The Analysis of an Audiological Protocol in Measuring Hearing Amongst People with Drug Resistant TB.

STUDENT: Zarreen Cassim

SUPERVISOR: Dr. Victor De Andrade

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Declaration

I hereby declare that this research dissertation is my own work. It is submitted for the degree of Master's of Audiology at the University of the Witwatersrand, Johannesburg. It has not been submitted for any other degree or examination at any other university.

Zarreen Cassim

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List of Abbreviations

* Listed in order of appearance

DR TB	Drug Resistant Tuberculosis
MDR TB	Multi-drug Resistant Tuberculosis
XDR TB	Extensively Drug Resistant Tuberculosis
TB	Tuberculosis (in this research, referring to pulmonary tuberculosis.) It may be used interchangeably with the term DR TB, due to the manner in which it is referenced in various policy documents.
ARVs	Antiretrovirals
HIV	Human Immunodeficiency Virus
HAART	Highly Active Antiretroviral Therapy
Pre-HAART	Prior to beginning Highly Active Antiretroviral Therapy
HPCSA	Health Professions Council of South Africa
WHO	World Health Organization
dB	Decibels
Hz	Hertz
OAEs	Otoacoustic Emissions
DPOAEs	Distortion Product Otoacoustic Emissions
PTA	Pure Tone Average

AC	Air Conduction
BC	Bone Conduction
FDA	Food and Drug Administration
PAS	Para-aminosalicylic Acid

Abstract

South Africa is in the midst of a DR TB pandemic, and due to treatment, ototoxic hearing loss has become a significant area for audiological intervention. Changes in DR TB treatment guidelines include non-ototoxic options, yet ototoxicity monitoring still continues as drugs such as amikacin are still prescribed. Thus, the focus is now placed on accuracy and precision in audiological service provision within ototoxicity. This study examined a specific ototoxicity monitoring protocol which used a KUDUwave audiometer operated by nursing staff and once cured, patients received full diagnostic evaluations from audiologists. Thus, the study explored patient related factors, and audiological findings using a KUDUwave and diagnostic audiometer, to determine trends within this population in a tertiary hospital in Gauteng. The experiences of nurses who operated the KUDUwave were explored, providing insight into factors affecting this process. A mixed methods approach, using a quantitative prospective review of 120 patient files, in conjunction with qualitative interviews of six nurses was utilized. Findings revealed that DR TB is multi-faceted, influenced by individual, and environmental systems, which affect DR TB, ototoxicity, and treatment. Results indicated that the KUDUwave was able to detect the presence of ototoxicity in a timeous manner. Challenges in the ototoxicity monitoring programme resulted in the omission of baseline hearing evaluations and inconsistencies in follow-up testing. Nurses viewed KUDUwave testing positively, however they require further support to enhance their knowledge and practice. Implications of this study include that audiologists should assume a more active role in ototoxicity monitoring programmes, and protocols should be developed and standardized, to ensure greater accuracy in ototoxicity monitoring, especially for patients on amikacin.

Key Words: Bedaquiline; DR TB; KUDUwave; nurses; ototoxicity

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Chapter 1

Introduction and Rationale

1.1. Introduction to the Study

During the course of treatment for drug resistant tuberculosis (DR TB) and prior to July of 2018, patients swallowed an average of 14 600 pills and had over 240 injections (Médecins Sans Frontières, 2018). South Africa is one of the countries with the highest rates of multi-drug resistant (MDR) and extreme drug resistant (XDR) TB, with statistics revealing that between 2009 and 2013, the number of patients receiving treatment for strains of DR TB more than doubled from 4143 to 10 179. This resulted in South Africa being classified as having a DR TB epidemic (WHO, 2014 as cited in Ndjeka et al., 2015). According to the National Health Laboratory Services (NHLS), KwaZulu-Natal has been ranked as the province with the highest number of cases, followed by the Western Cape and then Gauteng. It is predicted that there are 13 000 new MDR TB cases diagnosed in South Africa each year (Cox et al., 2010). While recent statistics have not been obtained, trends have shown that the numbers of MDR and XDR TB cases have continued to increase exponentially, with large amounts of patients lost to the system without receiving or completing adequate treatment (Dlamini, 2017).

Patients who have strains of drug resistant TB were previously treated with injectable aminoglycoside antibiotics as part of standard practice, and these were known to be ototoxic in nature, and particularly detrimental to those most at risk for acquiring ototoxicity (Petersen & Rogers, 2015). Ototoxicity is defined as the permanent damage of the organs of the inner ear, an irreversible side-effect of the administration of drugs used in the treatment of various diseases. It often results in disabling hearing loss, which negatively impacts upon the quality of life of patients (Adeyemo, Oluwatosin & Omotade, 2016). As such, the Department of

Health (2015) recommended that hearing levels be monitored regularly to promote practices of early identification and management of hearing loss within this population. Due to a general lack of guidelines regarding hearing monitoring and how this should be conducted, South African hospitals employ a variety of methods in monitoring the hearing of patients on treatment for DR TB.

Since July of 2018, most injectable aminoglycoside antibiotics have been removed from South African treatment regimens, to be replaced with the non-ototoxic drug bedaquiline (Department of Health, 2018). This research study was conducted during the period wherein the changes were made to include bedaquiline as a first drug of choice. However, the majority of participants utilized for the study, were treated before the change in guidelines and as such, were exposed to kanamycin prior to receiving bedaquiline. Despite kanamycin no longer being present within South African DR TB treatment regimens, research into ototoxicity in this area is still relevant and necessary, as there are still patients living with the consequences of ototoxic drugs. Furthermore, the ototoxic drug amikacin, still remains in the treatment regimen and hence, despite the removal of injectable agents from DR TB treatment, hearing monitoring for ototoxicity is still conducted for each and every patient accessing treatment. In fact, more emphasis is currently being placed on enhancing the accuracy and reliability of ototoxicity monitoring programmes, thus rendering a study which examines a specific protocol of ototoxicity in DR TB monitoring, particularly relevant for the current landscape of healthcare in South Africa.

As DR TB is significantly common amongst the South African population, and as a result of past aminoglycoside treatment, ototoxicity has become an emergent area for audiologists to intervene in terms of scope of practice (HPCSA, 2018). This research study is located within

the public health sector, and provides an overview of the DR TB ototoxicity monitoring programme at a specific tertiary hospital in Gauteng. It must be noted that despite there being policy documents in place, there is no standard ototoxicity monitoring protocol in South Africa, and protocols differ between contexts (Hollander, 2018). Furthermore, there is no mention made in existing policy documents of the role that nursing staff should play in the ototoxicity monitoring process (Department of Health, 2018; HPCSA, 2018). The research site makes use of a KUDUwave audiometer that is operated by nursing staff, for the monitoring of ototoxicity during the time in which patients are still infectious and smear positive. While studies have been conducted to prove the accuracy of the KUDUwave audiometer, these have focused on the comparison of hearing thresholds between a KUDUwave audiometer and a standard diagnostic audiometer. A review of literature revealed that currently no research exists on the application of the KUDUwave audiometer in ultra-high frequency testing within the context of ototoxicity monitoring in DR TB, yet this is what the KUDUwave is used for in many state hospitals countrywide.

Aside from the trends in hearing thresholds, this study further explored the contextual factors of patients with DR TB. It is well established that factors not directly associated with individual patients, have the power to influence the health and well-being of patients, as well as the successful treatment of patients once they have acquired diseases such as DR TB (Berben, Dobbels, Engberg, Hill & De Geest, 2012). Therefore, individuals cannot be separated from their context and environment, which necessitates the need for research to target factors not simply limited to the individual, but associated with the systems surrounding the individual, so that intervention can be targeted at each sphere (Neal & Neal, 2013). While most studies in health and DR TB have focused on individual patient factors, or isolated environmental factors (Berben et al., 2012) no known research has explored the presence of, or interaction between

the ecosystemic spheres which surround DR TB patients, effecting their health, well-being, and risk for ototoxicity. Thus, this study explored the contextual factors of patients with DR TB, in conjunction with the trends in hearing test results obtained using a KUDUwave and standard GSI audiometer, while considering the perspectives and experiences of the nurses who operated the KUDUwave machinery.

1.2. Rationale for the Research Study

While the well-known injectable drugs such as kanamycin have been removed from the DR TB drug regimen in South Africa since July of 2018, research within ototoxicity and the accurate monitoring, and identification thereof, is still a necessity within the current context of healthcare. This is due to the fact that the ototoxic drug amikacin, still exists within the regimen, and both the World Health Organization (WHO, 2018) and the South African Department of Health (2018) have recommended that ototoxicity monitoring continue, as patients may require amikacin at some point during treatment. Thus, the only modification with respect to ototoxicity monitoring, is that instead of being done monthly, it now occurs less frequently, at 3 month intervals following baseline assessment. This is for those on the non-ototoxic drug bedaquiline.

Both the WHO guidelines (2018) and the South African Department of Health guidelines (2018) note that ototoxicity monitoring has to be more accurate now than ever before, as alternative non-ototoxic drugs are available, and if the decision is made to place patients on amikacin, ototoxicity should be strictly monitored and prevented. Therefore, while the current study explored data from patients of whom the majority were treated with kanamycin as the first line of treatment, this research is important as well as relevant to the South African context as it provides a perspective on how patients can be managed, going forward. This study

explored factors which have the potential to impact upon the successful treatment of patients, regardless of the type of drugs used in management. Furthermore, it highlighted the processes involved in ototoxicity monitoring so that going forward, ototoxicity monitoring protocols can be refined, especially to aid those on amikacin. It must also be noted that as ototoxic drugs such as kanamycin were used for many years prior to the change in guidelines, many patients currently still live with the consequences of ototoxic hearing loss, and thus, audiologists should understand the process behind such an occurrence. The findings of this research have a further impact on international contexts where bedaquiline has not yet been introduced as a first-line drug, and ototoxicity monitoring protocols are heavily relied upon for ototoxicity prevention.

The introduction of bedaquiline as a first line of treatment, has implications for ototoxicity monitoring in the field of audiology in South Africa. While the number of DR TB patients accessing treatment may remain stable, the number of patients with ototoxic hearing loss, and who require monthly audiological intervention such as ototoxicity monitoring, is likely to decrease. However, with this decline, the demand in terms of accuracy and reliability of audiological results obtained, has increased. As such, a study which examines the ototoxicity protocol within the setting of a tertiary hospital, is necessary to determine the processes involved within the ototoxicity monitoring system. This is particularly important to maximize the potential for precision in testing especially when the KUDUwave, which falls under teleaudiology, is utilized.

People living with DR TB and who have the potential to acquire ototoxicity, are affected by a myriad of factors which have the potential to determine the success of their medical treatment. While these factors are common amongst the patient population, particularly in South Africa, most researchers, and health professionals tend to focus on the level of the

individual, without necessarily considering the contextual, and environmental factors which contribute to the well-being of the individual. Thus, the focus of this study shall go beyond individual level factors such as ototoxicity and medical diagnoses, to explore the contextual factors which affect those accessing treatment, in order to provide intervention that is contextually relevant.

While the KUDUwave 5000 has been widely distributed throughout South Africa for the purpose of ototoxicity monitoring in DR TB, no previous research could be found on its efficacy within the DR TB population, nor is there any research examining its application in the ultra-high frequency range beyond 8000 Hz. Furthermore, the equipment has been favoured for its ability to be operated by individuals who are not trained audiologists, yet no published studies exist regarding the experiences of those operating the KUDUwave who have no prior experience in hearing testing and monitoring practices. Thus, this study not only examines the use of the device within the context that it was designed for, but explores the experiences of nursing staff who operate the device, and the specific challenges and positive factors that affect the accuracy of testing within this context.

Lastly, there is limited research in the field of audiology which uses a mixed methods approach, thus, resulting in a gap in understanding the context within which research has occurred. Most studies have largely focused on the individual quantitatively, and have not considered the interaction of the individual with environmental factors. Thus, the current study which uses both quantitative and qualitative methods of inquiry together, not only confirms the results from each measure, but provides an overview of the milieu wherein the data observed occurred, thus enhancing the richness of findings and ensuring that results are interpreted contextually. Therefore, this study provides a unique approach to this aspect of research within

the field of audiology, and has the potential to provide a distinct overview of the factors affecting ototoxicity in DR TB.

1.3. The Choice of Research Study

The researcher completed the compulsory community service year of training as an audiologist and speech therapist at the chosen research site. It was noticed that there was the trend of quadruple burden of disease, whereby patients, especially those with DR TB, experienced a number of concomitant health difficulties. Furthermore, it was observed through patient interactions that the social settings from which patients had originated, appeared to have a marked impact upon their treatment and overall well-being. Thus, the researcher began to question if these factors were significant to consider when managing patients and whether this had a knock-on effect for the successful management of patients, especially those experiencing ototoxicity.

As a staff member within the department, the researcher saw a patient who had been treated for DR TB the previous year and was now presenting with hearing loss. It was discovered that the patient was previously unemployed, yet had found a job as a taxi driver and was referred by his employer to have his hearing evaluated, which had significantly declined following DR TB treatment. Upon evaluation, the patient had a severe to profound hearing loss, affecting the speech spectrum, particularly at the higher frequencies. He could not communicate with the audiologist verbally, unless she used written input to augment communication.

When the results of testing were explained, the patient appeared surprised that the hearing loss was related to his TB treatment and it was then revealed by the patient that his expectation was that the audiologist would be able to treat his hearing loss immediately, as his employer

was threatening to fire him if he did not have his hearing remediated on the day of the appointment. This experience had a profound impact upon the researcher, who wondered how such a situation was possible, when hearing monitoring was occurring during DR TB treatment, the hospital had access to the non-ototoxic drug bedaquiline, and audiologists were available within the hospital setting. The researcher realized that if the patient had been referred to audiology upon exit from the treatment programme, diagnostic testing would have been conducted and the patient would have already had hearing aids, perhaps avoiding job insecurity and social distress. Thus, questions were raised regarding the processes involved within the ototoxicity monitoring programme.

During the time at the hospital, it was noticed that some of the KUDUwave results did not correlate with what was expected, or with the diagnostic audiology results upon exit from the programme. As such, the researcher was curious as to why this was the case. At this time, the researcher was given the opportunity to train nurses from an external site, on behalf of the Department of Health, in areas such as what ototoxicity is, how to diagnose it, and what the role of the audiologist is within the context of ototoxicity. It was during this experience that the researcher began to further question the role of nurses within ototoxicity monitoring, and interrogated the idea of how well nursing staff, particularly at the given research site, were equipped to handle ototoxicity monitoring. The impact of such factors on testing procedures and patient care was of interest to the researcher. As such, this study was then conceptualized, with the assistance of various stakeholders and the guidance of the research supervisor who contributed to the inception of this research study.

1.4. Theoretical Framework

Three theoretical frameworks underpinned the conceptualization of this study, with a significant emphasis placed on Bronfrenbrenner's (1979) ecosystemic model and its application within the health setting. This is as this model was integrated with and had an influence on the other two theoretical frameworks, namely epidemiology and evidence-based practice. The findings from the application of the ecosystemic model was integrated with epidemiological factors, to influence evidence-based practices.

Bronfrenbrenner's (1979) theory acknowledged that an individual could not be viewed in isolation, but should instead be understood as part of an interacting ecosystem with a unique social, political, and economic set of circumstances all of which affect the individual directly. Such a setting is termed the ecological environment, which is made up of ecosystemic factors, with the individual as an active participant within this process. The manner in which the individual interacts within this setting has a marked impact upon both functioning and development, especially since ecological factors are constantly fluctuating (Hook, 2002). The theory categorizes the environmental settings that exist beyond the individual into multiple ecological tiers or systems, which shall be discussed in further depth in Chapter 2.

While Bronfrenbrenner's (1979) theory is well established, current research has illustrated that its assumptions are still applicable to the modern era. This is as it is useful in identifying contextual risk factors from a health point of view, so that intervention can be moulded around the needs of the individual at multiple levels (Neal & Neal, 2013). This theory is specifically applicable to the current research study, which examines not just the presence of ototoxicity amongst patients with DR TB, but explores the factors that exist beyond the level of individual patients, including nursing staff who operate the KUDUwave. These factors are examined

based on their effect on the patient, and their potential to effect overall treatment and susceptibility to ototoxicity.

The second framework utilized is that of epidemiology, which seeks to analyse trends amongst patients with specific diseases, so that assumptions can be made regarding what contributes to illness, and what aids in the remediation of various pathologies (Carter, Lubinsky & Domholdt, 2013). Epidemiology further involves the examination of diagnostic tools used to detect ill-health, based on whether these are accurate and reliable (Hartmann, Heitman & Brown, 2009). However, researchers have begun to note that simply addressing risk factors and the efficacy of diagnosis at an individual level, is too limited in its understanding of the complexities of ill-health and its associated factors. As such, models which include ecosystemic considerations should be used to augment other theories, as the analysis extends beyond the individual level, delving into other, more richer sources of information (Hay, 2012).

Lastly, evidence-based practice refers to the process whereby professionals, particularly those practicing within the healthcare setting, integrate research findings with their own clinical reasoning skills to form a basis for decision-making processes. This then informs clinical practice, by ensuring that patients are provided with the best care available (Straus, Glasziou, Richardson & Haynes, 2019). It includes the integration of bodies of knowledge obtained from research, in order to make informed decisions for patient management, giving health professionals the ease of knowing that their decisions are based on clinical data (Hoffmann, Bennett & Del Mar, 2010). This is pertinent to this study, as through the processes of epidemiology and ecosystemic theory, the research project will provide findings that can be used to inform clinical decision-making processes in the field of ototoxicity amongst DR TB patients.

1.5. Methodological Overview

The primary aim of this study was to investigate the overall trends in a specific ototoxicity monitoring programme at a tertiary hospital in Gauteng. There were 3 sub-aims of the study, the first of which was to provide insight into the personal variables of patients with DR TB who were attending the ototoxicity monitoring programme at a tertiary hospital in Gauteng. The second sub-aim involved the description of the audiological findings of patients with DR TB in this setting, while the third sub-aim explored nurses' experience of hearing screening within the context of the ototoxicity monitoring programme at the hospital. As there is a paucity of research in audiology that takes contextual factors into account (Knudsen et al., 2012), this research study has used a mixed methods design, including both a quantitative and qualitative phase to the study, both of which were conducted simultaneously. This was in order to provide a richer enquiry into the context of the research findings at the chosen site and to ensure triangulation of data, whereby findings from one research method, confirmed the findings of the other method (Barnes, 2012).

The quantitative phase used a within-subjects design and included a prospective file review of 120 patient files of people enrolled within the DR TB programme at the specialized DR TB centre at the chosen tertiary hospital. The qualitative phase which utilized a survey design, involved the process of face-to-face semi-structured interviews of six nurses who had experience operating the KUDUwave audiometer, and who worked at the TB centre. Thus, for both phases of the study, the purposive convenience sampling strategy was used. In terms of analysis, the quantitative data were evaluated using descriptive statistics and inferential statistics which included measures of dispersion, variability, and central tendency. Data from the qualitative phase of the study were analyzed using the qualitative method of thematic analysis described by Braun and Clark (2006). Calibration certificates for both the KUDUwave

audiometer and GSI audiometer were used to confirm the reliability and validity of test results, while the trustworthiness of qualitative data was upheld by employing various criteria detailed in Chapter 3.

1.6. Summary of Chapters

Following on from this chapter, is Chapter 2, which provides an overview of the three theories that were used to form the theoretical framework which was used in this study. Background literature within the fields of DR TB, ototoxicity, and teleaudiology as well as the interplay of various factors within the unique South African context will be discussed. The reader will be provided with an overview of the significance and potential contribution of the study, in relation to previous research in the field of enquiry. Chapter 3 outlines how the mixed methods approach has been used in this study, and highlights the importance of such a research design for the current context. Specific details are provided regarding the aim and sub-aims of the study, the research sample used for both phases of the study, the recruiting process, data analysis, and ethical considerations that were taken into account. Thereafter, Chapter 4 presents the results of the study, in relation to the aim and sub-aims of the study as set up by the researcher. This information includes the quantitative results obtained from statistical analysis, which is presented separately to the qualitative data obtained from interviews.

Chapter 5, the discussion, integrates the findings from both the quantitative and qualitative phases of the study, and provides critical input, as the findings of the study are integrated with previous research findings from the literature. Lastly, Chapter 6 is the concluding chapter and aims to provide the reader with an overview of the findings of the study. It provides recommendations for further research and notes the implications of the study for audiology practice in South Africa. The limitations of the study have been detailed in this chapter.

Chapter 2

Theoretical Framework and Literature Review

This chapter describes how Bronfrenbrenner's (1979) ecosystemic model has been applied to the context of health, in addition to the theories of epidemiology, and evidence-based practice to form the theoretical framework of this study. An overall review of the relevant literature pertinent to this study is provided, with emphasis on the exploration of the DR TB phenomenon, both globally and from a South African perspective. The recent adaptations to drug therapy protocols within DR TB are explored, with a focus on the way forward for DR TB management in the complex landscape of South African public health.

2.1. Theoretical Framework

This study is based on evidence-based practice within an epidemiological framework, while taking into consideration the contributions of Bronfrenbrenner's (1979) ecosystemic model and applying it to healthcare. Epidemiology is the study and analysis of trends that occur within the context of health and such a theory is used to predict causative factors for ill-health and predictive factors for the prevention of diseases (Carter et al., 2013). Epidemiology can be further used to examine the accuracy and reliability of diagnostic tools within health care settings (Hartmann et al., 2009). This is applicable to the current study which examines the application of the KUDUwave in an ototoxicity monitoring context. Specific risk factors and the distribution of health disorders within given populations are explored within epidemiological research and thus, it has the potential to inform policy guidelines and promote evidence-based practice (Hartmann et al., 2009).

The latest research within the fields of public health and communicable diseases acknowledges that epidemiology cannot be used to analyse patient care and management in

isolation, as this can limit the effectiveness of treatment outcomes as contextual factors are omitted (Marais et al., 2013). Therefore, Bronfrenbrenner's (1979) ecosystemic model has been applied to this context as it recognizes that health forms part of a complex puzzle of other factors such as social structures, contextual factors, and economic landscapes that patients exist within (Knudsen et al., 2012; Marais et al., 2013).

The ecosystemic approach which originates from psychological theory, recognizes that individuals do not exist in isolation, but are a part of a unique set of socio-political, historical, and economical circumstances, and these environmental systems are constantly in flux (Hook, 2009). As such, the ecosystemic approach recognizes the different environmental systems that surround an individual, with the individual nested in the centre of these systems (Bronfrenbrenner, 1979). The environmental systems have the potential to influence the behaviour of the individual, whereby they can either promote or hinder the growth of the self (Amod, Halana & Smith, 2019). This is especially important as the individual patient cannot be separated from the living context and environment (Berben et al., 2012). For the purpose of this research project, five of these systems, as displayed in Figure 2.1, will be discussed in further detail in the section to follow.

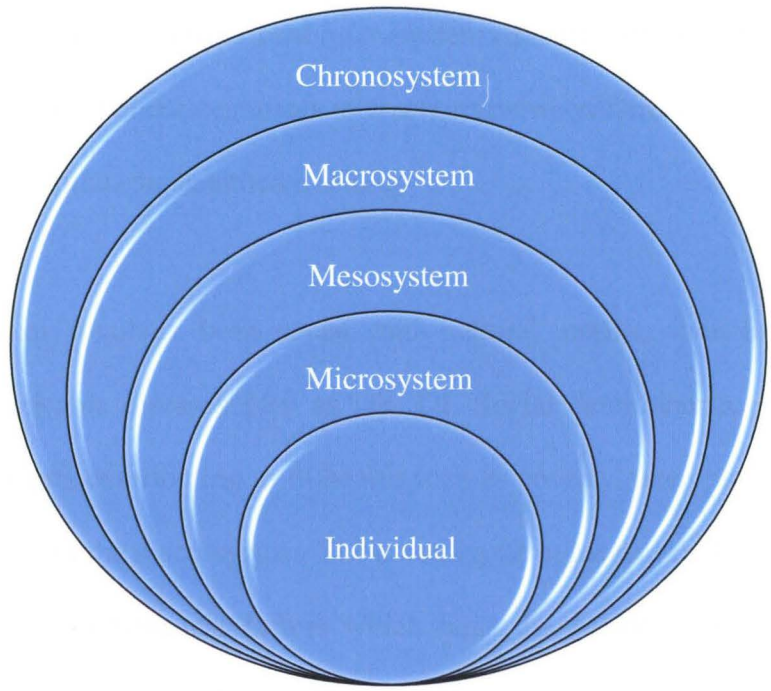

Figure 2.1. Systems Within the Ecosystemic Approach.

