pathology. I look forward to your positive consideration in this regard.

If you require any further information in this regard please do not hesitate to contact me at Tel: 011 717 4573 or Ben. Sebothoma@wits.ac.za or my research supervisor, Professor

Katijah Khoza-Shangase Tel: 011 717 4565 or Katijah.Khoza-Shangase@wits.ac.za.

Yours sincerely

Ben Sebothoma

Appendix H: Results form for ENT specialists

Thank you for agreeing to review the video otoscopic images.

Instructions:

Please note that if you tick under the section '*presence of middle ear pathology*' you will also need to name the middle ear pathology on the same row e.g. acute otitis media.

If you could not evaluate, please briefly indicate why it was difficult to evaluate the middle ear

Participant number	Ear	Normal Y/N	Presence of middle ear pathology Y/N	Type of middle ear pathology *(please name)*	Could not evaluate Reason
WBT0001	Left				
	Right				
WBT0002	Left				
	Right				
WBT0003	Left				
	Right				
WBT0004	Left				
	Right				
WBT0005	Left				
	Right				
WBT0006	Left				
	Right				
WBT0007	Left				
	Right				
WBT0008	Left				
	Right				

WBT0009	Left				
	Right				
WBT0010	Left				
	Right				

Appendix I: Participants information Sheet

Study title: The Clinical Utility of Wideband Acoustic Immittance in Adults living with HIV

My name is Ben Sebothoma. I am currently studying toward my Master's degree in Audiology at the University of the Witwatersrand. As part of my research requirements, I am required to conduct a research study. I am currently conducting a study titled: *The clinical utility of wideband acoustic immittance in adults living with HIV*. For the purpose of this study I am going to determine whether wideband absorbance tympanometry (new technique) can identifies middle ear pathologies better than the standard tympanometry with 226Hz (old technique). These two tests will be compared with the ENT diagnosis.

I would like to invite you to take part in this study. Before you take part in the study, you need to understand what will be expected of you. If you agree to take part in the study, I will look at your medical file in order to obtain information for this study. I will then ask you some questions regarding your medical history and hearing. I will the test your hearing. The hearing test will involve the following:

- I will look into your ear using otoscope (light)
- I will conduct a range of tests that include tympanometry with single probe tone (226Z) and wideband absorbance tympanometry to assesses the status of your middle ear
- I will then put the headphones to test your hearing

The tests will take approximately 30 minutes to complete. If I find that you have a problem with your ears or hearing you will be referred to the doctor or audiologist for further management. Your participation in this study is voluntary. You may decide not to

discontinue with the testing at any time without penalty. 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 for these and they will be provided to you. The data will be kept in a in a password-protected computer file and only the researchers will have access to it. The raw data will be destroyed after 5 years post the completion of the study.

Should you decide to participate, you will be asked to sign an informed consent form to confirm that you understand the purpose of the research and you are willing to participate in the study.

If you need any more information, please contact me 072 989 7648 or email: ben.sebothoma@wits.ac.za or my research supervisor Prof Katijah Khoza-Shangase on 011 717 4565 or email: Katijah.Khoza-Shangase@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.

Thank you very much for your help

Sincerely,

Ben Sebothoma

Appendix J: Permission to conduct study at Ndlovu medical centre

Dr H Templeman

Chief Executive Officer

Ndlovu Medical Trust

Dear Dr. Hugo Tempelman

My name is Ben Sebothoma and I am an Audiologist working at the University of Witwatersrand in Johannesburg. I am currently studying toward my Master's degree in Audiology at the University of Witwatersrand. As part of my research work, my study aims to investigate the clinical utility of wideband acoustic immittance in adults living with HIV I hereby request permission to conduct the study at Ndlovu Wits Audiology clinic. Participants will include adults living with HIV attending Ndlovu medical centre. Participants' medical records will be reviewed to confirm HIV status, CD 4 count and current treatment.

Participants' hearing will be tested using the following:

- Otoscopy: To check if there are no abnormalities in the ear canal and tympanic membrane
- Standard Tympanometry and Wideband tympanometry: To assess the functioning of the middle ear. This test involves placing a probe on the ear that sends wind-like pressure into the ear.
- Pure tone audiometry: To assess the hearing sensitivity

Participation is voluntary. There are no medical risks involved when participating in this study. There are no direct benefits from participating in this study. Participants have the right to withdraw from this study at any point, without any negative consequences.

No identifying information will be used, instead participant numbers will be used in the research dissertation. Every effort will be made to keep personal information confidential; personal information will only be reviewed by the researcher, research assistant and academic supervisor. Personal information will be stored in a password-protected file and destroyed after a mandatory period of five years.

Your permission to conduct the research at the Ndlovu Medical Centre and the Ndlovu Wits Audiology Clinic will be greatly appreciated. Evidence from this current study will contribute towards early detection and identification of middle ear pathologies in adults living with HIV.

If you require any further information in this regard please do not hesitate to contact me at Ben. Sebothoma@wits.ac.za or my research supervisors, Professor Katijah Khoza-Shangase at 011 7174565 and Katijah.Khoza-Shangase@wits.ac.za.

Yours sincerely

Ben Sebothoma