Note. Adapted for this research study based on Bronfrenbrenner's (1979) ecosystemic approach.

According to Bronfrenbrenner (1979), individual factors include characteristics of the patient such as age, gender, attitudes towards healthcare, knowledge, and level of education. Predisposing factors, and concomitant health issues including HIV (Human Immune Deficiency Virus) and other communicable and non-communicable diseases are also included within this tier. This level does not in itself, provide a holistic view of the individual patient, as the environmental factors surrounding the patient are not explored (Berben et al., 2012). Following this, the system located closest to the individual is the microsystem, which consists of relationships which directly impact upon the individual. These include social and familial support, interactions with healthcare professionals, and the relationship with employers in work settings. Thereafter, the mesosystem involves the individual as an active participant in

the environment and includes how the individual negotiates interactions between the different relationships which occur at the level of the microsystem (Bronfrenbrenner, 1979). An example of this is how the patient negotiates interactions between family members and medical professionals within the healthcare setting.

The macrosystem involves both social and cultural norms, including the stigma surrounding communicable diseases such as DR TB. Social determinants of health which include the social factors contributing to ill-health such as poverty, unemployment, and food insecurity all form part of the macrosystem. The chronosystem, located furthest away from the individual, involves socio-historical factors which have the potential to impact upon the individual (Neal & Neal, 2013). These include health policies which affect the healthcare system as a whole, such as when bedaquiline should be prescribed and how DR TB patients should be managed, in conjunction with policies such as the Bedaquiline Expansion Plan. Apartheid policies which have exacerbated the formation of previously disadvantaged groups of patients, also falls within the chronosystem of this theory.

Most research in the past has focused on characteristics of the individual patient and how these have affected the successful treatment of the patient, without addressing the risk factors occurring at the micro-, meso-, and macro-levels of the patient (Amod et al., 2019). Thus, a multi-level overview of a patient involving the analysis of all the systems surrounding the individual is necessary. This can provide a much-needed holistic perspective, while identifying specific risk factors and interacting variables which impact upon successful ototoxicity management in DR TB (Berben et al., 2012). Thus, the use of this model is recommended in conjunction with epidemiology, to inform evidence-based practices that take into account the circumstances of the patients accessing healthcare services. This research study, which

involved a combined framework of an ecosystemic approach with epidemiology, can be used to inform best practice within the field of ototoxicity. This is as the social, economic, and background history of patients was explored, in conjunction with the trends in hearing monitoring and ototoxicity management. The research findings can be used to inform policy guidelines as well as to gain information regarding how ototoxicity monitoring programmes can be tailored to improve service delivery and cater towards the diverse needs of patients.

2.2. Literature Review

2.2.1. MDR and XDR TB

According to the South African Department of Health (2013), South Africa is ranked as having the fifth highest burden of DR TB worldwide, with the two most common strains including MDR TB and XDR TB. MDR TB is defined as TB that is resistant to more than 2 first-line drugs, namely rifampicin and isoniazid, which are drugs used to treat normal strains of TB. If a patient has resistance to rifampicin in isolation, this is termed as mono-resistant TB, with South Africa having the highest rate of rifampicin resistant TB in the world (Department of Health, 2018). XDR TB is defined as MDR TB with additional resistance to both a fluoroquinolone and a second line injectable drug (Ndjeka et al., 2015) and Pre-XDR TB includes patients with MDR TB that have additional resistance to either a second-line injectable drug or a fluoroquinolone (Department of Health, 2018).

Awareness of the DR TB epidemic in South Africa has increased substantially since 2005. As such, South Africa has seen a positive shift in the recognition of DR TB and subsequently, healthcare professionals are now more vigilant in suspecting MDR and XDR TB. The Department of Health has allocated more resources to TB management and specific TB

programmes have been established throughout the country in order to manage the growing medical crisis (Gandhi et al., 2010). These changes appear to have translated into improvements in survival rates from 2005 to 2007 (Gandhi et al., 2010), however, XDR TB patients still remain classified as the group with the least favourable treatment outcomes. This is as approximately only 15% of patients with XDR TB are treated successfully in South Africa (Ndjeka et al., 2015). DR TB treatment regimens are lengthy, costly and are associated with adverse side-effects as protocols involve using second line aminoglycoside antibiotics often referred to as injectables (Harris et al., 2012). Despite the inclusion of injectable-free treatment regimens in South Africa, ototoxic drugs such as amikacin still remain part of the DR TB treatment regimen, and with the change in guidelines being relatively new, the majority of patients are still living with the consequences of ototoxicity.

The Department of Health (2014, pp. 74) has classified DR TB as a "man-made problem", as the development of drug resistant strains is attributed largely to the inefficient management of TB countrywide. This is reportedly due to factors such as poor management of drug supply rendering patients unable to take TB drugs as regularly as stipulated, as well as poor patient management in the prescription of the correct dosages per patient body weight. An overall lack of patient support and counselling is a further factor affecting adherence (Department of Health, 2014), especially due to the high pill burden and complexity of drug regimens (Berben, Dobbels, Engberg, Hill, & De Geest, 2012). Patient factors that result in poor adherence to TB drug regimens include poor access to health care, homelessness, drug or alcohol abuse, and exposure to family members who have been unsuccessfully treated (Department of Health, 2014).

Further social factors that predispose patients to defaulting medication include those of older age who require assistance to access health care services, and those who live far distances away from hospitals and clinics (Li et al., 2016). The attitude of health care workers towards patient care and management is a determining factor on the success or failure of patient treatment, as patient outcomes can directly be affected (Li et al., 2016). The patients' attitude towards treatment and healthcare systems also plays a large role in treatment success and can easily be influenced by side-effects of drug therapy. This is since adverse reactions to medication such as acquired hearing loss, can result in patients being less compliant with taking DR TB medication as prescribed (Berben et al., 2012). As such, an ecosystemic model which takes into account patient factors, environmental factors, policies and healthcare system factors as detailed by the World Health Organisation (WHO), is useful in addressing patient adherence to treatment protocols. This is especially since the systems which surround a patient determine the success or failure of treatment (Berben et al., 2012).

Recently, the trends found in DR TB reveal that the majority of patients have not acquired DR TB due to previous unsuccessful treatment, but have acquired the DR strain directly without a prior history of TB infection. This is noted in a South African study conducted by Gandhi and colleagues (2006), where more than half of the patients with XDR TB had not previously been treated for TB, suggesting that they were exposed directly to the XDR TB strain. The study further documented that of the total sample of patients with DR TB, merely 15% were previously treated for TB. This illustrated that currently, DR TB is being driven largely by transmission of resistant strains and not necessarily by decreased compliance with medical regimens (Cox et al., 2010). The Department of Health (2014) has recognized that patients with DR TB are highly infectious and are able to infect large numbers of people at a time, particularly those who are vulnerable such as HIV positive individuals. As such, early

detection and rapid treatment are of utmost importance in the guidelines. Thus, better infection control procedures and the early detection and management of drug resistant strains of TB are necessary, especially amongst patients with a higher risk for acquiring the disease (Duarte et al., 2018).

2.2.2. DR TB risk factors

Marais and colleagues (2013, pp. 443) describe TB as a "barometer" of the society that it occurs within, as the disease can be seen as measure of access to healthcare systems, poverty, and deprivation amongst people in a given population. As DR TB is driven by these socio-economic and social factors, the more prevalent the disease is, the more likely there is to be unemployment, poverty, low levels of education, and poor access to healthcare amongst people (Department of Health, 2018; Marais et al., 2013). Furthermore, the availability of functioning healthcare systems is inversely proportionate to the needs amongst patients accessing treatment. Poorer individuals who are in increased need, have reduced quality of healthcare, in comparison to people of higher socio-economic status. Patients dealing with other personal issues such as the lack of social support and concomitant health disorders including psychiatric disorders, kidney disease, sexually transmitted diseases, hepatitis, anaemia, HIV, and stress, are more predisposed to acquiring DR TB (Department of Health, 2018; Marais et al., 2013).

As noted previously, patients have a higher risk of directly acquiring DR TB than developing it due to complications after standard TB treatment. There are well established risk factors within the literature that place certain groups of patients at a higher risk of developing DR TB. Non-communicable diseases such as diabetes, and hypertension have a complex effect on the immune system, and can increase the vulnerability of patients to diseases such as TB

(Seegert, Rudolf, Wejse, & Neupane, 2017). DR TB is often detected amongst hospital in-patients admitted for other internal medicine related disorders (Marais et al., 2013). HIV results in an immunocompromised state, and its relationship to TB will be discussed in further detail in the next section. Diabetes in particular, increases the risk of acquiring TB by threefold, as it is a metabolic disease which can delay the immune response to viruses by 6 days or longer (Rodriguez-Rodriguez, Ruy-Diaz-Reynoso, & Vazquez-Lopez, 2015). Studies conducted in India revealed that 50% of patients who had TB also had diabetes (Marais et al., 2013). Furthermore, countries with higher rates of non-communicable diseases such as hypertension and diabetes, were the same countries where the TB rates were highest, and this was particularly noted in Sub-Saharan Africa (Rodriguez-Rodriguez et al., 2015; Marais et al., 2013). However, it must be noted that in Africa, diabetes is more prevalent in urban areas in comparison to rural areas or informal settlements due to lifestyle differences (Levitt, 2008).

The socio-economic determinants of health have been described by authors as the main driving force behind the current DR TB phenomenon and from an ecosystemic perspective, this forms part of the mesosystem surrounding the individual. Research over the past decade has established that the economic, personal, social, and environmental contexts wherein patients exist, predispose them to contracting diseases such as DR TB (Duarte et al., 2018; Marais et al., 2013). The risk for acquiring TB can be compounded by social risk factors such as incarceration, immigration, overcrowding in informal settlements, alcohol abuse, smoking, and low levels of education (Department of Health, 2013; Marais et al., 2013). The consumption of alcohol not only decreases patient adherence to medication, but impairs the immune system, rendering individuals vulnerable to TB infection (Seegert et al., 2017).

Those of a lower socio-economic status who stay in poor housing, with multiple people and who are unemployed have a much higher risk of contracting DR TB than others of higher socio-economic standing (Duarte et al., 2018). A study conducted in Iran found that DR TB cases were concentrated amongst people in impoverished areas on the outskirts of cities, who lived in poverty (Kolifarhood, Khorasani-Zavareh, Salarilak, Shoghli, & Khosravi, 2015). Malnourished individuals are at further risk for acquiring DR TB, due to a poor immune system that is unable to protect the body against infections. Research indicated that those without food in their systems when taking TB medications, developed more side-effects and adverse drug reactions to medications (Marais et al., 2013).

Due to the high comorbidities present within the DR TB context, the need for multi-disciplinary work and cross referrals between professionals is highlighted and proven to be beneficial, particularly in resource-constrained healthcare settings (Marais et al., 2013). As ototoxicity causes irreversible hearing loss which affects the social, emotional, economic, and employment capabilities of patients (Hollander, 2018), multi-disciplinary work and research, especially in the field of audiology, is necessary. This is as it provides a richer understanding of contextual factors to inform better health practices (Knudsen et al., 2012).

Most healthcare systems, especially in developing countries, are poorly equipped to deal with the double burden of disease, where communicable diseases such as DR TB overlap with non-communicable diseases in the patient population (Marais et al., 2013). The need for training of health care personnel, the up-skilling of healthcare workers and reciprocal screening of patients between health care providers allows for the optimum use of available resources, especially when human resources are combined and well co-ordinated (Marais et al., 2013). Prevention practices need to extend beyond the healthcare system, as DR TB and its associated

factors can only be eradicated by developing housing and infrastructure and boosting job creation, in order to meet the social and therefore, medical needs of society (Marais et al., 2013).

2.2.3. HIV and DR TB

As HIV causes a reduction in the functioning of the immune system, patients are left vulnerable and thus, are more susceptible to the acquisition of infections, particularly TB. Often in South Africa, patients with TB attend hospitals for treatment at which point it is discovered that they are HIV positive (Department of Health, 2014). People living with HIV and DR TB are considered to have advanced stages of HIV with an increased risk of mortality, especially if not on antiretroviral (ARV) treatment. The treatment procedure for patients who are co-infected with both HIV and TB is often complex, as the interactions of the drugs used to treat both the diseases can cause an enhancement of side-effects for the patient. In fact, commencing HIV treatment once TB positive, may cause the TB symptoms to worsen for the initial period of treatment. This triggers poor patient compliance with TB medication regimens, resulting in the increased likelihood for the development of DR TB (Department of Health, 2014). In cases such as these, the importance of patient education and counselling is highlighted (Department of Health, 2014). The concomitant treatment of HIV and DR TB may also cause thyroid dysfunction, a common complication of co-infection with the two diseases (Ige, Akinlade, Rahamon, Edem, & Arinola, 2016).

HIV positive patients may also acquire DR TB without having defaulted on their medication, as recent research has shown that HIV positive individuals are particularly susceptible to acquiring DR TB (Department of Health, 2014.) This is evident in the large

numbers of HIV positive patients with drug susceptible TB (non-resistant strains of TB), who while attending hospitals for treatment, acquired DR TB from the hospital facilities themselves (Department of Health, 2014). Regardless of the cause of DR TB amongst the HIV positive population, there exists an interactive relationship between HIV and DR TB, with research revealing that XDR and MDR TB are the highest causes of mortality amongst HIV positive South Africans (Gandhi et al., 2010). Furthermore, Sub-Saharan Africa contributes to 80% of the global HIV TB co-infection rates (Marais et al., 2013).

Research by Cox and colleagues (2010) found that in a population of people with MDR TB in Khayelitsha South Africa, 55% of newly MDR TB diagnosed patients and 71% of previously treated MDR TB patients were HIV positive. It must be noted that such statistics were obtained from the context of Khayelitsha, where the population density is high and poverty is rife, and thus findings cannot be generalized to all of South Africa (Cox et al., 2010). In another South African study by Gandhi and colleagues (2010), 90% of MDR TB patients and 98% of XDR TB patients were HIV positive. Thus, the incidence of co-infection is high, with the interplay of the two diseases becoming increasingly more difficult to treat, resulting in the rising incidence rates of DR TB noted countrywide (Cox et al., 2010; Department of Health, 2014, & Gandhi et al., 2010). This has placed a significant burden on the public health care system, as success rates in the treatment of HIV as well as TB have been severely affected. The World Health Organisation has recommended that service delivery must be curated for integrated TB and HIV treatment at all levels of healthcare. to combat the rising rates of coinfection (Marais et al., 2013).

2.2.4. Aminoglycosides and ototoxicity

Aminoglycosides are a group of broad-spectrum antibiotic medications used to treat life threatening diseases such as DR TB. Common aminoglycosides used to treat DR TB in South Africa include amikacin, kanamycin and streptomycin (Department of Health, 2011), which are classified by the World Health Organisation as second line anti-TB drugs (Xie, Talaska & Schacht, 2011). This is as they are used when the first-line of TB treatment has failed, and as such, aminoglycosides are indicated in the treatment of drug resistant strains of TB (Xie et al., 2011). Research has established that aminoglycosides cause irreversible, permanent hearing loss amongst humans, referred to as ototoxicity, due to its damage of structures within the inner ear, including the vestibulocochlear nerve and the cochlea (Petersen & Rogers, 2015). Damage to the cochlea begins in the outer hair cells and supporting cells of the basal end of the cochlea before progressing to the apex (Petersen & Rogers, 2015). Certain ototoxic drugs may also cause damage to the vestibular organs within the inner ear, resulting in symptoms such as vertigo (Duggal & Sarkar, 2007). However, vestibulotoxicity shall not be discussed, as it is not within the scope of this research study.

According to the American Speech-Language-Hearing Association (ASHA, 1994, as cited in Petersen & Rogers, 2015), the overall incidence of ototoxicity in patients receiving aminoglycosides is difficult to establish, due to different treatment regimens, inconsistent definitions of hearing loss, and a lack of information regarding hearing loss in the ultra-high frequencies. Despite the disagreement amongst authors in terms of the incidence of ototoxic hearing loss with aminoglycoside administration, recent studies have aimed to quantify the number of patients on aminoglycosides that acquire ototoxicity. A study by Duggal and Sarkar (2007), examined 64 MDR TB patients that were divided into 3 groups based on the

aminoglycosides that they were prescribed, namely, amikacin, kanamycin and capreomycin. All patients received baseline puretone audiometric assessments, and follow-up testing was conducted every 2 months until the completion of treatment. Patients with renal and liver function abnormalities were excluded from the study. The audiological assessments tested frequencies from 125 Hz to 8000 Hz, not evaluating the ultra-high frequencies. Findings of the study suggested that the overall high frequency hearing loss amongst all patients was 18,75% which the author concluded was indicative that all 3 aminoglycosides were ototoxic in nature.

A study conducted in Cape Town examined patients on MDR and XDR TB treatment and found that 47% of the 53 adult patients developed ototoxicity of varying degrees, with no difference in hearing loss between those on treatment for MDR TB and patients on XDR TB treatment (Ramma & Ibekwe, 2012). Another local study conducted with 52 adult patients on MDR TB treatment in KwaZulu-Natal, found that over time from baseline to 3 follow-up sessions, 100 % of participants were found to have ototoxic hearing loss by the last follow-up session (Appana, Joseph & Paken, 2016).

A study conducted in Botswana by Modongo and colleagues (2014), found that out of 437 MDR TB patients, 62% were diagnosed with ototoxic hearing loss. Only 54% of these patients' hearing loss was diagnosed using audiometry, while the remainder relied on patient report of hearing loss. The diagnosis of ototoxic hearing loss occurred at an average time of 170 days after beginning treatment. However, the researchers did not have access to baseline audiometry and as such, patients may have had pre-existing hearing losses before beginning aminoglycoside treatment. This reveals the weakness of many studies conducted in this field, whereby audiometry was not consistently conducted to measure ototoxicity and extended high

frequency audiometry was not used in the majority of cases. Nevertheless, it is evident that those on aminoglycoside treatment for DR TB are prone to developing ototoxic hearing loss.

2.2.5. Risk factors for acquiring ototoxicity

ASHA recommends that future research should document the trends in aminoglycoside induced ototoxicity so that higher and lower risk groups for ototoxicity can be identified and early intervention procedures be implemented (Frymark et al., 2010). While people on ototoxic drugs are at risk for developing ototoxicity, certain groups of people are further predisposed to acquiring ototoxic hearing loss. Evidence has suggested that cumulative dosages of aminoglycosides result in a greater risk for ototoxicity in comparison to single doses (Adeyemo et al., 2016; Seddon et al., 2012).

Longer treatment regimens are further associated with a greater risk for ototoxicity. Studies such as those conducted by Petersen and Rogers (2015) and by Seddon and colleagues (2012) provided a synopsis of previous research from 1979 to 2012 of ototoxicity with drugs such as amikacin, gentamicin and kanamycin. When hearing monitoring occurred within a short-term of less than 2 weeks, the ototoxicity incidence rate ranged from 18% to 28% and when monitoring occurred over a longer period such as months, the incidence of ototoxicity ranged from between 25% to 69%. This is similar to findings of another study where the incidence of ototoxicity during the first week of treatment was 2% while at 6 weeks it had increased to 12% (Sharma, Bhagat, Verma, Singh, & Singh, 2016). Modongo and colleagues (2014) also found that there was a strong correlation between a longer treatment time and an increased risk of developing hearing loss, thus, there may be a relationship between duration of treatment and increased risk of ototoxicity.

Most international literature suggests that specific genes can further predispose individuals to ototoxicity and as such, the risk for ototoxicity may be hereditary (Adeyemo et al., 2016; Konrad-Martin et al., 2005). However, in the South African population the likelihood of this gene mutation is less than 1% (Seddon et al., 2012), and thus, this risk factor may not be relevant to the South African context. Those with previous exposure to noise have an increased risk for ototoxicity and in terms of age, those who are elderly (above 65 years of age) are further at risk for ototoxicity along with people who are on multiple ototoxic drugs simultaneously (Konrad-Martin et al., 2005; Petersen & Rogers 2015; Seddon et al., 2012). Javadi and colleagues (2011) however, found that age was not related to ototoxicity risk, but multiple ototoxic drugs as well as being male contributed to an increased risk for ototoxicity. This was as 90% of men in their study were more susceptible to ototoxicity in comparison to 53% of women. However, according to the HPCSA (2018), females are more likely to be at risk for ototoxic hearing loss.

A study conducted in a tertiary hospital in India by Sharma and colleagues (2016) assessed the auditory function of 100 MDR TB patients on kanamycin. Ototoxicity was found to be more common in males, with 67% being affected in comparison to 33% of females. The results further revealed a strong correlation between risk for ototoxicity and low socioeconomic status as well as with co-morbid conditions such as diabetes and hypertension. This confirms Petersen and Rogers' (2015) findings that poor lifestyle and nutrition increased the risk for ototoxicity. Surprisingly, the correlation between age and ototoxicity risk was found to be statistically insignificant which was similar to the findings of earlier studies (Moore et al., 1984, as cited in Sharma et al., 2016). The authors suggested that a study with a long-term review of ototoxicity in aminoglycoside treatment is necessary to further understand trends and risk

factors for ototoxicity. Renal dysfunction, and anaemia were listed as risk factors for ototoxic hearing loss as per the HPCSA (2018) guidelines.

Of particular interest in South Africa and worldwide, is the co-infection of HIV and TB and as such, the question as to whether those who are HIV positive are at a greater risk for developing ototoxicity. Harris and colleagues (2012) conducted a study in Cape Town South Africa, with 153 MDR TB patients, using standardized puretone audiometry with extended high frequency testing. It was found that over 3 months, 57% of patients developed a high frequency hearing loss, of which 70% of these patients were HIV positive. This was the first study at the time to include such a large number of HIV positive patients, as most researchers used the factor of being HIV positive as an exclusion criterion. As such, the authors concluded that HIV positive patients were more at risk for developing ototoxic hearing loss when on aminoglycoside treatment.

Research shows that antiretrovirals (ARVs) used in the treatment of HIV may be ototoxic themselves, and may place HIV positive patients at an increased risk for developing ototoxicity (HPCSA, 2018). This is as most authors note that patients who are on multiple ototoxic drugs, are at a greater risk of developing ototoxic hearing loss (Konrad-Martin et al., 2005; Seddon et al., 2012). However, more research is required in this area, as the exact mechanism of hearing loss in relation to ARVs is still unknown, especially since HIV positive patients are prone to middle ear infections and as a result, some degree of hearing loss (Javadi et al., 2011).

Authors such as Petersen and Rogers (2015) recognize that ototoxic drugs cannot be completely eliminated from treatment regimens, and due to the cost of bedaquiline, it may not be consistently available, despite access programmes facilitating its distribution. Thus, it is

recommended that protocols be implemented, and a multi-disciplinary team approach be used to identify ototoxicity early for prevention purposes. Individuals should be educated, and informed regarding aminoglycoside induced ototoxicity. Hence, there is need for researchers and health care practitioners to clearly establish the risk factors associated with ototoxicity in aminoglycosides, so that there is a balance in decision making procedures between the need for intervention and the risk of acquiring ototoxic hearing loss.

2.2.6. Diagnosis and monitoring of ototoxicity in TB

According to the Health Professions Council of South Africa (HPCSA, 2018) the detection and monitoring of ototoxic hearing loss is an important area within the scope of practice of audiologists and forms part of early detection and prevention procedures. The primary aim of ototoxicity monitoring is to ensure that hearing loss is detected early, before the speech spectrum of frequencies are affected, in order to maintain the quality of life of patients (Govender & Paken, 2015). Therefore, it is the responsibility of audiologists to establish, design, and implement ototoxicity monitoring programmes, train the necessary personnel who perform ototoxicity monitoring practices, assess and manage ototoxicity symptoms in patients, and provide the necessary rehabilitation to those who have acquired ototoxic hearing loss (HPCSA, 2018).

Ototoxic hearing loss can be identified by a distinctive sloping pattern of hearing loss, effecting the high frequency range from 16 000 Hz and downwards, before effecting the mid and lower frequencies (Human et al., 2010). This is since the basal end of the cochlea responsible for high frequency hearing is damaged first, before the apex of the cochlea that is responsible for low frequency hearing transduction (Adeyemo et al., 2016). In some cases,

hearing loss becomes flat in configuration towards the end of treatment (Appana et al., 2016). Such a pattern is confirmed in studies conducted by Duggal and Sarkar (2007) where 6,25% of patients on aminoglycosides developed a flat hearing loss with time, and hearing loss was seen to progress from the higher frequencies to the mid and lower frequencies as time progressed. This was further noted in the study by Appana and colleagues (2016), where most patients developed hearing loss that was greatest in the ultra-high frequencies. As time progressed, the average thresholds in the mid and lower frequencies declined, providing evidence for why ultra-high frequency hearing testing is essential in ototoxicity monitoring.

The majority of research conducted in ototoxicity in TB recognizes a lack of standardized audiological protocols to reliably identify hearing loss in patients receiving aminoglycosides (Adeyemo, et al., 2016; Javadi et al., 2011; Petersen & Rogers 2015; Sharma et al., 2016). While some literature suggests that the monitoring of hearing loss with aminoglycoside use should occur once to twice a week (Campbell, 2004; Konrad-Martin et al., 2005), most researchers have recognized that this is not feasible in terms of cost and time constraints for both professionals and patients (Adeyemo et al., 2016; Duggal & Sarkar, 2007; Mdongo et al., 2014). In South Africa particularly, there is disagreement regarding which audiological findings are indicative of ototoxic shifts especially since there are no set criteria for grading scales of ototoxicity, which is important to consider when reviewing any DR TB programme (Hollander 2018; Phanguphangu & Ramma, 2018).

Patients' report of hearing function cannot always be relied upon to assess hearing functioning. While health professionals are encouraged to inform patients of the symptoms of ototoxicity so that patients are empowered and can facilitate early detection and management (HPCSA, 2018), patients may classify their hearing as normal when in fact, hearing loss exists.

This is as patients rate their functioning based on their own perceived expectations of hearing and communication, and what their own environment demands of them as individuals. Therefore, the same hearing loss may not be significant for some patients, while it is debilitating for others (Borg, 1998). This is as patients who do not have high communication or listening demands placed upon them during daily interactions, may not notice the effects of their hearing loss, whereas other patients who rely heavily on their hearing abilities, may notice changes more readily. Thus, while diagnosis focuses on the cause of hearing loss and the consequences thereof, the process is more dynamic and needs to address the holistic functioning and expectations of individual patients (Berben et al., 2018).

Due to the lack of universal methods established internationally for the monitoring of hearing in patients exposed to aminoglycosides, practitioners rely on different assessment methods to monitor hearing loss. One such method is distortion product otoacoustic emissions (DPOAEs) an objective hearing assessment that assesses outer hair cell damage within the cochlea, before a high frequency loss is detected with conventional audiometry (Konrad-Martin et al., 2005). However, a drawback of this method is that otoacoustic emissions (OAEs) are unable to detect hearing loss less than 40dB's which is problematic for those who enter their baseline assessments with a mild pre-existing hearing loss. Furthermore, OAEs cannot be reliably assessed in those with outer or middle ear pathology (Harris et al., 2012). Such pathologies are common amongst patients on aminoglycosides, as most patients are co-infected with HIV, which due to poor immunity, predisposes patients to otitis media and other outer and middle ear complications (Konrad-Martin et al., 2005).

A further assessment method used is conventional puretone audiometry between the frequencies of 125Hz to 8000 Hz. However, high frequency puretone audiometry assessing the

extended high frequencies up to 16 000 Hz is most sensitive to detecting ototoxic hearing loss early (Adeyemo et al., 2016). Thus, puretone audiometry assessing the extended high frequency range beyond 8000 Hz is necessary for effective ototoxicity monitoring. This is as a decline in hearing due to ototoxic effects would occur in the ultra-high frequencies first, and thus, would indicate the presence of ototoxicity before the frequencies in the speech spectrum are affected (Petersen & Rogers, 2015). This is important for early detection and prevention procedures especially since ototoxic hearing loss once present, is irreversible.

Research has revealed that the frequencies most sensitive to ototoxic shifts include those in the ultra-high frequencies of 8000 Hz, 9000 Hz, 10 000 Hz, 11 200 Hz and 12 500 Hz (Hollander, 2018). The importance of ultra-high frequency testing is confirmed by a study conducted in the Himalayas whereby, 70% of patients displayed hearing loss in frequencies from 10 000 Hz to 20 000 Hz after beginning aminoglycoside treatment. Only 30% of the sample displayed hearing loss in the frequency range from 250 Hz to 8000 Hz (Chauhan, Saxena, & Varshey, 2011). Similar findings were noted in a study conducted in a district hospital in KwaZulu Natal in South Africa, where earlier on in treatment, ototoxic hearing loss in the ultra-high frequencies was most common (Appana et al., 2016). As such, both authors concluded that without high frequency audiometry, a large portion of patients with ototoxic hearing loss would have gone undetected until vital speech frequencies were affected (Appana et al., 2016, & Chauhan et al., 2011).

The above studies utilized a standard manual audiometer to test hearing loss. The only research in ototoxicity and the use of a KUDUwave audiometer is the framework of a potential longitudinal study that is currently being conducted in Nigeria by Adeyemo and colleagues (2016). The study aims to investigate the incidence of hearing loss experienced by patients who

are on streptomycin for DR TB. Hearing levels will be monitored using a KUDUwave audiometer, whereby patients will receive a full diagnostic test ranging from 250 Hz to 16 000 Hz at baseline. Follow-up tests will be conducted by testing only 3 frequencies, namely 250 Hz, 500 Hz and 1000 Hz to establish the Pure Tone Average (PTA), which is representative of hearing in the low to mid frequencies. The extended high frequencies will only be tested if the patient notes any symptoms of hearing loss. While this study has the potential to significantly add to existing research on aminoglycoside induced ototoxicity, the method of hearing screening at follow-up sessions may be ineffective if only the PTA is tested. This is as aminoglycoside ototoxicity effects the higher frequencies first, and thus, changes in the PTA may not occur until much later in treatment (Human et al., 2010). Additionally, patients may not detect symptoms of hearing loss until the loss progresses to lower frequencies affecting speech discrimination (Sharma et al., 2016). Thus, the future findings of the study may be inaccurate in reflecting the true number of people with ototoxic hearing loss, as hearing loss may go unnoticed. Hearing loss may also be detected too late, when prevention procedures may be ineffective.

The World Health Organisation (WHO, 2016) suggests that baseline hearing assessments should be conducted prior to beginning aminoglycoside antibiotics. Hearing should then be monitored periodically and results should be compared to baseline results to detect ototoxic shifts in hearing. However, the WHO has no guidelines regarding how hearing should be tested and how frequently this should be done (Seddon et al., 2012). The South African Department of Health is more detailed in their guidelines and has stipulated that MDR and XDR TB patients should have a baseline hearing assessment prior to being initiated on aminoglycosides. If drug initiation has already happened, patients must receive a baseline hearing assessment within the first 72 hours of starting medication (Department of Health, 2011). As per the

recommendations of the Department of Health (2015), baseline hearing testing should include case history, otoscopy and tympanometry for middle ear assessment. Lastly, puretone audiometry must be conducted and the Department of Health (2015) as well as the HPCSA (2018) have specifically stipulated that testing must include the ultra-high frequencies.

During the administration of ototoxic drugs, hearing monitoring should include high frequency puretone audiometry conducted monthly or if resources allow for it, weekly (Department of Health, 2015). The HPCSA (2018) has stipulated that ototoxicity monitoring should occur with equipment that is sensitive to ototoxic shifts, to reduce false positive rates and equipment should be reliable with few changes in results with repeated testing. The HPCSA (2018) further details that hearing monitoring should occur up to 6 months after finishing DR TB treatment, and DPOAEs should be conducted bilaterally at every session. This is as the effects of ototoxicity can manifest over long periods of time when medication is no longer being taken. Patients should receive a full diagnostic audiological evaluation when leaving the TB programme, and this testing must include the extended high frequency range. For difficult to assess patients, the HPCSA (2018) suggests that the number of frequencies tested can be reduced, with the focus on the high frequencies from 4000 Hz to 12 500 Hz. Objective assessment measures such as DPOAEs should be used for these patients.

In the South African Department of Health policy guidelines as well as in guidelines available worldwide, there does not appear to be a definitive and universally accepted description of what specifically quantifies an ototoxic loss. As such, the ASHA (1997) guidelines are widely used by researchers and practitioners assessing ototoxicity in aminoglycosides (Adeyemo et al., 2016; Sharma et al., 2016). ASHA (1997) defines ototoxicity in comparison to baseline results, as a 20 dB decline in hearing at one frequency,

or a 10 dB decline at any two adjacent frequencies or a loss of response at 3 consecutive frequencies at which responses were previously present. Patients should be managed in collaboration with other professionals including doctors, nurses, and social workers, during which patients should be empowered to detect early signs of ototoxicity (HPCSA, 2018)

While South Africa has adequate policy guidelines which stipulate how to conduct ototoxicity monitoring, and how often to do so, in practice, these policies are not always well implemented. This is evident in a retrospective file review conducted by Khoza-Shangase and Stirk (2016), which revealed that out of five South African state hospitals, only one had a formal ototoxicity monitoring programme in place. Once ototoxicity was identified, no clear management procedure was used. While some audiologists made recommendations to change the medication of these patients, the overall conclusion of the study highlighted the need for integrated ototoxicity monitoring programmes based on evidence-based practices for South Africa. Furthermore, there is no set ototoxicity protocol for use across South Africa and thus, all hospitals appear to use their own ototoxicity monitoring programmes (Khoza-Shangase & Stirk, 2016). This makes it difficult for physicians to determine when medication adjustments should occur, as the significance of ototoxic shifts are not always clear, and lines of communication between professionals are not optimal (Hollander, 2018).

Another research study conducted in South Africa by Govender and Paken (2015), aimed to document the practices of 93 audiologists in the management of adults with MDR TB. The findings revealed that only 87% of audiologists conducted baseline hearing assessments due to a reported lack of appropriate equipment for infectious patients as well as shortages of staff. Merely 19% of audiologists conducted high frequency audiometry and only 68% of respondents were familiar with the ASHA international guidelines for ototoxicity monitoring.

As such, the authors concluded that due to a lack of South African guidelines, DR TB patients were inconsistently managed, which may have resulted in an under identification of hearing loss. Thus, there is a significant gap in the current literature both locally and internationally, as the majority of research examining ototoxicity in MDR and XDR TB has not assessed the extended high frequencies when conducting hearing testing (Duggal & Sarkar, 2007; Modongo et al., 2009; Sharma et al., 2016). This results in various inaccuracies in hearing findings, as potential ototoxicity may have been overlooked.

2.2.7. The KUDUwave Audiometer

Puretone audiometry conducted in a sound proof booth using a standardized manually operated audiometer has been established as the gold standard of hearing assessment internationally (ASHA, 2004; Maclennan-Smith, Swanepoel & Hall, 2013). However, such a testing environment with adequate equipment and trained audiologists is not widely accessible to the majority of individuals, especially those living in under-resourced environments where the need is often greatest (Maclennan-Smith et al., 2013). With advances in technology, developers have aimed to address this issue in order to provide audiological screening and diagnostic hearing services to a wider population. This is through the creation of mobile assessment devices, such as the KUDUwave. The KUDUwave audiometer was developed by a South African company, GeoAxon Holdings, with the aim to address the limited access that those with hearing loss have to hearing assessment devices and professionals (Storey, Munoz, Nelson, Larsen & White, 2014). The KUDUwave audiometer is portable and has both a manual mode and an automatic mode that threshold searches using a modified Hughson-Westlake procedure, similar to that which is used in conventional audiometry (Storey et al., 2014).

The KUDUwave comes standard with insert earphones covered by circumaural ear cups for the purpose of providing attenuation to noise, as the KUDUwave does not require the sound proof environment that is necessary in conventional audiometry (Swanepoel & Biagio, 2011). Insert earphones alone, allow for more accurate assessment of hearing thresholds as it adapts to the external auditory canal of each individual patient, and can attenuate noise more effectively (Oda, Marangoni, & Gil, 2014). Thus, double attenuation occurs with the KUDUwave, as the simultaneous use of circumaural earcups with insert earphones provides maximum attenuation (Swanepoel, Matthysen, Eikelboom, Clark, & Hall, 2015). There are microphones both on the outside and inside of the ear cups that monitor environmental noise in relation to the amount of attenuation provided and as such, thresholds are only obtained when the noise floor is low (Storey et al., 2014.) Thus, the developers claim that it can be used in sub-optimal noisy environments (Swanepoel & Biagio, 2011). However, it must be noted that the insertion depth of insert earphones affects how well the background noise can be attenuated (Clark & Roeser, 1988, as cited in Swanepoel et al., 2015).

While the KUDUwave uses double attenuation as discussed above, if the insert earphones are inadequately inserted, ambient noise may affect the degree to which thresholds can be accurately obtained, particularly in the low frequency range (Swanepoel et al., 2015). So far, no research study has evaluated the use of insert earphones in ultra-high frequency testing (Oda et al., 2014) nor has automated testing been validated on the DR TB population (Hollander, 2018). Additionally, it has been reported that nursing staff who operate automated audiometers such as the KUDUwave, often struggle particularly with the accurate placement of foam insert earphones (Hollander, 2018).

The KUDUwave falls under the category of computerized audiometry and teleaudiology, where hearing testing procedures are automated and controlled by computer software. The main advantage of this form of testing is that it allows for specialized testing to occur in settings where trained audiologists and specialists are not always available (Swanepoel & Biagio, 2011). It allows for results from hearing assessments to be shared via a server so that audiologists are able to review the data obtained while off-site and thus, make necessary recommendations without being physically present (Swanepoel & Biagio, 2011). While teleaudiology has an important role to play in audiological service provision in the 21st century, it must be implemented in collaboration with other professionals. This is especially important since interdisciplinary work within ototoxicity monitoring is not always optimal (Hollander, 2018).

The KUDUwave is operated using eMoyo software and there are various models of KUDUwave audiometers, with the KUDUwave 5000 (KUDUwave Plus) commonly used as the standard audiometer. This is as it offers all the tests that form part of audiometric testing, including air conduction, bone conduction and speech audiometry with word lists available in other languages such as isiZulu and Sesotho, so that testing is not limited to the capabilities of the administrator (Smith, Carling, Griffiths-Brown, Rhad & Koekemoer, 2018). The KUDUwave also provides a real time analysis of the reliability of the patient being tested, as information on false positives and no responses is tabulated at the bottom of each hearing tracing. The KUDUwave Pro is being distributed in association with the South African Department of Health, with 38 units having been dispersed for the purpose of ototoxicity monitoring in state hospitals (Govender, 2015). This is as it has all the features of the KUDUwave 5000, with the addition of ultra-high frequency testing which extends to

16 000 Hz. Hospitals do not require on-site audiologists or sound proof booths for it to be operated (Smith et al., 2018).

In terms of research into the accuracy of the KUDUwave audiometer, studies have only used the KUDUwave 5000 and no literature exists on the use of the KUDUwave Pro. Previous research has not examined the accuracy of the KUDUwave at frequencies above 8000 Hz and as such, no information exists regarding its precision in ototoxicity monitoring protocols. This is despite its extensive use within ototoxicity management in the context of South Africa. All of the studies conducted have compared results obtained by the KUDUwave to those obtained using conventional puretone audiometry using a GSI audiometer within a sound treated environment. It must be noted that the majority of research in the area has been conducted or co-authored by the same authors, and by authors who are known to have interests within the field of portable audiometry, due to their roles in the development of such devices. Most of the studies have not examined the accuracy of the KUDUwave in noisy, non-optimal environments, yet this is one of the main purposes for which the KUDUwave and its attenuators have been designed.

In a study conducted by Swanepoel and Biagio (2011), the air conduction (AC) and bone conduction (BC) hearing thresholds of adult patients were assessed using the GSI audiometer and the KUDUwave audiometer. Only 8% of ears in the testing sample had a hearing loss. The study found that the results for the KUDUwave audiometer were within 5 dB of the thresholds obtained by the GSI audiometer, for 90% of cases. A 5 dB difference in test re-test variability is acceptable and is within normal range (Swanepoel & Biagio, 2011). The largest difference between the results occurred at the lowest and highest frequencies of 250 Hz and 8000 Hz respectively and the same trend was found in another research study, which was conducted in

a different testing environment (Storey et al., 2014). This highlights the need for investigation into frequencies beyond 8000 Hz, to ascertain whether the same trend persists.

The results are similar to a study by Maclennan-Smith and colleagues (2013) who had a larger sample of patients and found that AC and BC results were within 5dB of a GSI audiometer for 95% and 86% of cases respectively. As the study had a larger sample, with a significant amount of people with hearing loss, this study further concluded that the KUDUwave was as accurate in determining thresholds amongst those who had normal hearing and those with hearing loss. The authors from both studies concluded that the KUDUwave is reliable for use in healthcare settings, with more research into less optimum environments necessary (Maclennan-Smith et al., 2013 & Swanepoel & Biagio, 2011).

One of the few studies to factor in background noise was conducted by Storey and colleagues (2014), who measured the accuracy of the KUDUwave in comparison to the standard GSI audiometer, when 40dBA of noise was present in the environment. The study revealed that 96% of results with the KUDUwave used in quiet and 94% of results with the KUDUwave used in noise, were within 5dB of the thresholds obtained with the GSI audiometer, indicating that the KUDUwave was reliable in non-sound treated environments. There was a high level of statistical correlation between results obtained with the KUDUwave and those obtained by a conventional GSI audiometer. In 5% of cases, the KUDUwave audiometer thresholds were over-estimated by as much as 60dB in comparison to the GSI audiometer. The authors could not provide suitable reasoning for this but concluded that it was not due to patient variables. Instead, the placement of the foam probe tips might have affected the recording of results. Even though this occurred in merely 5% of the population, it is

noteworthy for future research in order to establish whether this is a frequent occurrence and how best to counter act it.

Another study into the use of the KUDUwave in noisy environments was conducted in a busy Kenyan hearing clinic by Turunen-Taheri (2014) and aimed to validate the use of the KUDUwave in comparison to puretone audiometry. Eleven patients were tested over a short period of 4 weeks across the frequencies of 125 Hz to 8000 Hz using both types of equipment. Quantitative results using a dependent t-test revealed a significant difference in the lower frequency results between the two test environments, with the KUDUwave yielding higher thresholds than the puretone audiometer. This was evident in the 250 Hz to 2000 Hz region in the right ears of patients and the 250 Hz to 1000 Hz region in the left ears. However, there was evidence that the puretone audiometer was not used in a completely sound proof room, and thus, noise which largely impacts upon results in the lower frequencies, could have resulted in less accurate results for the puretone audiometer. This study therefore highlights the KUDUwave's ability to attenuate noise within a non-optimal hearing testing environment.

A pilot study conducted in Australia by Brennan-Jones, Eikelboom and Swanepoel (2017) examined the sensitivity and specificity as well as the measure of agreement between the KUDUwave hearing thresholds and thresholds obtained by a standard audiometer. This was conducted when assessing patients for a specific type of hearing loss. The results found that sensitivity and specificity values were high amongst the two conditions, with an 86% level of sensitivity and specificity in detecting normal hearing and a 97% level of specificity in identifying disabling hearing loss. Cohen's Kappa agreement revealed the agreement between results of the two types of equipment ranged from substantial agreement to almost perfect agreement. As such, the authors concluded that the KUDUwave was reliable, especially when

used to assess a specific type of hearing loss. It was noted that more studies with larger samples using these methods of analysis are necessary.

Lastly, a research master's study conducted in Ghana by Adjekum (2014) revealed that the mean unmasked threshold difference between a GSI audiometer and the KUDUwave at each frequency was less than 5dB bilaterally. The author noted that future research should compare the two methods of testing in the setting of ototoxicity monitoring and should examine its effect on difficult to test populations. Thus, the current study has a gap to fill in the literature, as patients with MDR and XDR TB are often difficult to test due to acute illness. Furthermore, there is a paucity of literature in the practical use of the KUDUwave within contexts that it was specifically designed to service, especially in low to middle income countries.

2.2.8. Nursing curriculum

In the context where this research study was conducted, the KUDUwave audiometer was operated by nursing staff who performed the test and sent it to the audiologists for reporting. As discussed above, the primary rationale behind the KUDUwave audiometer is that it was designed to be user-friendly for individuals who are not qualified audiologists, in order to increase as well as diversify access to audiological services. Due to the role nurses performed in hearing monitoring within the context of the current study, an insight into whether they were sufficiently trained and prepared for such a task, was necessary.

Throughout the world, nurses are the largest portion of health care workers in any given healthcare system, and are at the frontline of health promotion and patient management (Blaauw, Ditlopo & Rispel, 2014). The 21st century poses a unique challenge for nursing

practice, and education based on changes to how healthcare is delivered. There are now more individuals living with acute and chronic diseases worldwide than ever before (Larkin, 2011), with a growing awareness and emphasis placed on the relationship between healthcare and environmental factors which affect patient health and well-being (Tompkins, 2001). Nursing staff who are linguistically and culturally diverse, are a strength to any healthcare system, as it enhances contextual relevance and by extension, the treatment process (Nelson & Welch, 2006).

Currently, more patients receive services in settings that are removed from traditional models of service delivery. This is especially true in the era where the landscape of medicine is ever changing, with advances in technology and telemedicine. Research has in fact, shown that technology is viewed to be the most valuable resource within the healthcare setting (Tompkins, 2001). This is the case within the current DR TB management context, where technological advances have made technology such as the KUDUwave audiometer possible and feasible for use in the public health sector. Not only does this affect how services are delivered, but it implies that nursing staff have to become proficient in the use of technology, something that nurses are not always well prepared for, in order meet the demands of the new working environment. Thus, there is a need for training programmes and nursing curricula which equip nurses with an understanding of the demographical variables of patients, and how best to cater towards the needs of patients' families, and their communities (Keating, 2014).

Due to contextual and global factors, the field of nursing has experienced a paradigm shift over the past decade. Nurses now find themselves having to assume novel roles and responsibilities, in conjunction with having to respond to new and increased demands, particularly with regards to educational requirements (Keating, 2014). Not only are nurses

expected to assume roles that previously were not within their delegation, but nurses have to learn to become dynamic in their practice, while identifying and responding to gaps in their own knowledge by practicing collaboratively with other healthcare professionals (Hebert, 2014). As such, nursing services are no longer simply focused on individual patient care, but are expanded to include the training and supervision of fellow nursing professionals to equip others to deal with the ever-changing backdrop of nursing in health (Nelson & Welch, 2006).

In terms of nursing in South Africa, a new curriculum was developed over a 10 year period, which was then inculcated into nursing colleges and universities from 2013. The focus of the new curriculum was to up-skill nurses and transform the curriculum, which was originally influenced by apartheid laws and practices, to a curriculum which was more socially and contextually relevant for the modern needs of South African patients (Blaauw et al., 2014). A few nursing curricula both locally and internationally were reviewed, and most programmes included anatomy, physiology, and the practical aspects on how to nurse critically ill patients. While health awareness and promotion were included in nursing curricula, none of the curricula that were reviewed seemed to have specific details on hearing screening (Keating, 2006; Nelson & Welch, 2006; South African Nursing Council, 2019; Tompkins, 2001), despite professionals working within these contexts. This was due to the fact that nursing curricula are often generic, and form a foundation upon which further knowledge and specific training can be built (Nelson & Welch, 2006). Thus, it is expected that if nurses are to work within the contexts of hearing screening, training would be provided by the institution, and should be designed to build up upon the pre-existing medical knowledge that nurses already possess from their tertiary education.

2.2.9. Bedaquiline as an alternative

Up until July 2018, MDR and XDR TB treatment involved a long treatment regimen with injectable drugs associated with adverse side-effects, resulting in poorer outcomes and reduced adherence amongst patients (Brigden, Hewison & Varaine, 2015). As such, globally there has been a need for novel treatment options as MDR and XDR TB have become increasingly more prevalent and complex to treat. Bedaquiline and delamind are the first two new drugs introduced to TB treatment in over 50 years (Brigden et al., 2015). However, as delamind is costly and not yet widely available in South Africa, bedaquiline will be the focus of the present research project.

In 2012, bedaquiline received accelerated FDA (Food and Drug Administration) approval in the United States, following initial phases of clinical trials yielding positive results. Subsequently, The World Health Organisation (WHO, 2013) recommended the use of the drug bedaquiline specifically for the treatment of MDR TB and XDR TB (Brigden et al., 2015). Bedaquiline belongs to a new group of antibiotics called diarylquinolines and uses a novel mechanism of action to specifically target resistant strains of TB, thus, it has been registered solely for the treatment of DR TB (WHO, 2016). As such, the WHO has developed guidelines as to how bedaquiline should be administered including other TB drugs to be combined with bedaquiline, the dosage for the medication as well as the frequency of treatment.

The WHO has also stipulated strict inclusion and exclusion criteria for patients receiving Bedaquiline. Patients must have a diagnosis of MDR or XDR TB to receive bedaquiline and it is not recommended for pregnant women, individuals under the age of 18, those with pre-existing liver difficulties or people with a predisposition for cardiac complications (WHO,

2016). Prior to July 2018 when the bedaquiline prescription laws in South Africa changed, The National Department of Health adopted the same inclusion and exclusion criteria, however, patients with pre-existing hearing loss or those who developed ototoxic hearing loss during aminoglycoside treatment, were candidates for bedaquiline (DOH, 2014). Interestingly, the WHO did not consider ototoxicity as a factor in any of their previous guidelines, while South African policies have recognized the risk of ototoxicity and the role of bedaquiline in its prevention.

In a study conducted in 2013 which examined the treatment of 351 patients who received bedaquiline according to the WHO guidelines, two thirds of patients were successfully cured of DR TB (WHO, 2016). Of most significance is that in international studies on the reported side-effects of bedaquiline, ototoxicity or symptoms of hearing loss were not reported by any patients receiving such treatment (WHO, 2016). Therefore, bedaquiline has a significant role to play in providing an alternative to ototoxic aminoglycosides, as injectables can be replaced by bedaquiline within treatment regimens (WHO, 2016).

South Africans have been able to access bedaquiline through the Bedaquiline Clinical Access Programme which began in 2013, and allowed patients compassionate access to the drug, while facilitating research in the treatment protocols (Department of Health, 2018). By January of 2018, approximately 15 000 South African patients with rifampicin resistant TB had received bedaquiline under these guidelines. Outside of clinical trials in the United States, South Africa has had the largest access to the compassionate use of bedaquiline, with France and Armenia closely behind (Bennett & Brown, 2008). Compassionate use of drugs aims to provide new, unregistered drugs to countries such as South Africa that have no access to clinical trials using the drugs and as such, no access to life saving medications for the successful

treatment of diseases (Bennett & Brown, 2008). Data on the use of bedaquiline was collected in all countries where it was administered, with South Africa contributing significantly by having the highest rate of patients (59,3 %) co-infected with HIV and TB (Brigden et al., 2015). The impact of bedaquiline on the South African health system, has been profound, with a notable decrease in patient mortality rates by a factor of 4 in comparison to those on kanamycin (Department of Health, 2018).

Studies examined how well bedaquiline caused culture conversion in patients, with sputum results of culture conversion from positive to negative indicative of a patient recovering from TB (Conradie et al., 2014). In the South African study conducted by Ndjeka and colleagues (2015), results found the use of bedaquiline in the South African context to be both safe and efficacious, with 76% of patients having culture conversion on sputum at 6 months (Ndjeka et al., 2015). In the French study, a cohort of 35 patients with MDR and XDR TB received bedaquiline treatment, which yielded a 97% rate of culture conversion after 6 months of treatment (Guglielmetti et al., 2015). In all studies, there were no reports of severe adverse health effects with bedaquiline use, and this was of particular interest in the South African study, for there was previously no research on the effects of co-usage of ARVs and bedaquiline (Brigden et al., 2015). Limitations of the above studies include that they were based on interim results, over short periods of time with reliance on culture conversion, which does not necessarily reflect the curing of DR TB as relapses in the long term may have occurred (Brigden et al., 2015; Ndjeka et al., 2015; Guglielmetti et al., 2015). More results from longitudinal studies are expected by 2020 (Brigden et al., 2015; Guglielmetti et al., 2015).

Despite bedaquiline's potential to revolutionize DR TB treatment, on a global scale, very few people have had access to the drug (Brigden et al., 2015), despite it being available in over

70 countries (WHO, 2016). A large barrier to patients receiving bedaquiline lies mainly in the high costs involved in importing the drugs, which is especially noted in low to mid-income countries such as South Africa (Brigden et al., 2015). Bedaquiline has been known to be expensive, with a 6-month regimen in the United Kingdom, costing approximately £20 000 (Tiberi et al., 2018). In South Africa, the approximated cost of bedaquiline for the first month of treatment is R 1952, 96 in comparison to other DR TB drugs which cost between R31 and R50 (Wong & Reddy, 2018).

Historically, bedaquiline had to be approved before it could be dispensed, to prevent the misuse of drugs. This was detrimental as patients could not immediately receive bedaquiline when it was clinically indicated (Tiberi et al., 2018). The National Department of Health, Right to Care and Médecins Sans Frontières worked collaboratively to obtain the medication for South African patients (Conradie et al., 2014). With all 9 provinces of South Africa having MDR and XDR TB treatment facilities, The Department of Health aimed to have bedaquiline available at a provincial level, with a center in every province dispensing the medication (Department of Health, 2015). While this aim has been achieved, South Africa has been striving to provide national access to bedaquiline so that it could be widely available in healthcare settings throughout the country (Department of Health, 2015). As such, changes were made to treatment regimens from July of 2018, with South Africa at the forefront in the fight to reduce ototoxicity in DR TB treatment.

As South Africa has one of the highest rates of DR TB in the world, and since bedaquiline treatment regimens showed marked success within the South African context, steps needed to be taken to ensure that bedaquiline was largely available to all patients, as and when it was required. Thus, from July of 2018, The South African National Department of Health

announced that injectable-free regimens were to be phased into routine DR TB treatment ahead of recommendations by the World Health Organisation. This was done using the Bedaquiline Expansion Plan Policy as set out by the National Department of Health (Department of Health, 2018). These bold steps taken by South Africa ensured that a non-ototoxic DR TB treatment protocol was inculcated, while keeping ototoxicity monitoring systems in place.

2.2.10. New treatment regimens

Following the new Department of Health Guidelines released in July of 2018, the World Health Organisation (WHO, 2018) released new global treatment guidelines in August of 2018. These guidelines were based on research from 26 countries, including South Africa, and was in response to the global call for alternative treatment to aminoglycosides such as kanamycin, due to the negative side-effects of these drugs (Tiberi et al., 2018). It was found that despite kanamycin being cheaper, it became more expensive in the long-term as patients had high rates of treatment failure and relapse. Typically, MDR TB treatment lasted 18 months or longer, and included the combination of both first-line and second-line injectable drug treatment. Now, the WHO has encouraged a shorter drug regimen of 9 to 12 months for MDR TB, including an intensive phase of 6 months of oral treatment with the omission of injectable aminoglycoside antibiotics such as kanamycin and capreomycin (Tiberi et al., 2018; WHO, 2018).

The longer regimens of DR treatment are still recommended and are used for more complex cases, but have been adapted to exclude kanamycin. Kanamycin has been replaced with bedaquiline, in all regimens, however, bedaquiline cannot be prescribed for children, and pregnant women (Tiberi et al., 2018). Despite the removal of kanamycin from the new WHO drug regimens, the ototoxic aminoglycoside amikacin, still remains part of the drugs that can

be used for DR TB treatment. This is as amikacin does not show the same pattern of drug failure, and adverse drug reactions as kanamycin or capreomycin (WHO, 2018). When amikacin is used, the precautions for injectable drugs including hearing monitoring, must be observed (Department of Health, 2018; WHO, 2018). In fact, it is recommended that clinical safety monitoring programmes are intensified during this period, especially for those on amikacin, so that at the first sign of ototoxicity, these patients can be changed to other medication (Department of Health, 2018; WHO, 2018) The drug Para-aminosalisylic Acid (PAS) which is not known to have ototoxic effects, still remains in the DR TB regimen (WHO, 2018).

As per the new WHO (2018) guidelines, patients are to receive counselling when entering the DR TB programme, and given social support from a patient-centred approach in order to encourage adherence. The new regimens are to be placed into effect without waiting for kanamycin stocks to finish, and in the interim, patients who were initiated on injectable drugs and have been on them for a month or longer, should be switched to amikacin instead of kanamycin (Department of Health, 2018; WHO, 2018; Wong & Reddy, 2018). These patients are then to receive strict ototoxicity monitoring as part of the treatment process. As there is a possibility that amikacin may be indicated during treatment, patients are to receive hearing testing and ototoxicity monitoring according to the pre-existing ototoxicity monitoring protocols (Wong & Reddy, 2018).

Due to the complex nature of DR TB treatment, there is a need to explore the system factors that occur beyond the level of the individual, where specific variables have the power to impact upon the health, well-being, ototoxicity monitoring, and successful treatment of patients with DR TB. The protocols used to evaluate the presence of ototoxicity at an individual

level should also be explored, where the KUDUwave is evaluated in conjunction with external factors at the level of nursing staff who operate the machinery. This can then provide a holistic overview and understanding of the DR TB monitoring protocol in its entirety, considering the patients, the nurses providing ototoxicity monitoring, and the external environmental factors and systems which affect the overall process.

Chapter 3
Methods

This chapter outlines the mixed methods approach that was used to conduct this study, and its application in relation to the aims and sub-aims of the research project. The research design and sampling methods are detailed, and a description is provided of the nurse participants and patient population involved in the study. The research instruments, and methods of data analysis are explained, and the principles of reliability, validity, and rigor have been considered. Lastly, some of the ethical considerations pertinent to the study have been explored.

3.1. Main Aim and Sub-Aims

3.1.1. Aim:

The aim of this study was to interrogate overall trends in a specific ototoxicity monitoring programme at a tertiary hospital in Gauteng. Detailed below are the sub-aims of the study.

3.1.2. Sub-Aims:

- To provide insight into the personal variables of patients with DR TB, attending the ototoxicity monitoring programme at a tertiary hospital in Gauteng.
- To describe the audiological findings of patients with DR TB, attending the ototoxicity monitoring programme at a tertiary hospital in Gauteng.
- To provide insight into the nurses' experience of hearing screening within the context of the ototoxicity monitoring programme at a tertiary hospital in Gauteng.

3.2. Research Design

According to Knudsen and colleagues (2012), reality can be interpreted in various ways, especially since knowledge and understanding is dependent on the experiences of individuals within diverse contexts. In the past, thematic analysis has been used extensively in health research, particularly in nursing (Knudsen et al., 2012). However, there is limited research within the field of audiology that uses a mixed methods approach, which is significant as health experiences are often influenced by contextual factors, and if these are taken into account, a richer set of findings are obtained. Thus, the concurrent mixed methods approach, which combined the simultaneous use of both quantitative and qualitative research methods (Barnes, 2012), was utilised in this study. The approach provided the opportunity for a much richer enquiry than what was possible through the use of one method in isolation (Burke Johnson & Onwuegbuzie, 2004, as cited in Barnes, 2012).

The mixed methods approach further allows for the triangulation of data, whereby one research method is used to support the findings of another research method (Jick 1979, as cited in Barnes, 2012). It facilitates the discovery of different aspects of an overlapping phenomenon (Barnes, 2012), and thus, both the qualitative and quantitative aspects of this study were conducted concurrently to enhance this process (Morgan & Sklar, 2012). The use of a mixed methods design further strengthens a study as it articulates the context that the researcher is exploring (Henning, van Rensburg & Smit, 2009). It is of particular value within the South African context as it facilitates the development of protocols or interventions that are both beneficial and relevant to the diverse cultural and linguistic context (Barnes, 2012).

The quantitative phase of the study involved a non-experimental method of research, namely a prospective study using a within-subjects design. In a prospective research study,

participants are included within a study based on specific characteristics and participants are tracked over time for the development of these traits (Bacchieri & Della Cioppa, 2007). The benefits of such studies include that multiple diseases can be studied simultaneously whilst analyzing various predictive factors, allowing the researcher to control the process of data collection by accounting for events such as the deaths of patients, as they occur (Jekel, Katz, Elmore, & Wild, 2007). Disadvantages of such a study include that patients may be lost to follow-up, and data collection can be time consuming in nature (Jekel et al., 2007). The present study was classified as prospective in nature, as the researcher reviewed files that were created after the date that ethics clearance was obtained. This renders the study prospective and not retrospective in nature. The study used a within-subjects design, as all participants were exposed to all levels of a factor (Roberts & Russo, 2014). Such a design was appropriate as the patient files reviewed were all from the same TB and ototoxicity monitoring programme, resulting in all patients being exposed to the same tests and procedures.

The qualitative phase of the study included a non-experimental, research design, namely a survey design which involved the selection of a specific group of participants for the purpose of conducting interviews. This allowed the researcher to describe the participants' attitudes, beliefs, and knowledge regarding a topic of interest, while using a small sample of individuals to gain an understanding of a wider population (Seabi, 2012). This form of research design was best suited to this study, as the researcher was interested in exploring the knowledge and attitudes of nurses using the KUDUwave to test hearing amongst patients exposed to ototoxic medication.

3.3. Participants

3.3.1. Sampling Strategy

A purposive convenience sampling approach was used to select participants for this study. A purposive sampling method allows for participants to be chosen based on set criteria stipulated by the research topic (Ritchie et al., 2014), while the convenience sampling approach involves using a sample of patients that are easily at the researcher's disposal (Matt & Matthew, 2013). This was appropriate since this study required participants to have specific characteristics outlined by the inclusion criteria, and purposive sampling ensured that the research topic was relevant to the participants selected for the study (Knudsen et al., 2012). The same sampling method was used for both the quantitative and qualitative portions of the study. For the quantitative aspect of the study, a total of 200 files were reviewed by the researcher, with only 120 files included in the study, as these met the inclusion criteria stipulated for the research study. The 120 files included the records of patients enrolled in the DR TB programme at the TB centre within the chosen hospital. On the other hand, the qualitative part of the study included six qualified nurses who had experience testing patients using the KUDUwave audiometer, and these were the only nurses working at the TB centre at the time when the study was conducted.

The inclusion criteria for the quantitative sample were that patients needed to be currently or previously on treatment for MDR or XDR TB and be enrolled within the DR TB programme at the hospital. To be included in the study, patients needed to have had approximately two KUDUwave tests, to allow for sufficient data points for statistical analysis. More than one KUDUwave test was required, as research shows that initial hearing assessments are not as accurate as follow-up sessions, as patients do not always understand

test protocols in unfamiliar situations (Schlauch & Nelson, 2009). Moreover, follow-up hearing tests reveal that hearing can differ within 5dB to 10dB from initial testing (Schmuziger, Probst & Smurzynski, 2004).

The exclusion criteria were patients with DR TB that were not enrolled at the TB centre at the hospital or that had one or no KUDUwave hearing tests. Those that had hearing testing using other means of assessment other than the KUDUwave, were also excluded as there were no KUDUwave test results available. Patient files where the research consent document (see Appendix E) was not filled in and signed by the patient, were omitted from the study. People below the age of 18 were also excluded from the study, as these individuals are not eligible for bedaquiline prescription due to drug regulations. Furthermore, those who did not have DR TB or who were concurrently receiving chemotherapy or other ototoxic drugs during their DR TB treatment, were excluded from the study. This is as chemotherapy medications may cause ototoxic shifts that cannot be controlled for within the study (Konrad-Martin et al., 2005). One participant in the study was diagnosed with Kaposi sarcoma, however, the participant was included in the study as chemotherapy began after DR TB treatment had finished and as such, the ototoxic shifts observed could not be affected by the cancer treatment.

The inclusion criteria for the qualitative sample of nurses included professional nurses who had operated the KUDUwave audiometer and used it in the hearing testing of patients on ototoxic medication at the TB centre at the chosen hospital. Nursing staff that were not from the TB centre, who were not trained on the KUDUwave audiometer or had no experience operating it, were excluded from the study. The rationale for the exclusion of these nurses

was that they did not have the necessary background information to answer the interview questions appropriately.

3.3.2. Description of Participants

The quantitative phase of the study included a review of 120 files of patients who had previously received treatment or were currently enrolled in the DR TB treatment programme at the TB centre, having met the inclusion criteria for the study as detailed above. The age range of the participants when beginning treatment was 18 to 73 years of age. The mean age of participants was 36 years old, and in terms of gender, 52% (n = 63) of the total sample were males while 48% (n = 57) were females. The participants were on DR TB treatment for an average of 14 months, with certain patients being on treatment for a maximum of 24 months. In the sample, 118 patients were diagnosed with MDR TB, of which 72,5% (n = 87) were classified as having mono-resistant TB with resistance only to the drug rifampicin. The remainder of patients (25,8%, n = 31) were resistant to two drugs, namely rifampicin and isoniazid. Two patients in the sample were diagnosed with Pre-XDR TB, with resistance to the drugs rifampicin and oxfloxacin. Of the total sample of 120 patients, 8,3% (n = 10) reported being in contact with an individual such as a prison cell mate, spouse or family member who had previously had TB.

The majority of participants in the quantitative sample did not live in an urban area, with 28,3% (n = 34) living in informal settlements and 20,8% (n = 25) living in various townships across Gauteng. The remainder of the sample lived in urban areas (47,5%, n = 57) while three patients were prisoners in Gauteng. More than half of the participants were unemployed (52,5%, n = 63) and the remaining participants were employed as domestic workers, gardeners, factory workers, store managers, assistants at fast food outlets, and health care workers. A

small number of participants were not employable as they were either prisoners or scholars at the time of treatment (5,8%, $n = 7$). One patient was dismissed from his place of employment when his employer found out that he had DR TB and one patient attended the clinic for treatment irregularly as his employer would not give him time off to attend the appointments.

The qualitative sample comprised of nursing staff within the age range of 32 to 60 years of age. Their years of professional experience is detailed in Table 3.1. The training each nurse received on how to operate the KUDUwave audiometer is also shown in Table 3.1. Three of the six nurses worked in HIV specific settings (such as at ARV clinic at the hospital) while one participant was a TB co-ordinator in the wards at the same hospital, before transferring to the TB centre.

Table 3.1

Participant	Age	Years as Nurse	Years at TB centre	Training Received	Period Using the KUDUwave (Years)
1	60	38	3	Nurse trained	1.5
2	36	8	1	Nurse trained	1
3	32	3	3	KUDUwave and nurse trained	1.5
4	36	8	1	Nurse trained	1
5	42	9	1	KUDUwave and nurse trained	1
6	58	18	4	Nurse trained	1.5

Participant Demographics of Nurses

Note. Nurse Trained: the nurse was trained on the KUDUwave audiometer by the sister at the TB centre. KUDUwave and Nurse trained: the nurse was trained on the KUDUwave audiometer by a representative of Emoyo as well as by the senior sister at the TB centre.

3.4. Instruments

For the quantitative phase of the study, a prospective file record review was used, as patient files from both prior to and during the data collection period were analyzed to answer the research questions, classifying this study as prospective in nature (Matt & Matthew, 2013). Information from the files were recorded on a self-developed data recording sheet (see Appendix Q) and later transferred to an excel spreadsheet. The files reviewed were of patients

enrolled at the TB centre, and contained biographical information such as the date of birth, gender and address of each patient. A further insert within the file, developed by the South African Department of Health and filled out by nursing staff, was reviewed. The information included previous DR TB treatment, the referral source, the patient's living situation, level of education, HIV status, marital status and food security. Habits such as smoking, drinking, and drug use, as well as known TB contacts and referrals that were made to other professionals were included. The doctors' notes were reviewed to gain information about acute and chronic diseases as well as the type of DR TB for which the patient was treated.

The audiological results reviewed included data from two sources. Firstly, the results obtained from the KUDUwave tests conducted by nurses at baseline and during treatment at follow-up sessions were reviewed. Thereafter, where available, the results of patients who had received exit diagnostic audiograms after completing treatment were reviewed. These diagnostic audiograms were conducted by an audiologist in a sound proof booth using a standard GSI audiometer, upon exit from the TB programme. Only 28 patients from a sample of 120 received these audiograms, despite it being part of the standard monitoring protocol. Those who had developed ototoxic losses were closely examined to establish possible associated factors.

The qualitative phase of the study included the use of face-to-face semi-structured interviews (see Appendix J) that were conducted with the nursing staff who were operating the KUDUwave audiometer at the TB centre. Semi-structured interviews, the most direct form of data collection, involves the researcher gaining responses directly from the participants in a one-on-one environment using both open-ended and closed-ended questions that are pre-determined (Galletta, 2013). Semi-structured interviews are the most common method of data

collection in qualitative research in the field of audiology, and the dialogue between the researcher and participant provides an in-depth account of the phenomenon being studied (Knudsen et al., 2012). Such an interview structure was beneficial for the current study as even though the interviews were framed around the research questions, participants were provided with the opportunity to freely share their knowledge, experience, beliefs and attitudes in a less constricted environment (Brink, Van Der Walt & Van Rensburg, 2006). It also allowed the researcher to amend follow-up questions based on how the participants responded, in order to expand upon and add richer detail to the data obtained (Brink et al., 2006). The interview questions included aspects such as nurses' knowledge of KUDUwave testing, their experience of using the machine, and their views on further training that was required.

While it is noted that it is best for interviews to be conducted in the home language of participants as it allows the researcher to gain an accurate analysis of the perspectives, experiences, and world views of participants (Goyal, 2013), the interviews were conducted in English. This is because English is the common lingua franca used at the TB centre, and the participants were all qualified nurses who have had a formal tertiary level of education in English. Thus, a certain competency in the English language, specifically at a conversational level, was assumed by the researcher and appeared to be present amongst the participants, rendering it appropriate for use in the interviews

3.5. Procedure

Following ethical clearance from both the ethics committee at the hospital research site and from the University of the Witwatersrand Health Research Ethics Committee (HREC - Medical) (see Appendices B, C, and D, Ethics Protocol Number: M180407) the researcher conducted a prospective file review of both the hospital files of patients as well as the

audiological diagnostic test results kept at the audiology department, in order to collect quantitative data which was coded and inputted onto a Microsoft Excel spreadsheet. The data from the Excel spreadsheets was then analyzed by a statistician who performed various statistical analyses of the data in order to provide quantitative information that answered the research questions.

The qualitative data collection process began concurrently with the quantitative file review. Nurses working at the TB centre who matched the participant inclusion criteria were invited to participate in the study using a participant information document (see Appendix G.) This document detailed the purpose of the research study and what was expected of them as participants should they choose to participate in the study. The nurses who agreed to participate in the study were asked to fill out a consent form (see Appendix H) indicating that they had given consent to participate in the study. A separate consent form (See Appendix I) was signed which stated that the nurses had given their permission to have the interview audio recorded for transcription by the researcher at a later date. The interviews followed the structure of the interview schedule and both open ended and closed ended questions were utilized. Where necessary, follow up probing questions were posed for clarity purposes (Brink et al., 2006). The interviews were approximately 20 to 30 minutes in length, and took place in a private office at the TB centre at a pre-arranged time that was convenient for nursing staff. The audio recorded raw data were then transcribed verbatim by the researcher for the purpose of analysis.

3.6. Data Analysis

For the data obtained from the prospective file review, quantitative data analysis involving both descriptive statistics and inferential statistics was utilized. Descriptive statistics analyzes data using summaries and descriptions, such that patterns in the data can be identified (Polit

& Beck, 2008). Descriptive statistics for the categorical data obtained, involved measures of frequency dispersion. Measures of central tendency such as the mean, measures of dispersion and measures of variability were used for the data involving continuous variables (Brink et al., 2006). These methods were used to analyze characteristics and trends amongst patients with DR TB, and those presenting with ototoxicity. However, it must be noted that descriptive statistics does not allow for conclusions to be drawn from the data or for causational relationships to be established (Polit & Beck, 2008). Thus, inferential statistics, a method of data analysis used to draw conclusions from a sample and generalize these to a larger population using statistical measures (Mendenhall, Beaver & Beaver, 2012) was necessary.

Inferential statistics was used to analyze various relationships between the quantitative data obtained. Specifically, in this study, a chi-square test of association was utilized as it allowed for the analysis of the categorical data from the study. This was done in a manner that determined whether two specific sets of data were related to one another, or independent of one another (Lang & Secic, 2006). As part of the chi-square test, both the P value which represents the test statistic as well as the degrees of freedom which represents the probability distribution, have been detailed in the results of the study. This is as part of best practice, so that the data obtained can be deemed both accurate and authentic (Lang & Secic, 2006).

The data gathered from the nurse interviews were analysed using qualitative data analysis, specifically thematic analysis. This method of analysis was beneficial as the researcher was able to access reality through the subjective analysis of transcribed interview responses which were obtained from the original audio recorded data (Ehnert, 2008). Thematic analysis provides a data driven overview of participant responses, and allows the researcher to integrate the data

obtained while forming associative links between the findings within the data (Knudsen et al., 2012). It further captures the main ideas within the data that are required for interpretation, thus minimizing the amount of content the researcher needs to interpret (De Vos, 2002). This was done using the 6-step process of thematic analysis as outlined by Braun and Clark (2006).

Using Braun and Clark's (2006) 6-step process, the audio recorded interview data was first transcribed and then the researcher became familiar with the data by repeatedly reading the content before assigning codes to meaningful parts of the data as they emerged within the data set. Coding is a method utilized to break down the data for analysis allowing for the formation of theories as the data is reorganized in new ways (De Vos, 2002). More specifically, in this study, open coding was utilized as phenomena within the data were named and categorized through the separation of data into specific parts, allowing for the analysis of the similarities and differences (Braun & Clark, 2006).

Axial coding was then utilized, allowing the researcher to piece the data back together thereby facilitating the formation of relationships between the items of data, resulting in the formation of themes (Braun & Clark, 2006). These themes were then assigned names and it was ensured that all the meaningful data that emerged was represented appropriately. During the transcription of data into text form, the process of indexing was used, whereby each line of the transcript was numbered in the margin in numerical order so that direct reference could easily be made to the original data set during data analysis (Ritchie & Spencer, 1994). This process allows the researcher to easily identify patterns within the natural context wherein they occurred, and facilitates the accurate interpretation of results (Ritchie & Spencer, 1994).

3.7. Reliability and Validity

Reliability refers to how consistently a research instrument measures a specific construct over time, while validity addresses how accurate the instrument is in identifying a specific construct. Validity also includes the degree of preciseness and truthfulness of research results (Brink et al., 2006). Within a mixed methods study, the terms reliability and validity are applicable to the quantitative data collected (Heale & Twycross, 2015). The KUDUwave portable audiometer requires annual calibration to ensure that the machine is functioning optimally and measures hearing thresholds appropriately (eMoyo, 2015). Thus, a calibration certificate as proof of recent calibration (See Appendix K) is indicative of the reliability and validity of the results obtained. As the KUDUwave is an automated audiometer, hearing thresholds are tested without having to account for operator variables. Additionally, once the test has run, it provides a summary of false positives and false negatives based on the patient's response to testing (eMoyo, 2015). Thus, operator variables affecting the reliability of testing procedures are not of concern.

For diagnostic audiometry testing, the standard GSI diagnostic audiometer used in a sound proof booth is calibrated annually to ensure the validity and reliability of testing results (Roeser, Valente & Hosford-Dunn, 2011) and as such, the calibration certificate (See Appendix L) confirms the recent calibration. Audiological testing is conducted manually with the audiologist following an internationally recognized standardized procedure known as the modified Hughson Westlake Protocol (Carhart & Jerger, 1959; Hughson & Westlake, 1944, as cited in Schlauch & Nelson, 2009). This is used to ensure that the procedures used in determining the softest sound an individual can hear, is consistent across different audiologists, and different test sessions, ensuring reliability (Roeser et al., 2011).

Lastly, the concept of triangulation further adds to the reliability and validity of a study and is often achieved when different sources and types of data are used in conjunction with various methods of data collection (Di Fabio & Maree, 2012). Triangulation was used in this study which involved gathering data from multiple sources, as data from both a prospective file review as well as semi-structured interviews were utilized. This facilitated greater depth in the exploration of the research problem as well as allowed for the integration and confirmation of results (Di Fabio & Maree, 2012).

3.8. Rigor

An important aspect of qualitative analysis is rigor which assesses whether the research tool accurately measures what it intends to measure and how well it does so (Flanagan, 2005), forming part of the trustworthiness of the study. Trustworthiness is the qualitative equivalent of reliability and validity and refers to the manner in which data are collected and organized, specifically in verbal or in text form (Knudsen et al., 2012; Di Fabio & Maree, 2012). The criteria for evaluating trustworthiness include credibility, dependability, confirmability and transferability. Credibility, which addresses how accurate the research findings are, was established by consulting individuals not directly involved in the research, including the research supervisor, and peers. In the current study, these individuals reviewed the data and the corresponding analysis, in order to reduce researcher bias and confirm that the researcher's interpretation of the findings was reflective of the data obtained (Di Fabio & Maree, 2012).

Dependability, which involves how consistent the results of the study remain over time, was established by providing the interview schedule used in the interview process so that methodologically, the study can be replicated in similar contexts (Di Fabio & Maree, 2012). Confirmability ensures that there is no researcher error as the evidence of results should be

obtainable directly from the participant and not solely from the researcher's subjective opinion. As such, direct quotes from the responses of participants during interviews have been included in the results of the research study (Di Fabio & Maree, 2012). Transferability which addresses how well the results can be generalized from one context to another, was not the focus of the interviews conducted, as qualitative analysis aims for an in-depth understanding of a phenomenon rather than generalizability of research findings (Flanagan, 2005). Pilot studies are often conducted to ensure the rigor of the interview schedule utilized; however, this was not possible in the current study due to the small sample of nurses that met the inclusion criteria for the study. Therefore, to compensate for this and to ensure the rigor of the tool used in the semi-structured interviews, individuals other than the researcher proof read the interview schedule (Henning et al., 2009). These included the reviewers of the ethics committee, the research supervisor as well as peers. The necessary adaptations were made to the tool based on this feedback.

3.9. Ethical considerations

Ethical clearance (Protocol Number M180407) was granted by the University of the Witwatersrand Human Research Ethics Committee (HREC Medical) stating that the researcher had full ethical clearance to conduct the research at the research site (See Appendix C). To better reflect the aim of this research study, and to provide a richer investigation, the title of the research was amended, and the nurse interviews were later added into the study for triangulation purposes. As such, Appendix D shows that the changes were both acknowledged and approved by the HREC Medical Ethics Committee. A letter of information (Appendix A) was given to the Chief Executive Officer (CEO) and the Head of Department (HoD) of Speech Therapy and Audiology at the chosen hospital in order to provide the necessary information regarding the research study and what it entailed. As the chosen hospital has its own ethics

board, approval was obtained from the hospital in the form of a research permission letter (Appendix B.)

As the chosen hospital is an academic hospital, the hospital policies stipulate that patient hospital records are for use for research purposes. As such, each patient who was enrolled at the TB centre, had signed a consent document for their file data to be used for the purpose of any research conducted at the hospital (See Appendix E), and as such, further individual consent from each patient for this study was not required. The researcher has a copy of each signed consent document from the files that were reviewed for this study. A copy of the Wits HREC ethics certificate once obtained, was made available to the Hospital CEO and the Head of the Hospital's ethics committee.

In addition to the above, permission was requested from the head of nursing at the TB centre (Appendix F), to grant permission for the researcher to interview the nurses from the TB centre for the qualitative phase of the study. Thereafter, the potential nurse participants were invited to participate in the study with an information sheet (Appendix G) which informed them about the purpose of the research study, the duration of time required for the interviews as well as the assurance that their anonymity and confidentiality would be as far as possible, strictly maintained. It further detailed that there would be no risk or direct benefit to them for participating in the study and that they had the right to withdraw at any point during the study with no consequences. Participants were given the opportunity to ask questions or request for further clarity which ensured that informed consent was obtained from the nurse participants (Henning et al., 2009). Participants who were willing to participate were then requested to sign the consent form (Appendix H) stating that they agreed to be interviewed by the researcher and that they had understood the aims of the research study and what would be expected of them.

As the interviews were audio recorded, the nurse participants who agreed to participate in the study were given an opportunity to sign the audio recording consent document (Appendix I) stating that they had given their consent to have their interview audio recorded. Ethically, the researcher was required to inform the participants that the interviews were recorded to ensure that the participants were comfortable with this and were aware of this before partaking in the interview process (Henning et al., 2009). As far as possible, the anonymity and confidentiality of the research participants, inclusive of nurses and patients, has been maintained. This is as the patient participants from the quantitative phase of the study were traced using their hospital numbers, and then assigned a unique study number by the researcher. The nurse participants from the qualitative phase of the study were also allocated unique study numbers by the researcher, and these were used when direct quotes from the interviews were referred to in the dissertation. This process further aided in maintaining participant anonymity, as information recorded by the researcher did not allow the participants in question to be identified (Matt & Matthew, 2013). However, the researcher could not prevent other nurses from knowing who was interviewed, as nurses practiced in close quarters with one another and there was a small pool of nurses that met the inclusion criteria for the study

The researcher will share the preliminary results of the study with the necessary stakeholders within the hospital by providing them with a summary of the research findings, as part of good ethical and clinical practice (Vogt, Gardner, & Haeffele, 2012). During data collection, the patient files and medical records remained at the TB centre, in a locked office. Both the quantitative and qualitative data including excel spreadsheets, audio recordings of the interviews, and transcriptions of the interviews have been kept on a password protected computer and only the researcher and supervisor have access to the data. The research dissertation will be available on the Wits University WIReD Space, and the data collected may

be retained for publication purposes but if not used within 5 years, will be destroyed based on best ethical practice (Whitehead, LoBiondo-Wood & Haber, 2012).

Chapter 4

Results

As previously discussed in the Chapter 3, this research study followed a mixed methods framework of analysis, whereby two phases of data collection occurred simultaneously. Phase 1 was a retrospective file review of 120 files of patients with DR TB and the data was analysed quantitatively. Phase 2 of the study included qualitative semi-structured face-to-face interviews, and took place towards the end of Phase 1 of the study. Phase 2 of the study took into account some of the trends observed by the researcher in Phase 1, to provide the context for certain observations that were noted in Phase 1. As such, this chapter presents the results obtained from Phase 1 of the study, followed by that of Phase 2. The context of the research site has been detailed so that the results and observations can be grounded within the specific environment within which they have taken place.

4.1. Context of the Research Study

The study was initially part of a collaboration with the Health Economics and Epidemiology Research Office (HERO) research team, which forms part of the Wits Health Consortium. However, the HERO researchers lost their international funding due to changes in the bedaquiline laws in South Africa. Thus, subsequently, due to these changes within the HERO project this study moved to be a standalone study as described in this dissertation. The study took place at a specialized TB centre at a Gauteng hospital, located in Johannesburg. The hospital is classified as a Level 3 tertiary hospital with 21 in-patient wards with a total of approximately 750 beds. It services a diverse population and has 7 specialist out-patient clinics including a specialized clinic for HIV management, and the TB centre for DR TB treatment.

The team at the TB centre include doctors who have specialized in TB management, nursing staff, social workers, researchers as part of the research unit, and a team of data capturers who ensured that all patient details were accurately recorded and updated to the national TB database. Before July 2018, the TB centre was one of two sites in Gauteng with the resources to access and dispense bedaquiline. As such, referrals were received from hospitals and clinics all over Gauteng as well as from health care settings in other provinces. Thus, vast numbers of patients have been seen at the hospital, from diverse backgrounds and with various healthcare needs. Table 4.1 summarises the total number of patients seen at the TB centre from January of 2016 to October of 2018, and the outcome of each patient seen has been detailed.

Table 4.1

Overall DR TB Trends at the TB Centre

Outcome	2016	2017	2018	Total
Cured	28	19	2	49
Defaulted	8	11	0	19
Died	16	19	8	43
Transferred Out	25	29	7	61
On Treatment	40	58	66	158
Total	117	136	77	330

Note. The results for 2018 included October and not November and December as the researcher's data collection ended in October.

In terms of hearing testing, the protocol at the TB centre stipulates that patients with DR TB are to receive a hearing test at baseline, before starting any medication so that if changes to the regimen are necessary, this can be done by the doctor. Thereafter, patients attend the TB

centre for an appointment after 2 weeks, and then monthly until the medication regimen is completed. Patients are supposed to have their hearing tested at each of these follow-up appointments. This testing is done with a KUDUwave audiometer, operated by nursing staff. A flow chart of when patients should receive KUDUwave evaluations is present on the walls at the TB centre, and has been included in Appendix M.

As the audiology department does not have the appropriate infrastructure to test patients who are smear positive and contagious, patients can only receive diagnostic hearing tests with an audiometer once they are non-contagious. As such, part of the programme stipulates that patients must be booked at audiology for a full diagnostic test once they have completed treatment, and this is referred to as the exit audiogram. If complications have occurred during the course of treatment, patients can be booked for a diagnostic audiology evaluation while on treatment, but when they have been on medication long enough to no longer be contagious.

The researcher was trained at the TB centre at the start of the year, and training included how to operate the KUDUwave machinery and software. This facilitated the researcher's understanding of how the machinery functions and what is expected of the nursing staff when conducting the hearing testing. There was a head nursing sister (referred to as sister K in the transcriptions to maintain anonymity) who had worked at the TB centre for over 10 years and was experienced in hearing testing and patient management. She was responsible for training the other nurses and for establishing the ototoxicity and DR TB management programs. She has just left the hospital and no other nurse has taken her position. The head nurse's personal laptop was used to operate the KUDUwave software as previous laptops from the hospital had been stolen. When she left this year, the nurses have been unable to use the KUDUwave as no

laptop was present. In December 2018 Emoyo supplied a new laptop and the co-ordinator of TB for the province came in to re-train the nursing staff on how to operate the KUDUwave.

4.2. Phase 1: Quantitative Data

4.2.1. Trends amongst DR TB patients

From the total sample of 120 patients, 43% of patients (n = 51) had previously been treated for TB, of which 4% of these patients (n = 5) had previously been treated for DR TB. The patients previously treated for DR TB had been exposed to second line injectable drugs, while the remainder of patients were previously treated with first line anti-TB drugs. Those that were previously on TB treatment, were treated for an average of 6 months, and 54% of patients (n = 28) that had previously been treated for TB had completed the treatment course and now had experienced relapse. However, 23% (n = 12) of these patients had defaulted their TB treatment, and as such, now required DR TB treatment. The majority of patients had never been hospitalized for TB, while 4% (n = 5) had a history of hospitalization at a specialized TB hospital for tropical diseases. As the TB centre is a specialized clinic for DR TB, patient referrals came from a number of sources as detailed in Figure 4.1.

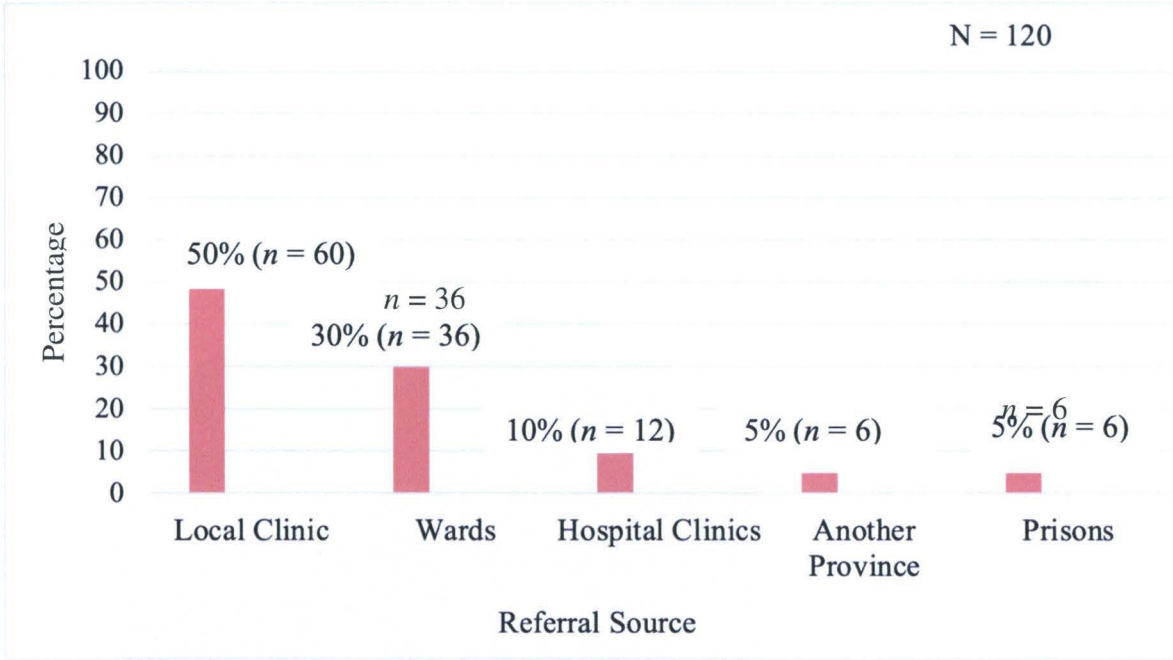

Figure 4.1. Referral Source

Note. Wards refer to patients referred from the wards at the hospital. Hospital clinics refers to referrals received from the various out-patient specialist clinics at the chosen hospital.

Figure 4.1 displays the various places that referred DR TB patients to the TB centre, represented as percentages. The majority of patients visited their local clinic prior to being referred to the TB centre. A large number of patients were referred internally, either from the 11 medical wards within the chosen hospital or from the specialist clinics within the hospital, including the HIV Clinic, or polyclinic which forms part of family medicine. Patients were also referred to the TB centre from hospitals and clinics in other provinces, and prison inmates were referred directly from the prisons.

Figure 4.2 displays the various drugs patients were given upon initiation at the TB centre. The majority of patients were initiated on ototoxic second-line aminoglycoside antibiotics upon entry in to the DR TB programme, with 81 patients on kanamycin and 1 patient on amikacin. A quarter of the sample was switched from kanamycin to PAS during treatment, due to ototoxicity or side-effects experienced on kanamycin. As illustrated in Figure 4.2, a small

portion of patients were initiated on non-ototoxic drugs such as PAS and bedaquiline from the start of treatment.

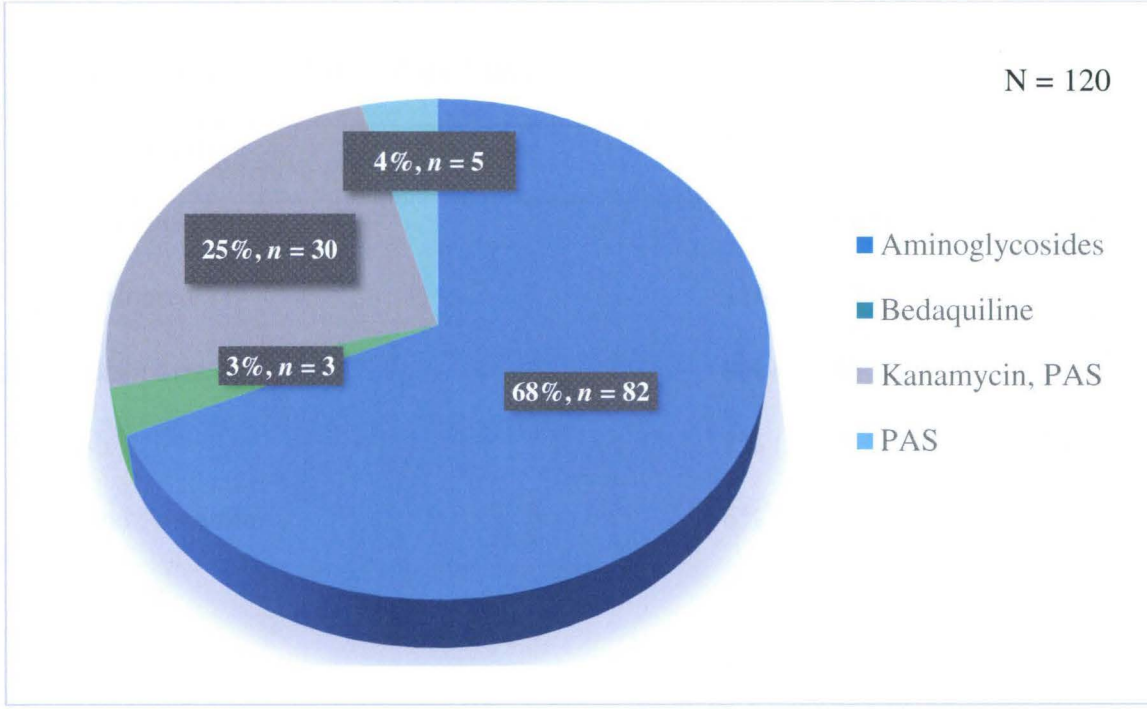

Figure 4.2. Anti-TB Drugs Patients Received at Initiation.

Note. Illustration of the different TB drugs that patients in the sample were initiated on. Aminoglycosides include kanamycin and amikacin. Kanamycin, PAS refers to patients who were initiated on kanamycin and then switched to PAS.

Aside from DR TB treatment, patients were often on short-term or long-term treatment for multiple acute or chronic conditions. In the total sample of patients (N = 120) The prevalence of acute diseases was 54% (n = 65) in comparison to the prevalence of chronic diseases which was at 49% (n = 59) thus, indicating that acute diseases were slightly more prevalent amongst DR TB patients. However, it must be noted that at least half of the sample of DR TB patients were living with a chronic disease, with 15% of people (n = 9) living with more than one chronic disease. Amongst patients with various acute diseases, 22% (n = 14) suffered from more than one acute disease. HIV has not been included in this section, as it is presented

separately further on in this chapter. The description of the different acute and chronic diseases present amongst patients in the sample has been detailed in Table 4.2 and Table 4.3.

Table 4.2

Acute Diseases in the Patient Population

Acute Diseases	Frequency in Population (N = 65)
Acute Kidney Injury (AKI)	15% (n = 65)
Disseminated TB	11% (n = 7)
Skin disorders	9% (n = 6)
Thrush	8% (n = 5)
AKI and Anaemia	6% (n = 4)
Pneumonia	6% (n = 4)
Abscess	5% (n = 3)
Gastroenteritis	5% (n = 3)
Dysphagia	3% (n = 2)
Anaemia	3% (n = 2)
Psychosis	3% (n = 2)
AKI and Disseminated TB	3% (n = 2)
Genital Herpes and Thrush	3% (n = 2)
Herpes	2% (n = 1)
Hepatitis	2% (n = 1)
Kaposi Sarcoma and Thrush	2% (n = 1)
Thrush and AKI	2% (n = 1)
Shingles	2% (n = 1)
Dysphagia and Shingles	2% (n = 1)

Thrush and Shingles	2% (n = 1)
Thrush and Motor Vehicle Accident	2% (n = 1)
Underweight	2% (n = 1)
Deep Vein Thrombosis	1% (n = 1)
Motor Vehicle Accident	1% (n = 1)

Note. The sample size is less than the total of 120 as certain patients in the sample did not have an acute disease and thus have been omitted. Disseminated TB refers to TB that affects other organs of the body aside from the lungs, such as the brain or abdomen.

As per the results in Table 4.2, the rate of opportunistic infections in the patient population was high, with 42% (n = 27) of acute diseases related to disorders of low immunity. These included thrush, shingles, hepatitis, disseminated TB, and sexually transmitted diseases such as herpes. Acute Kidney Injury (AKI) was a common acute disorder in the population, and often co-occurred with other disorders. AKI in this sample, was most often due to a drug induced complication from the DR TB medication and once adjustments were made to the medication, kidney function improved. Despite three patients in the sample presenting with dysphagia, no referrals were made to a speech therapist.

Table 4.3

Chronic Diseases in the Patient Population

Chronic Diseases	Frequency in Population (N = 59)
Hypothyroidism	22% (n = 13)
Hypertension	19% (n = 11)
Anaemia	10% (n = 6)
Hepatitis	10% (n = 6)
Kidney disease	8% (n = 5)
Diabetes and Hypertension	5% (n = 3)
Diabetes	4% (n = 2)
Psychiatric disorders	4% (n = 2)
Cancerous Mass	3% (n = 2)
Liver dysfunction	3% (n = 2)
Epilepsy	3% (n = 2)
Asthma / Allergies	3% (n = 2)
Cerebro-Vascular Accident (CVA)	2% (n = 1)
Cholesterol	2% (n = 1)
Hypertension and Hypothyroidism	2% (n = 1)

Note. The sample size is less than the total of 120 as certain patients in the sample did not have a chronic disease and thus, have been omitted. Cancerous mass includes Non-Hodgkin's Lymphoma as well as Kaposi Sarcoma.

The results from Table 4.3 revealed that hypothyroidism was the most common chronic disease amongst DR TB patients. There was a high rate of non-communicable diseases such as hypertension, diabetes, cholesterol, and anaemia amongst patients in the sample, with 41% (n = 24) of people presenting with one or more of these diseases. Hepatitis, and organ

dysfunction in the kidneys or liver, were also relatively common in the sample. A chi-square test of association was conducted to test whether a relationship existed between having hypertension and developing ototoxic hearing loss. There was found to be no significant relationship between hypertension and ototoxicity within this sample, χ^2 (1, N = 120) = 1.662, $p > 0.05$ and as such, hypertension did not appear to increase the risk for ototoxicity in the current sample.

Table 4.4

Social Habits Amongst Patients

Lifestyle Factors	Probability
Smoking	27% (n = 30; N = 113)
Alcohol consumption	22% (n = 23; N = 105)

In terms of lifestyle choices, a minority of patients from the total sample either smoked or consumed alcohol. From the total sample of patients who drank alcohol, 44% (n = 10) were heavy drinkers, drinking during the week as well as consuming 3 to 4 bottles of alcohol over the weekend. A chi-square test of association was conducted to ascertain whether the consumption of alcohol was associated with the development of ototoxicity during DR TB treatment. There was found to be no significant relationship between the two, χ^2 (1, N = 105) = 2.475, $p > 0.05$ which meant that drinking alcohol in this sample, did not relate to acquiring ototoxicity.

Within the sample, 47% of patients (n = 54) had children, most of whom resided with the patients as the children were below 7 years of age. Half of the patient sample was single, and half of the patient sample was in a relationship either with a partner or a spouse, thus resulting

in them having social support during treatment. One patient in the sample experienced stigma in her family home, whereby, her sister-in-law refused to live with her because of her DR TB diagnosis. As such, she had to relocate and reside elsewhere while on treatment. The majority of the patients were South African citizens (88%, n = 105) and the remainder of patients were citizens of other African countries such as Zimbabwe, Botswana and Malawi. Food security was emphasized during DR TB treatment, and referred to whether patients had sufficient food to survive on a daily basis. In the total patient sample, 47% of patients (n = 56) had no food security, with 16% of people (n = 19) requiring grant applications to buy food so that their DR TB medication was not taken on an empty stomach. In terms of the level of education of patients, 75% had received a secondary level of education (n = 74) and 14% had a tertiary level of education (n = 14). No formal education was present in 3% of patients (n = 3) while 8% (n = 8) had primary school education.

Due to the high levels of concomitant diseases, patients often required referrals to other professionals during treatment. These referrals were made by the doctors when they saw the patients at their follow-up appointments. A third of the total sample of 120 patients (n = 37) did not require any referrals to other professionals, and thus, received counselling as part of the standard treatment procedure at the TB centre. The remaining 83 patients who required referrals, and the professionals that they consulted for treatment, have been detailed in Table 4.5.

Table 4.5

Referrals to Other Professionals

Professionals	Frequency (n = 83)
Social work	31% (n = 26)
HIV clinic	20% (n = 17)
Dietician	19% (n =16)
Multiple referrals	19% (n = 16)
Medical specialists	11% (n = 9)

Note. Multiple referrals refer to patients who required consults from more than one of the following professionals: social work, HIV clinic, and dieticians.

The greatest number of referrals was to social work, as patients required grant applications to pay for their medication and for transport to the TB centre. Three patients in the sample were South African citizens but did not have ID documents, either because they were prisoners or had no access to the application process. Other patients were foreigners and did not qualify for South African disability grants. Those patients who did not qualify for grants or had no documents to apply for them, were then referred by the social workers for food parcels at the local clinics. The social workers also followed up regarding patients who defaulted their medication and appointments, to ascertain where the problem was and how best to remediate it. They also provided general counselling for patients struggling with the acceptance of their DR TB diagnosis.

Patients referred to HIV clinic often required counselling regarding their HIV diagnosis in order to begin ARV treatment. Others who had defaulted their ARV treatment, and had a high viral load of HIV were referred to the clinic for re-counselling on the importance of adherence. Dieticians were required by patients who had displayed dramatic weight loss during DR TB

treatment, or who displayed symptoms of malnourishment. A portion of patients required referrals to medical specialists which included gynaecologists, orthopaedic surgeons and dermatologists. More significantly, dermatologist referrals were required as patients displayed symptoms of Kaposi Sarcoma, which is a complication of poor immunity, commonly associated with HIV infection. The majority of DR TB patients in the sample were HIV positive, as displayed in Figure 4.3.

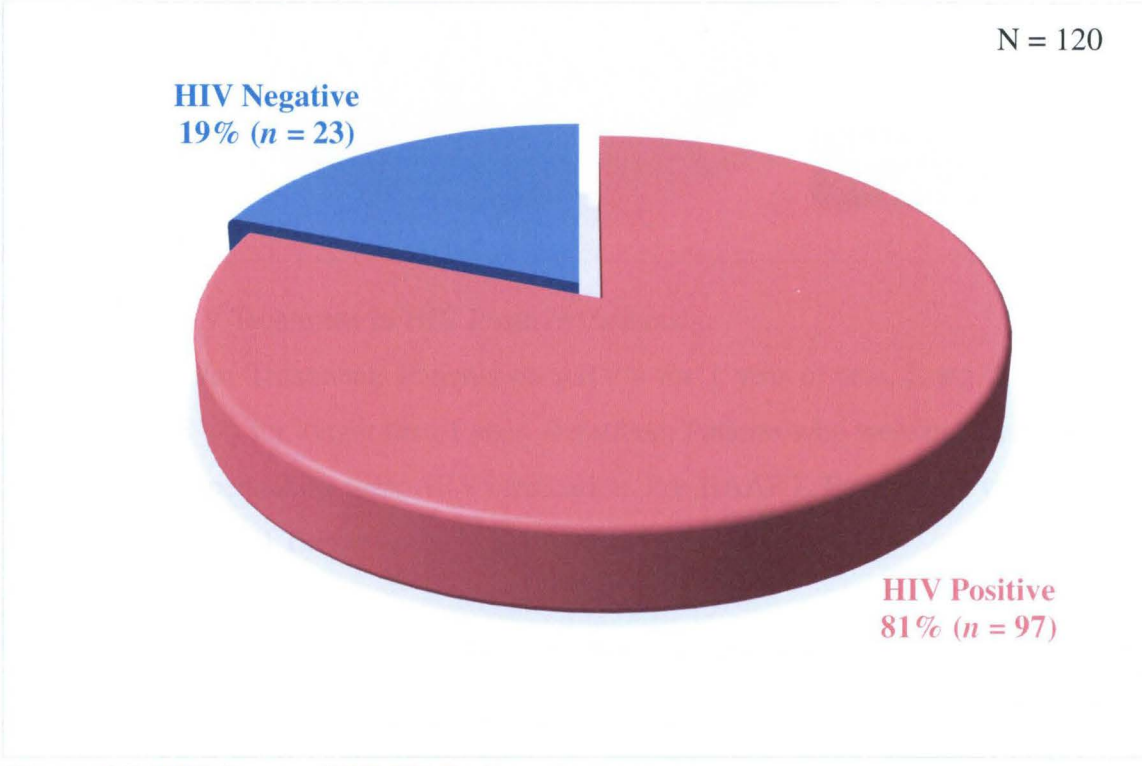

Figure 4.3. HIV Status of DR TB Patients

The majority of patients who were HIV positive, were aware of their diagnosis upon entering the program, however, approximately 30 patients were unaware that they had HIV, and found out when the testing was done upon initiation at the TB centre. At this point patients were then given HIV counselling in conjunction with DR TB counselling, and were initiated on ARV's by the doctors. As a large proportion of the patient sample was concurrently treated for HIV, Figure 4.4 below represents whether or not patients were on ARV treatment when initiated on DR TB medication.

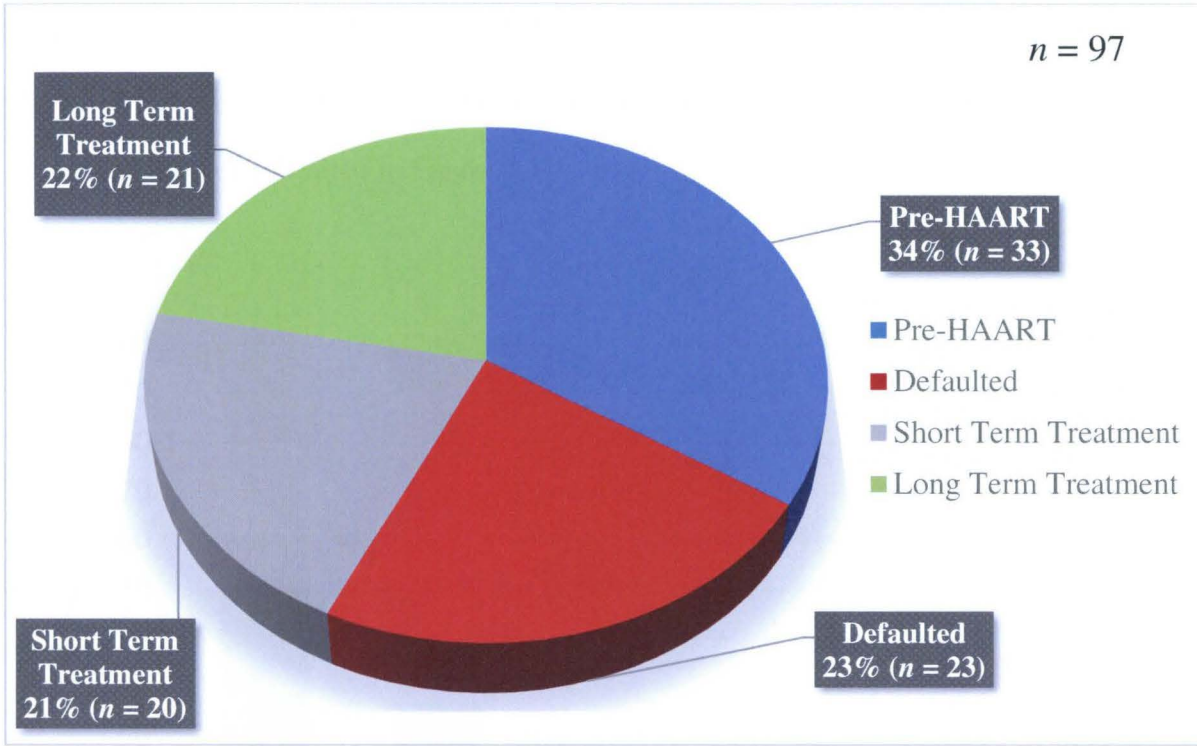

Figure 4.4. ARV Treatment in HIV Positive Patients.

Note. Short Term Treatment: Patients on ARV's for 1 year or less, Long Term Treatment: Patients on ARV's for longer than 1 year. Defaulted: Patients who were not on ARV treatment as they had stopped taking their ARV medication. Pre-HAART: Patients are yet to start Highly Active Antiretroviral Therapy.

The sample size reflected in Figure 4.4 is smaller than 120, as patients who were HIV negative have been omitted from this sample. The majority of patients in the sample were Pre-HAART, as they were HIV positive, but had not yet been initiated on ARV treatment. This was either because patients were unaware of their HIV status or they had not pursued treatment, despite having knowledge of their diagnosis. The second largest portion of the sample had defaulted ARV treatment, and when they were initiated at the TB centre, were not on ARV's, often having a high HIV viral load. Therefore, overall, 57% of patients (n = 55) were not on ARV treatment when entering the DR TB programme and a small portion of the sample had been on ARV's for long periods of time. The outcome of patients initiated within the DR TB

programme at the TB centre was documented and tracked for both national health surveillance as well as for internal statistics. A synopsis of the outcome of patients included in this sample (N = 120), has been detailed in Figure 4.5

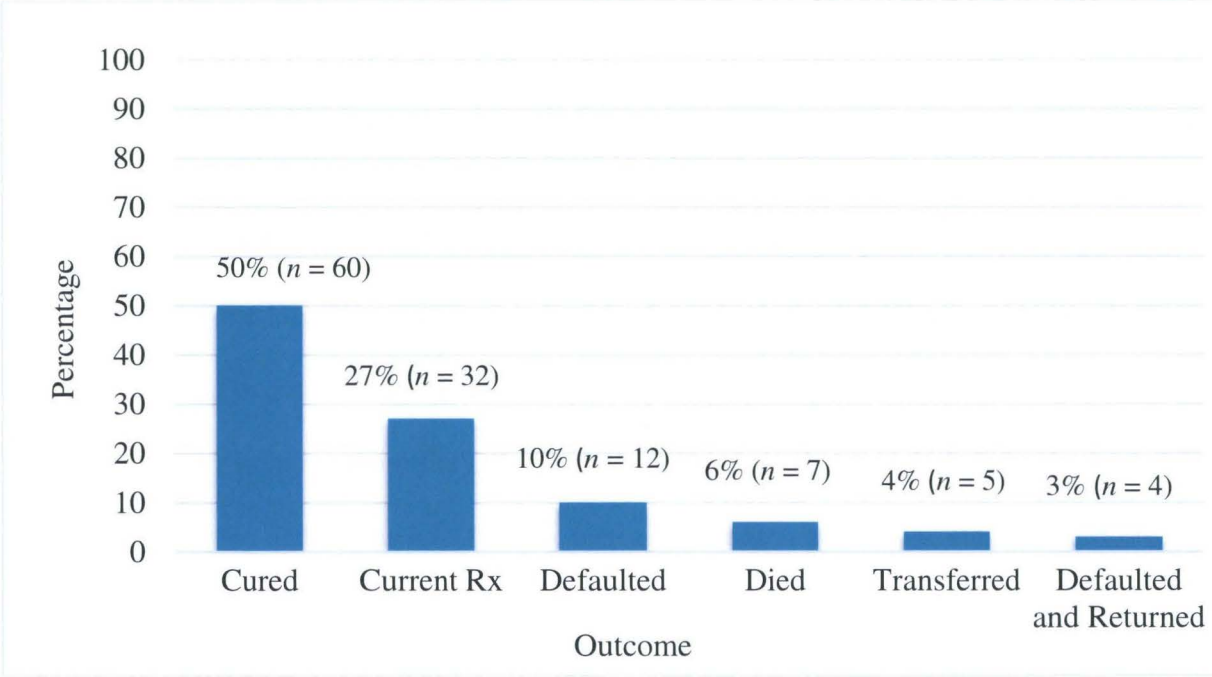

Figure 4.5. Patient Outcome.

Note. Cured: patients who were treated for DR TB and exited the programme cured of the disease. Current Rx: patients who were still on treatment. Defaulted: those who stopped attending their appointments at the TB centre, despite not yet being cured of DR TB. Transferred: patients referred to another hospital to continue their DR TB treatment. Defaulted and Returned: patients who stopped following up with their treatment, only to return at a later date.

Half of the patients in the sample were cured of DR TB, while approximately a third of patients were still on treatment. The TB centre attempted to contact the patients who defaulted via the social worker who works at the clinic, however, despite phone calls and attempts to track down these patients via their next of kin, these individuals did not return to continue their treatment. A small number of patients were transferred out to Sizwe Hospital and this was due to treatment complications such as a patient being pregnant and a patient who did not show

response to DR TB treatment. One of the patients that defaulted and returned was incarcerated during the interim, and as such, defaulted his medication until the prison re-referred him back to the TB centre. Other patients returned after having travelled to other African countries to visit family, without notifying the team at the centre.

4.2.2. Audiological findings

This section of results addresses the trends in hearing amongst patients receiving ototoxic drugs as part of the DR TB programme. Results from both the KUDUwave testing that was conducted during treatment, as well as from standard audiometry on a GSI audiometer that was conducted upon discharge from the DR TB programme, have been included. Table 4.6 below provides a summary of both the KUDUwave testing sessions as well as the standard audiometry sessions.

Table 4.6

Summary of Each Audiological Test Conducted and Recorded in Files

Test Type	Number of Patients (N = 120)	Average Days Between Tests
Baseline	77	2.2
Repeated baseline	5	0
Follow up test 1	119	41.1
Follow up test 2	94	58.17
Follow up test 3	58	81.53
Follow up test 4	34	67.88
Follow up test 5	17	97.41
Follow up test 6	4	35.5
Follow up test 7	1	85
Follow up test 8	1	85
Audio Diagnostic test 1	28	115.45
Audio Diagnostic test 2	4	28
Audio Diagnostic test 3	1	28

Note. Summary of each hearing test, the number of patients who had the test and the average time in days between each test. Baseline, Repeated baseline and Follow-up tests 1 – 8 were all done using a KUDUwave audiometer. Audio Diagnostic tests 1 – 3 were conducted using a standard GSI audiometer.

The results displayed in Table 4.6 revealed that at baseline, 35% of patients (n = 42) did not receive a hearing test when initiated on ototoxic injectable drugs. Certain patient files had motivations for why the baseline assessments were not conducted. These reasons included that patients were initiated on kanamycin at other hospitals before referral to the TB centre, and as

such, either the assessment was not conducted at the other hospitals or the results were not included in the hospital transfer paperwork. Other patients were transferred to the TB centre after the injectable phase of treatment had already ended. Aside from these, reasons specific to the context of the TB centre included that the KUDUwave was either broken or that patients were admitted into the general wards when initiated on kanamycin and were not referred by the ward doctors to the centre for baseline assessment. In the majority of cases however, no reason was stated as to why the baseline assessment was not done. This was especially noted in patients that began their treatment at the TB centre, and yet still did not have a baseline assessment.

Most of the participants who received a baseline audiogram had the test conducted on day 0 when initiated on treatment. However, 16 of the 77 participants received the baseline testing after initiation on kanamycin. Ten of these patients only received the baseline hearing test 2 weeks after commencing the injectable treatment. On average, patients received follow-up testing within a time period greater than 30 days, and the average days between each test increased in length the further the patient was into the treatment regimen.

In terms of the diagnostic audiological evaluations, there was on average, 115,5 days between the last KUDUwave test and the evaluation at audiology, as patients received the diagnostic test after the completion of DR TB treatment, when ready for discharge from the programme. A small number of patients returned for a second or third follow-up diagnostic assessment, and these patients were either referred for an ENT appointment followed by a re-test or received a re-test as part of the work-up for hearing aids. The remaining patients were either referred to their local clinics to access hearing aids or were counselled regarding ototoxic

hearing loss and informed regarding the value of annual hearing monitoring. The audiologist's recommendations given after the diagnostic session will be detailed further on in this chapter.

4.2.2.1 Results from KUDUwave testing

The KUDUwave audiometer was operated on automatic mode by the nurses, which meant that they did not require training on threshold searching in order to operate the test. The nurses were required to place the ear cups and insert foam plugs as well as instruct the patients for testing. They were also required to operate the software on the computer so that the correct tests were selected, and the patient data was inputted. The KUDUwave recorded various statistics during testing including how many times the tester presented and no response was given from the patient, and the number and percentages of false positives during testing, where patients would press the button despite no sound being presented by the machine. The KUDUwave also displayed the number of frequencies and presentations that occurred in noise, as well as a figure of true positives, which reflected the number of reliable responses given by the patient during the test sitting. While no specific trends in these measurements could be found, it was noted that patients who were more difficult to test, often had very large numbers of presentations without response, indicating that the response button was pressed many times by the patient, when the machine was not presenting any sounds.

The mean hearing thresholds obtained from the KUDUwave testing at baseline as well as at follow-up sessions have been detailed in Figure 4.6 and Figure 4.7 for the left and right ears respectively. It must be noted that test results from the third follow-up session onwards have been omitted from the analysis, as the sample size of patients that had a third follow-up session was less than half of the total sample size. The sample size continued to decrease at the

following assessment sessions, and this trend can be seen in Table 4.5 displayed previously. The diminished sample size rendered the results from other follow-up sessions as not an accurate reflection of the total sample of patients. As such, Figure 4.6 and Figure 4.7 denote the hearing thresholds obtained at the baseline and the first two follow-up testing sessions.

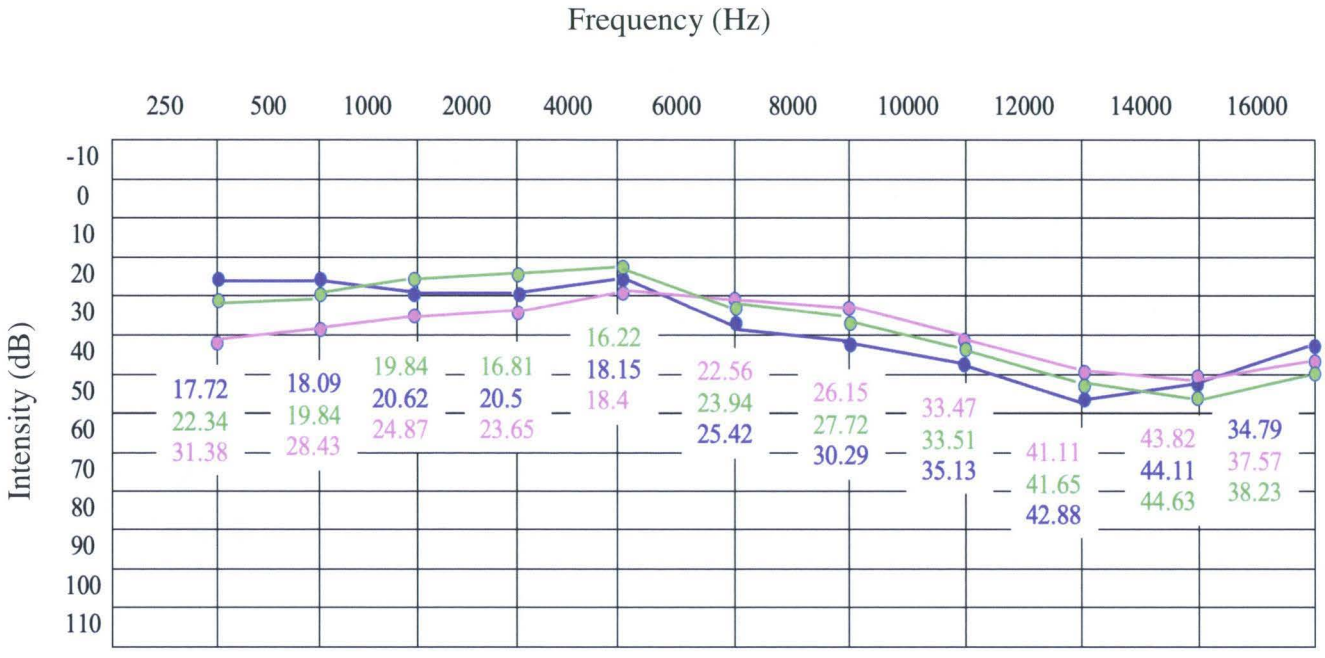

Figure 4.6. Average KUDUwave Results for 3 Follow-up Tests in the Left Ear

KUDUwave Baseline Assessment, $n = 78$

KUDUwave Follow-up 1, $n = 119$

KUDUwave Follow-up 2, $n = 93$

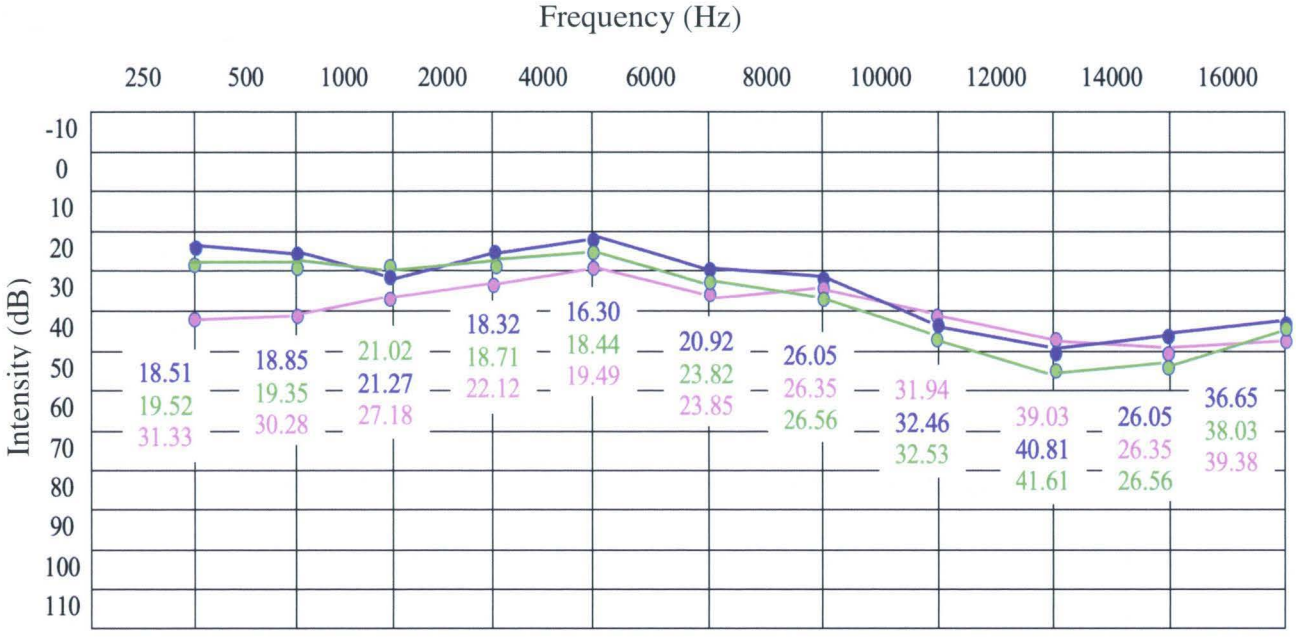

Figure 4.7. Average KUDUwave Results for 3 Follow-up Tests in the Right Ear

KUDUwave Baseline Assessment, $n = 78$

KUDUwave Follow-up 1, $n = 119$

KUDUwave Follow-up 2, $n = 93$

Figures 4.6 and 4.7 represent the mean hearing thresholds per frequency for the baseline KUDUwave test and for the two follow-up tests. It must be noted that thresholds for the low frequencies of 250 Hz and 500 Hz were not always assessed. Merely 30 patients out of the total of 78 who received baselines, had these low frequencies tested, and 47 out of 119 patients had the low frequencies assessed at the next follow up session. At the second follow-up test, 15 out of 57 patients had their hearing thresholds assessed at 250 Hz and 500 Hz.

When evaluating the mean thresholds obtained by the KUDUwave audiometer, it is noted that the thresholds at baseline assessment in both the right and the left ears, are significantly lower in comparison to the thresholds obtained at the follow-up sessions. This is indicative of hearing being worse at baseline than at follow-up sessions where hearing is noted to improve.

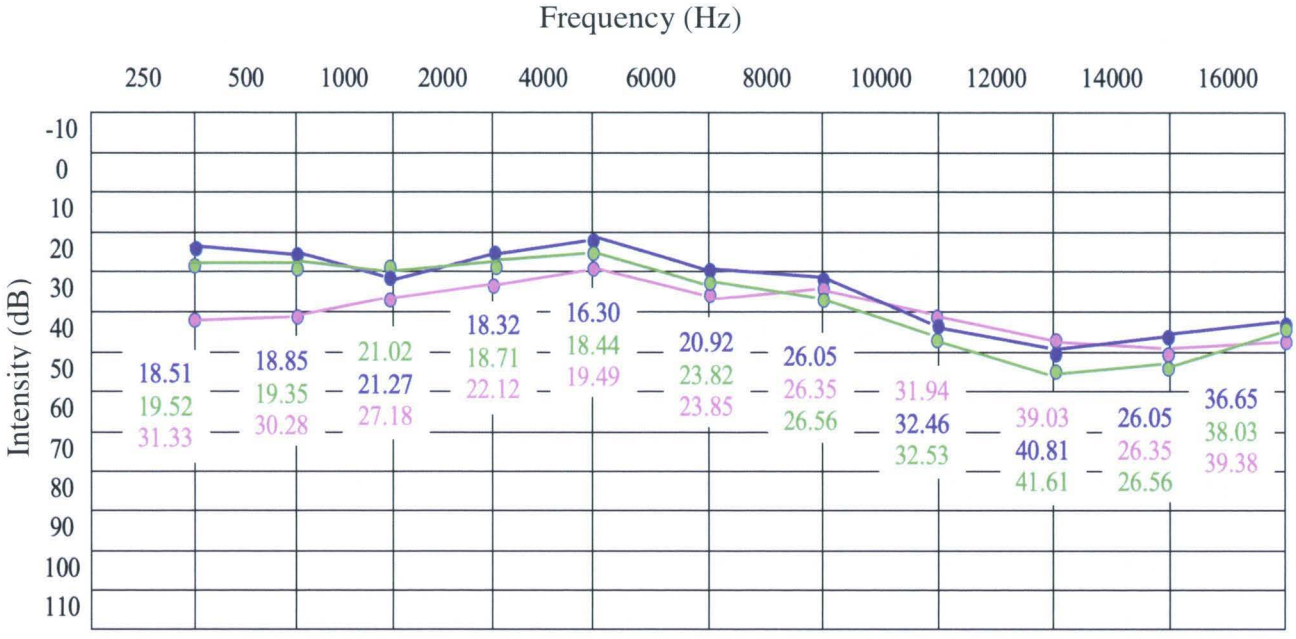

Figure 4.7. Average KUDUwave Results for 3 Follow-up Tests in the Right Ear

KUDUwave Baseline Assessment, $n = 78$

KUDUwave Follow-up 1, $n = 119$

KUDUwave Follow-up 2, $n = 93$

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When evaluating the mean thresholds obtained by the KUDUwave audiometer, it is noted that the thresholds at baseline assessment in both the right and the left ears, are significantly lower in comparison to the thresholds obtained at the follow-up sessions. This is indicative of hearing being worse at baseline than at follow-up sessions where hearing is noted to improve.

The trend is particularly noted at the lower frequencies, at 250 Hz and 500 Hz, where the baseline thresholds are within the range of a mild hearing loss (thresholds greater than 25 dB). However, by the second and third follow-up sessions, these results return back to being within normal limits (less than 25dB). Frequencies up until 4000 Hz bilaterally, reveal worse thresholds at baseline, and then improvement at follow-up sessions.

The overall configuration of results in this population is sloping, whereby, hearing thresholds are notably lower within the ultra-high frequency range where ototoxicity typically manifests. Aside from baseline results, the results for the two follow-up sessions reveal hearing within normal limits from 250 Hz to 6000 Hz bilaterally, with a mild loss present in both ears at 8000 Hz. While the results between the two ears appear to be symmetrical, the thresholds in the left ear seem to be worse in comparison to the right ear, particularly within the ultra-high frequency range. At each testing session, the patient's report of hearing functioning was recorded by the nurses, with details of any symptoms of hearing loss or ear related pathology reported by the patient. This has been displayed in Table 4.7.

Table 4.7

Patient Report of Hearing Function

Test Type	Patient Report				Hearing Loss Detected
	Normal	Middle Ear Symptoms	Hearing Loss	Not Done	
Baseline (n = 78)	56% (n = 44)	5% (n = 4)	12% (n = 9)	27% (n = 21)	36% (n = 28)
Follow Up 1 (n = 119)	57% (n = 68)	4% (n = 5)	12% (n = 14)	27% (n = 32)	63% (n = 75)
Follow Up 2 (n = 94)	46% (n = 43)	3% (n = 3)	14% (n = 13)	37% (n = 35)	73% (n = 69)

Note. The patient report of hearing functioning has been detailed according to baseline and follow-up sessions, in percentages. This has been compared to The Hearing Loss Detected column, which represents when hearing loss was physically present on KUDUwave test results. Not Done: cases where the patient report was not recorded by nursing staff

The findings in Table 4.7 revealed that the majority of patients, both at baseline and at follow-up sessions, reported their hearing to be within normal limits. This was despite hearing loss being detected with the KUDUwave audiometer, in situations where patients had reported no symptoms of hearing loss. When hearing loss was reported by patients, it was most likely to be general symptoms of hearing loss such as difficulty hearing or the experience of tinnitus. Middle ear symptoms represented signs of conductive pathology such as aural fullness, otalgia, and itching ears, and this was the least common report amongst patients at all testing sessions. Approximately a third of results at each testing session did not have the patient's report of hearing function attached to the KUDUwave results. This missing information gave rise to

there being little to no case history information attached to the puretone KUDUwave results, affecting the decision-making process of the audiologists reporting on the results. Aside from the patient report of hearing functioning, the audiologists were required to report on the KUDUwave results, when they were sent upstairs to audiology for analysis. Table 4.8 below represents the audiologist's report of hearing thresholds, after the testing was conducted by the nursing staff at the TB centre. The recommendations made by the audiologist based on the KUDUwave results have also been detailed in Table 4.8.

Table 4.8

Audiologist Report of KUDUwave Results

Test Type	Reported by Audiologist		Audiologist Recommendation			
	Yes	No	Unreliable	Adjust Meds	Monitor	Test High Frequencies
Baseline ($n = 77$)	88% ($n = 68$)	12% ($n = 9$)	13% ($n = 10$)	38% ($n = 29$)	32% ($n = 25$)	8% ($n = 6$)
Follow-up 1 ($n = 119$)	92% ($n = 109$)	8% ($n = 10$)	3% ($n = 4$)	34% ($n = 40$)	51% ($n = 61$)	1% ($n = 1$)
Follow-up 2 ($n = 94$)	89% ($n = 84$)	11% ($n = 10$)	4% ($n = 4$)	40% ($n = 36$)	46% ($n = 42$)	0%

Note. Adjust Meds: the DR TB medication required changing, likely to bedaquiline as ototoxic shifts had been noted. Monitor: no ototoxicity was present, and thus, monitoring of hearing was necessary. Test High Frequencies: the ultra-high frequencies beyond 8000 Hz were not tested, thus, testing of these frequencies was recommended.

While the majority of KUDUwave results were reported on by an audiologist, 32% (n = 29) of results across all of the testing sessions were not interpreted by an audiologist, despite this being part of the established protocol. One patient at every test session above, had their KUDUwave testing results reported on by the audiologist on a date much later than when the testing was conducted. This often happened when the doctor noticed that the results had not been sent to the audiologists and then requested that the results be sent upstairs to audiology for interpretation. At times, when audiologists detected an ototoxic shift and recommended a change in medication, doctors did not agree with the recommendation and continued kanamycin, referring regularly for KUDUwave monitoring. If results were reported as unreliable, the audiologist expected the testing to be repeated.

In terms of the audiologist report, the baseline test had the highest rate of results reported as unreliable, however, as the patients returned for follow-up sessions, this number decreased significantly. Audiologists deemed results unreliable if there was no indication of middle ear pathology, yet patients presented with a significant loss as the lower frequencies. If the case history information displayed no link to the severity of hearing loss reflected on the KUDUwave test results, they were interpreted as unreliable. The baseline session had the highest number of patients who did not receive ultra-high frequency testing as part of the KUDUwave test battery. This resulted in difficulties for the audiologist in ascertaining at the next follow-up, if results in the higher frequencies were related to ototoxic shifts or were representative of normal hearing levels for that specific patient. By the third test, however, the ultra-high frequencies were tested for all patients, illustrating that the audiologist recommendation to test the high frequencies was adhered to by nursing staff.

The type of hearing loss that patients presented with at each testing session was classified into the following categories: hearing within normal limits, the presence of hearing loss in the speech spectrum frequencies of 250 Hz to 8000 Hz, and the presence of ototoxic shifts in the ultra-high frequencies from 9000 Hz to 16 000 Hz. Unfortunately, hearing loss could not be classified according to conductive loss, mixed hearing loss, and sensori-neural hearing loss, as bone conduction results were not available for the majority of KUDUwave assessments. At baseline assessment and at the first follow-up sessions, the majority of patients presented with hearing that was within normal limits. During the second follow-up session, 43% of patients (n = 41) which constituted the majority, presented with ototoxic shifts in the ultra-high frequencies. Following this, hearing loss in the frequencies from 250 Hz to 8000 Hz was the second most common type of loss at the second follow-up session. The type of hearing loss between the two ears was relatively similar, indicative of symmetry between the two ears. Five out of the 10 patients in the sample had repeated baseline assessments on the same day as the initial test, as the audiologists had deemed the initial results to be unreliable. Only one patient had the low frequencies of 250 Hz and 500 Hz tested at the repeated baseline assessment. Furthermore, following the re-test, there did not seem to be much change in hearing thresholds and in fact, patients tended to perform worse in the lower frequencies at the second repeated test.

4.2.2.2. Results from diagnostic audiometry

The results in this section represent the audiological results obtained at the exit diagnostic assessment, conducted by an audiologist in a sound-proof booth using a standard GSI audiometer. The results from the first diagnostic hearing test have been used, as only four patients had a second follow-up diagnostic test, and one received a third test. As such, the first

diagnostic test reflected the most information required for statistical analysis. The mean hearing thresholds for the left and right ears across the frequency spectrum, have been represented in Figure 4.8 and Figure 4.9 respectively.

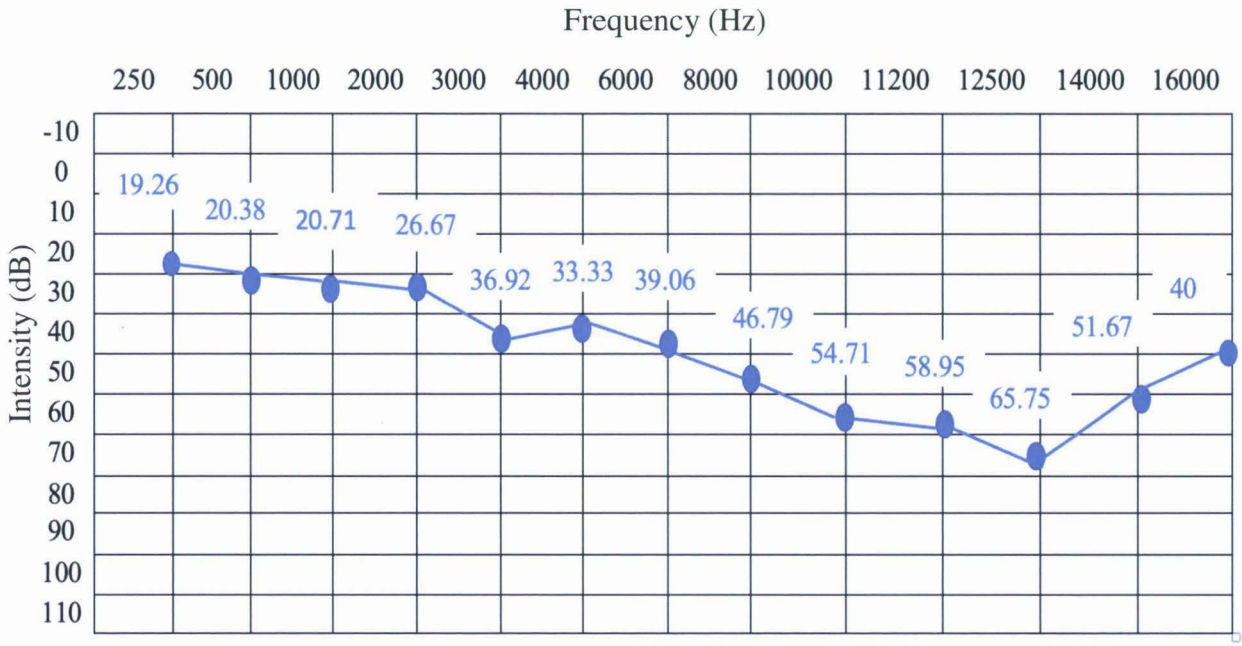

Figure 4.8. The Average Audiogram Results for the Left Ear

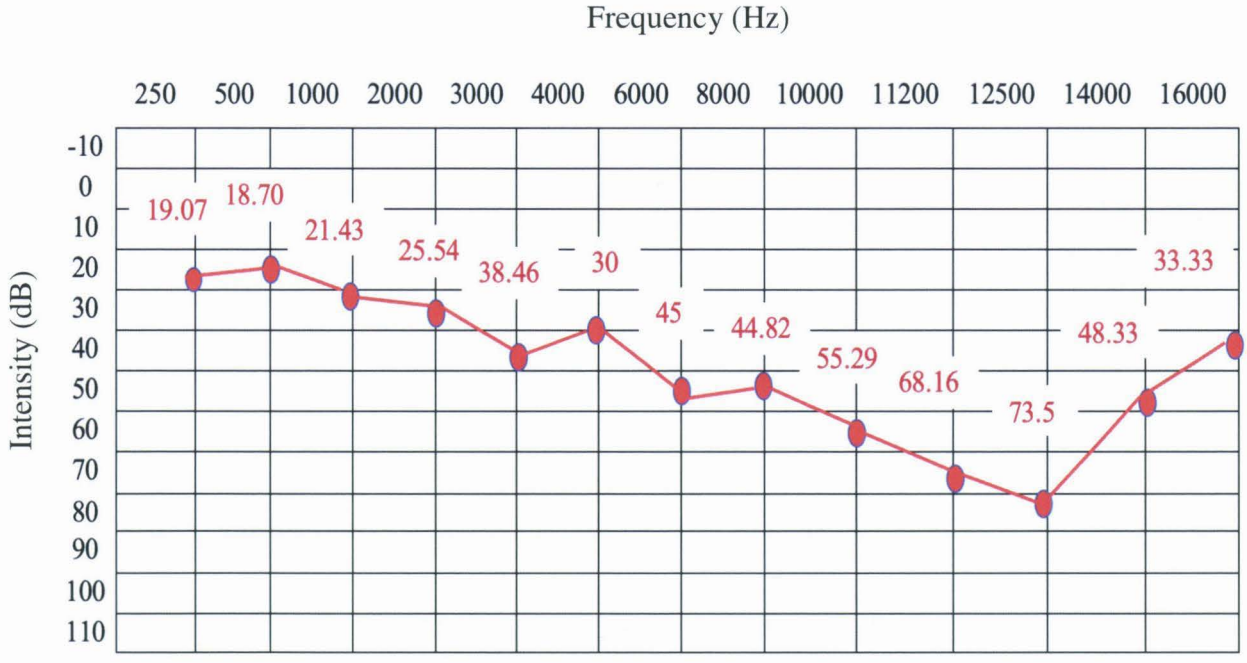

Figure 4.9. The Average Audiogram Results for the Right Ear

Figures 4.8 and 4.9 represent the mean hearing thresholds for the frequencies spanning from 250 Hz to 16 000 Hz, and 28 individuals out of the total sample of 120 received this testing. The frequency spectrum included irregular frequencies such as 11 200 Hz and 12 500 Hz, as this is part of the ultra-high frequency testing protocol on the GSI audiometer. The audiograms plotted in the two figures above, revealed a sloping configuration of hearing loss, whereby hearing loss was noted from 3000 Hz onwards in both the left and right ears. Thus, hearing loss had not only affected the ultra-high frequencies, but frequencies within the speech spectrum.

Hearing appeared to be symmetrical between the two ears, and hearing loss could not be classified according to type, as bone conduction results were not available for all diagnostic tests. Out of the total sample, only 14% of patients (n = 4) had bone conduction testing conducted on 1 or both ears. The most severe loss was noted at 12 500 Hz in both ears and thereafter a recovery in thresholds was noted at 14 000 Hz and 16 000 Hz bilaterally. Due to absent bone conduction testing, the results were classified according to the following: hearing within normal limits, ototoxic shifts in the ultra-high frequencies and hearing loss in the speech spectrum in frequencies from 250 Hz to 8000 Hz. It was noted that in 36% of cases (n = 10), patients presented with different patterns of hearing loss between the two ears. In left ears, hearing loss which affected the speech spectrum was most common, with 43% of patients (n = 12) displaying this pattern of loss, while in right ears, significant ototoxic shifts and hearing loss in the ultra-high frequencies was present in 32% of cases (n = 9). Left ears had a higher rate of displaying hearing within normal limits with 29% of patients (n = 8) with normal hearing, in comparison to 21% (n = 6) of right ears displaying hearing within normal limits.

Table 4.9

Indications of Ear Pathology

Result	Prevalence
Hearing loss reported	57% (n = 16; N = 28)
Abnormal Tympanometry	17% (n = 4; N = 24)
Cerumen occlusion on otoscopic exam	14 % (n = 4; N = 28)

Note. Three patients in the sample did not have tympanometric testing conducted, and thus, the sample size for abnormal tympanometry differs.

As per Table 4.9, in terms of case history factors the majority of the sample reported symptoms of hearing loss including tinnitus and decreased hearing acuity, while the remaining patients reported having hearing that was within normal limits. Amongst patients who had no concerns regarding their hearing, 27% of them (n = 3) in fact, presented with hearing loss in the speech spectrum, in the frequencies ranging from 250 Hz to 8000 Hz. The presence of middle ear pathology upon otoscopic examination and tympanometry, was relatively uncommon.

Table 4.10

Decision Made After Diagnostic Evaluation

Outcome	Probability
Counselling and annual monitoring	64% (n = 18; N = 28)
ENT referral	17% (n = 5; N = 28)
Hearing aids	11% (n = 3; N = 28)
Inappropriate discharge	7% (n = 2; N = 28)
Difficult to assess	7% (n = 2; N = 28)

Note. Inappropriate discharge: the patient was discharged from audiology when further intervention was still warranted. Difficult to assess: these patients were difficult to test both at diagnostic testing and during KUDUwave tests.

Following diagnostic testing, the majority of patients were counselled regarding hearing loss and DR TB treatment, and were told to assess their hearing annually or return should there be a change in hearing. This was necessary as hearing loss was noted in the higher frequencies amongst these patients, beyond the frequency range in which hearing aids could be of benefit. ENT referrals were necessary where tympanometric results were abnormal or middle ear pathology was indicated. In one such case, the patient presented with unilateral hearing loss and tinnitus, with 0% speech discrimination in the pathological ear, warranting an urgent ENT referral for retro-cochlear investigations. A smaller portion of the sample was referred for hearing aids and some patients were discharged by the audiologist while still on DR TB treatment. Certain patients who were difficult to test on the KUDUwave also displayed difficulties at diagnostic evaluation.

A total of 59 patients out of the sample of 120 were cured of DR TB and should have received an exit audiogram before leaving the programme, however, 46 of these patients did

not receive an exit diagnostic assessment. In terms of testing protocols for the overall sample of 28 patients that received diagnostic audiometry, 10% of patients (n = 3) did not have tympanogram testing and 28% of patients (n = 8) did not receive extended high frequency audiometry. This was despite seven of these patients presenting with ototoxicity during the KUDUwave testing conducted throughout the course of treatment. These patients simply received assessments from 250 Hz to 8000 Hz, the standard frequency range for hearing testing. This is significant, as according to Figures 4.7 and 4.8, the most significant decline in hearing was noted in the ultra-high frequencies, beyond 8000 Hz. Speech audiometry was only performed in 7 out of 28 patients, with the remainder only having received puretone audiometry.

Twenty three patients entered the DR TB programme with a pre-existing hearing loss, however, only nine of these patients were referred for an exit diagnostic audiological evaluation, with two of the nine patients defaulting the appointment booked at audiology. Therefore, 70% (n = 16) of patients with hearing loss, inclusive of the two patients who defaulted the final appointment, were lost to the system and did not receive further audiological intervention, despite having pre-existing hearing difficulties. Furthermore, 26% (n = 24) of patients who were detected as having ototoxic hearing loss during KUDUwave testing, and 57% (n = 52) of patients who presented with hearing loss affecting the speech frequencies from 250 Hz to 8000 Hz, were not referred for diagnostic audiometry. Lastly, a total of four patients did not arrive for diagnostic audiometry, and one patient was not booked for it despite the doctor specifically requesting for the assessment.

4.2.2.3 Trends in ototoxicity

The purpose of KUDUwave testing during treatment was to detect the presence of ototoxicity early, so that patients could either be placed on bedaquiline, or alternative medication adjustments could be made. In 47% of patients ($n = 56$) out of a total sample of 120, ototoxicity was noticed at the first follow-up KUDUwave test. This was on average, conducted 41 days after the initial baseline assessment, as displayed in Table 4.6 earlier in the chapter. Following the first test, ototoxicity was then most commonly detected at the second follow-up test, as displayed in 22% of patients ($n = 26$). As such, within the sample of this study, ototoxic shifts occurred fairly early on in DR TB treatment for patients on kanamycin treatment. Figure 4.10 below represents the presence of ototoxicity within the sample

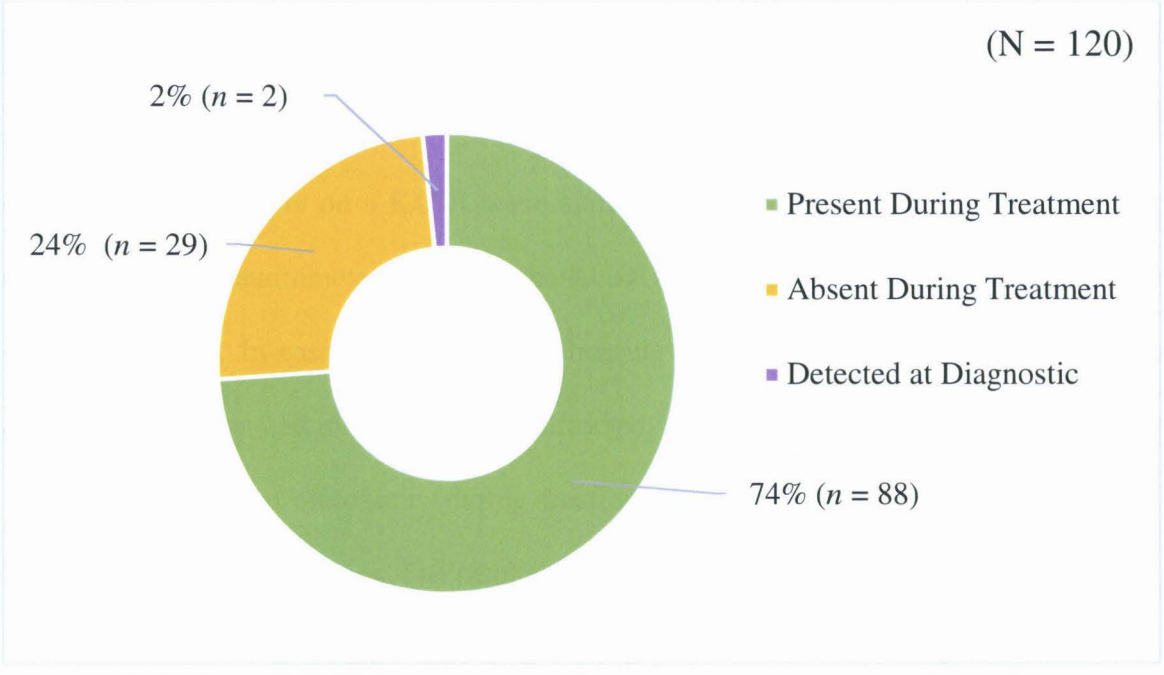

Figure 4.10. Prevalence of Ototoxicity in the Sample.

Figure 4.10 is an illustration of whether ototoxicity was present or absent amongst patients during DR TB treatment. If ototoxicity was noted, it was either detected during treatment at the KUDUwave follow-up tests or at the end of treatment, at the exit diagnostic audiological evaluation. Almost a quarter of the sample did not present with ototoxic hearing loss during

treatment, despite the fact that the majority of these patients (90%, $n = 26$) were exposed to kanamycin during treatment. Amongst the patients who were on kanamycin treatment but did not develop ototoxicity, certain trends were noted which will be discussed in further detail in Chapter 5. One patient entered the DR TB programme with pre-existing ototoxic hearing loss due to previous DR TB treatment. However, the bulk of patients developed ototoxic hearing loss during treatment, as ototoxic shifts in hearing occurred when exposed to kanamycin treatment. These ototoxic shifts were noted at KUDUwave hearing monitoring tests during the course of treatment.

The Pearson chi-square test of association was conducted to examine the relation between the presence of ototoxicity at KUDUwave testing and the presence of ototoxicity when a standard GSI audiometer was used at the exit diagnostic session. The relation between these two sessions was significant, χ^2 (1, N = 28) = 15.46, $p < 0.05$. Therefore, this meant that the detection of ototoxicity on a KUDUwave audiometer correlated with it being detected on a standardized GSI audiometer. As such, the KUDUwave audiometer is able to detect ototoxic shifts in hearing. In cases where ototoxic hearing loss was detected, analysis was done to establish which ear was most likely to be affected. The sample did not include the 29 patients who did not develop ototoxicity during treatment as well as the one patient who had pre-existing ototoxic hearing loss. The results are presented in Figure 4.11.

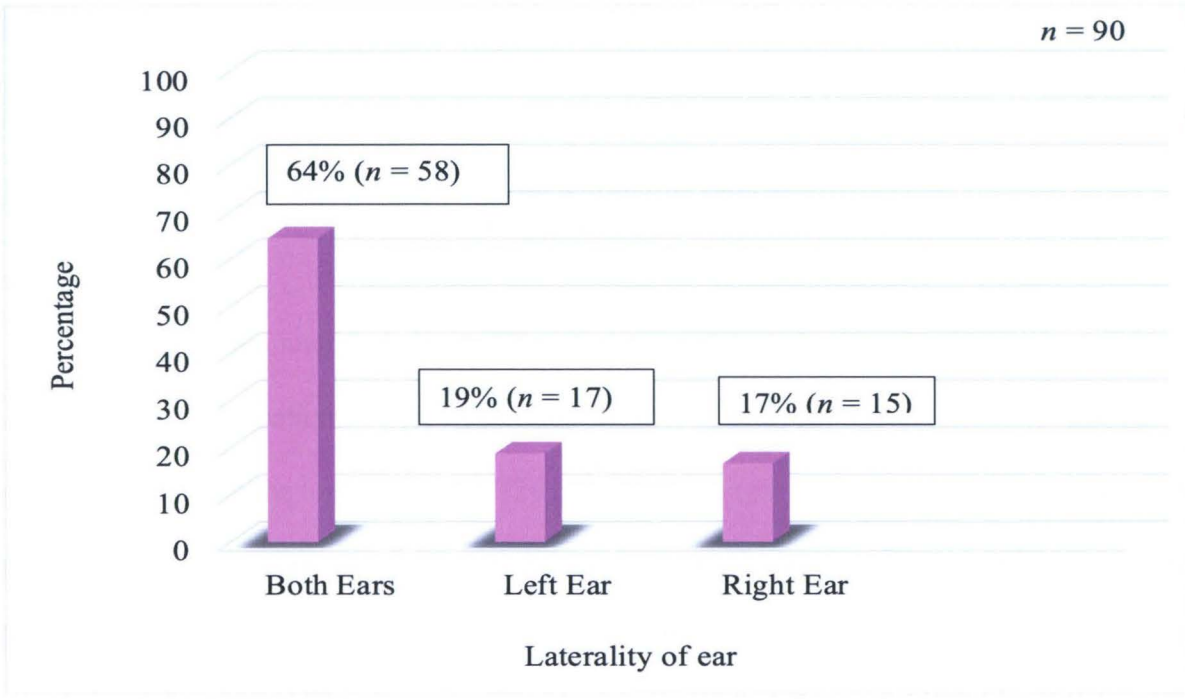

Figure 4.11. Ototoxicity Distribution According to Ear

Figure 4.11 illustrates whether ototoxicity presented in both ears simultaneously, or if ototoxicity presented in one ear before another. The majority of patients displayed ototoxic hearing loss in both the left and right ears simultaneously while in the remaining portion of the sample, ototoxic shifts occurred in one ear first before the other ear was affected. For these cases, ototoxic shifts were more likely to begin in the left ear before the right ear was affected.

As detailed in Chapter 3 under the description of the sample, the majority of the patient sample was male, and the mean age amongst the population was 36 years of age. As such, a chi- square test of association was conducted to ascertain whether gender had an effect on the development of ototoxicity, and the results revealed that no significant relationship existed between the two, χ^2 (1, N = 110) = 0.903, $p > 0.05$ and as such, being male or being female did not relate to developing ototoxicity. Furthermore, the same statistical test was performed to assess if advanced age was related to the development of ototoxicity during treatment.

The results revealed that no significant relationship was present χ^2 (1, N = 120) = 1.404, $p >$ 0.05. Thus, it could be concluded that patients with advanced age had no specific relationship to the development of ototoxic hearing loss within this sample.

In patients who manifested symptoms of ototoxicity, the medication regimens were adjusted such that patients were taken off of the kanamycin injectables and placed on bedaquiline. Within the total sample of 120 patients, 58% (n = 70) were placed on Bedaquiline while 42% of patients (n = 50) did not receive the drug during DR TB treatment. Amongst those who did not receive bedaquiline, 13% (n = 15) were recommended to start bedaquiline by an audiologist but for various reasons, did not start the drug. An analysis of when bedaquiline was prescribed by audiologists in comparison to when the drug was given to patients has been detailed in Table 4.11. These patients were instead changed to PAS or had the kanamycin dosages decreased by the doctors to reduce the ototoxic effects of the drug.

Table 4.11

Trends in Bedaquiline Prescription (n = 105)

Follow-up Bedaquiline Prescribed	Bedaquiline Recommended	Changed to Bedaquiline
3.18	45.04	81.87

Note. The sample size above may be less than the total sample of 120, as bedaquiline was not recommended for all patients within the sample. Follow-up Bedaquiline Prescribed: the average number visit at which patients received bedaquiline. Bedaquiline Recommended: The average number of days since starting treatment that bedaquiline was recommended. Changed to Bedaquiline: When the patient actually received bedaquiline.

Bedaquiline was commonly prescribed between the third and fourth follow-up session and on average, there was longer than a month's difference between when the audiologist recommended bedaquiline and when the patient received the medication. Furthermore, merely 27% (n = 26) of 105 patients in the sample received bedaquiline when the audiologists recommended it, and once having received bedaquiline, 41% (n = 28) of these patients no longer received follow-up KUDUwave tests. Table 4.12 provides details as to why bedaquiline was not prescribed according to the audiologist's recommendation, and this was tabulated based on how often each of the various reasons were given.

Table 4.12

Reasons for Bedaquiline Prescription Discrepancies

Reason	Frequency (n = 66)
Awaiting bedaquiline approval	24
Unspecified	14
Changed to bedaquiline for medical reasons	12
Unsupported by doctor	7
Post injectable phase	5
Bedaquiline unavailable	3
Not approved for bedaquiline	1

Note. The sample size was less than 120, as this did not apply to patients where bedaquiline was not recommended. Additionally, not all of those on bedaquiline had such discrepancies.

Table 4.12 provides reasons are for why bedaquiline was not given to patients immediately when the audiologist recommended it based on ototoxicity being present. The most common reason for bedaquiline being prescribed later than recommended, was that patients were awaiting approval for bedaquiline from the liaising office at the Department of Health. As such, there was a waiting period between the time bedaquiline was recommended and the time the patient was approved to receive the medication. Often in these cases, kanamycin was removed from the treatment schedule and replaced with PAS until bedaquiline became available. This was also applicable in the cases where bedaquiline was unavailable due to low stock or when patients were not approved for bedaquiline. Particularly concerning was that in 14 cases, no specific reason was documented as to why bedaquiline was not prescribed at the time when the audiologist recommended it. Other patients were changed to bedaquiline not due to ototoxicity, but due to other side-effects experienced, such as renal dysfunction. This was done at the discretion of the doctor. In seven cases, the doctor did not support the audiologist's decision to

change the medication based on the ototoxic shifts observed, and as such, patients remained on kanamycin. Other patients were already finished with the intensive injectable phase of treatment by the time the audiologist recommended bedaquiline.

4.3. Phase 2: Qualitative Data

As thematic content analysis has been utilized, this section of the results will provide an overview of the themes and sub-themes that emerged from the transcriptions of the interview data. Where necessary, quotes from the participants have been provided to corroborate the findings described. Table 4.13 below, details the themes and sub-themes that arose during qualitative data analysis.

Table 4.13

Themes and Sub-themes

Themes	Sub-themes
Nurses' Perceptions Towards Hearing Testing	Knowledge of Testing Procedures
	Attitudes Towards Hearing Testing
Views on the Role of the Audiologist	
Training Received	
Patient Factors Influencing Testing	
Gaps in Service Provision	
Thoughts on Future Training	Information and Training Needs
	Training Skills

4.3.1. Nurses' perceptions towards hearing testing

4.3.1.1. Knowledge of testing procedures

The nurse participants all acknowledged that hearing testing is both important and necessary within the context of DR TB treatment as they described that a side-effect of the injectable medication was hearing loss. As such, the participants described a feeling of responsibility to conduct hearing testing correctly, especially at baseline, in order to identify patients who already had a pre-existing hearing loss. Participants noted that those with pre-existing hearing pathologies would need to be identified early so that they did not get initiated on injectable drugs from the start of treatment. Others noted that from a legal perspective, it was important to do the hearing testing particularly at baseline, to avoid litigation. This is noted in the response by Participant 1: *"If the patient came with good hearing and after taking the treatment he has*

hearing loss, we will be held liable... because patients can sue us" (Lines 19-20). However, despite the participants knowing that they were required to perform the hearing testing, they were unsure of what to look for in the hearing testing results. This was noted in the following: *"No I don't know* [what we are looking for] *we just do it and then we take the results to audiology"* (Participant 3, Lines 26-27.) This illustrated the nurses had limited knowledge on what was actually being tested and what the results meant in terms of hearing loss.

All six participants described knowing that patients' hearing needed to be tested at baseline as well as at each follow-up assessment. The participants described the value of testing at every follow-up appointment as it ensured that the medication was not having a negative effect on the patients. This is evident in the following statement by Participant 6: *"I think it's important to test the hearing so that if the medication is related to the loss of hearing it can be stopped. The patient can be changed to something else"* (Lines 23-25.) The same participant noted that this information is communicated to patients so that if they experience symptoms of a hearing disturbance, they are welcome to come to the clinic regardless of the dates of their appointments. This illustrated that the participants had knowledge of the importance of hearing evaluations in this context and were able to communicate this to their patients. However, the participants were unsure of why the patients had to be booked for an exit appointment at audiology, once the medication regimen was completed. Currently, the participants are unsure of why hearing testing is still conducted with patients that are on bedaquiline but reported doing the testing for these patients at baseline, every 3 months, as well as at exit from the programme.

The nurse participants acknowledged the importance of instructing patients appropriately before commencing with the hearing testing. They often described having to explain in the patient's home language where possible and speaking to the patients at a slow pace, ensuring

understanding. Participant 1 explained this process in the following words: *"You tell a person, when you hear a sound you must click. In fact a person must be slow so that the patient can understand."* Despite having knowledge in how to instruct patients appropriately, the nursing staff felt that they did not know what to do with patients who did not respond well to testing. While they were able to identify the difficult to test patients in advance, they reported not knowing how to modify their testing procedures to accommodate such patients. Furthermore, when the results for such patients were inevitably reported as unreliable by the audiologists, the nursing staff then repeated the testing in the same manner in which they had done it previously, without using any further modifications. Participant 4 described this phenomenon as follows: *"And when we take it there they say repeat and we get annoyed as well. We don't have that thing that we can repeat it, because we find out the patient can't concentrate"* (Lines 64-66). This illustrates how nurses don't feel equipped to deal with difficult to test patient populations, and required further support in aiding them to do so, especially to reduce their frustration levels.

On some occasions, the nurses reported being shocked that the hearing test results had come back as unreliable, and as such, all the nurses came together to try and problem solve what had gone wrong. This process is described in the following quote by Participant 5: *"Then when the patient comes back we will all come – 'what happened? Why is he coming back?' then the sister will show us what she had done then we will correct her"* (Lines 171-174). Firstly this illustrated that the participants were not always able to judge the reliability of testing results unless the patient showed signs of being difficult to test or instruct. Secondly, it described the learning process and how the nursing staff sought knowledge within their environment, as they used this as a dynamic opportunity to learn from the mistakes of others. This was further corroborated by Participant 6 who described the experience of using the

KUDUwave as "a learning curve" (Line 66), where she was constantly learning as she was working.

Participants described feeling uneasy when the audiologists reported the results as unreliable, as they did not understand what had gone wrong and what more to do when the patient was tested the second time around. Participant 3 described this: *"When you take the results to the audio, they just write re-test. So I don't know, the mistake, was it me? Did I not connect right or is it the patient? I don't understand"* (Lines 115-118). This describes a knowledge gap particularly in understanding unreliable test results and what to do when such a finding is present. Furthermore, while the participants felt that they were able to identify patients who were unreliable during testing, they were not able to identify unreliable results from the findings alone. The participants believed that this was because they were not as familiar with the testing machinery and how the hearing testing actually functioned.

The nurse participants in the study noted that they did not feel confident in placing the ear probes in to the patients' ears themselves. As such, the nurses often asked their patients to place the ear probes into their own ears so that they could avoid hurting the patients or placing the probes in a manner that was uncomfortable for their patients. This was noted in the following response by Participant 3: *"When you put it* [the inserts] *inside, you think like maybe the patient may be uncomfortable so sometimes I ask the patient to put it inside"* (Lines 145-146). They further noted that certain patients struggled with placing the insert probes into their own ears, as evidenced by: *"Sometimes the patient couldn't put the plugs nicely in their ears... There's times when you have to ask patients to put it because you feel like you might be hurting him or her"* (Participant 6, Lines 99-102). Thus, as noted by the participants, insert probes were not

necessarily inserted by the nurses doing the testing, but by the patients themselves, who likely had no pre-existing knowledge of how to do so.

As the KUDUwave audiometer has an automatic setting, once nurses have started the test the threshold searching occurs automatically, and thus, nurses do not have to have knowledge in how to threshold search and obtain results at every frequency. As such, the nurse participants were often not able to give reasons for why the full frequency spectrum in some patients was not assessed. Furthermore, the participants appeared to have a limited understanding of the significance of ultra-high frequency testing in ototoxicity monitoring, as evidenced in this excerpt: *"No, I don't know why, I've never asked about it"* (Participant 6, Line 217). The participants further described not knowing where ototoxicity begins and described relying on the audiologist for the more detailed audiological interpretations. Most participants in the sample were not able to name any other forms of hearing testing, with only two participants describing tuning fork tests. Overall, the participants felt that the KUDUwave machinery was accurate and if for some reason it was not, the audiologists were relied upon to identify any issues. However, the participants noted that they did not understand bone conduction testing, how to place the bone conductor and how to instruct the patients for the bone conduction assessment. They appeared to be familiar with standard procedures such as positioning the patient facing away from the KUDUwave laptop so that visual cues were not given to the patient. This knowledge was obtained when they watched the head sister testing.

4.3.1.2. Attitudes towards hearing testing

The attitudes of participants towards hearing testing was explored. The participants described feeling empowered in knowing how to perform hearing testing. They felt that by doing the

testing themselves, they were better able to understand what the patients were experiencing and how best to manage the patients going forward. Participant 4 described this feeling: *"You know, I feel great neh. The first time they just showed me how to do it, you press this, you put it like that. I liked it very much"* (Lines 112-113). Participant 6 described the same feeling: *"No we felt good* [about doing the hearing testing] *although it was a lot of work"* (Lines 70-71) and Participant 3 described the same: *"To do the KUDUwave? Ya I am happy"* (Line 79).

Other participants in the sample noted that the hearing testing was often time consuming and at times difficult, especially on days where there were increased demands placed on them in terms of patient load and work. However, the nurses in these cases all expressed a sense of responsibility towards the patients, acknowledging that the hearing testing had to be done for the benefit and well-being of the patients that were being treated. Participant 1 described this aptly: *"Sometimes we haven't got time, we have many patients. But we can't let the patient go, we have to test him"* (Lines 89-90). Participant 2 noted that while she often felt that doing the hearing testing meant that she was overstepping her scope and doing the job of another professional, she was happy to do the testing for the benefit of the patient. She described this as follows: *"I'm worried that maybe I'm taking someone else's job. But I will do anything for the patient so I am happy to do it."* Participant 1 noted that if nurses have an interest and a positive attitude towards hearing testing, then it becomes easier for them to do the testing and to learn how to do the testing properly. Thus, the participants felt motivated to do the testing especially since they linked it directly to patient well-being.

While most of the participants had a positive attitude towards hearing testing, a minority of participants described feelings of frustration towards audiology, particularly when the audiologists simply wrote "re-test" (Participant 3, Line 115) on the results without giving

further explanations. This was especially confusing for participants as they viewed the KUDUwave as being reliable and thus, were surprised when the audiologists reported that the results were not accurate. Another factor adding to the frustrations of the participants was that they did not like having to deliver the results to the audiologists for reporting, as they felt that this was a poor use of their limited time. This sentiment was noted in the following:

> *Eish, we are not supposed to run up and down. We are taking time and leaving our job by taking the results up and coming back to give it to the doctor. But if there is someone trained who just does the KUDUwave and gives the report the patient can go straight to the doctor* (Participant 4, Lines 70-74).

The notion of feeling over-burdened with work was echoed in the responses given by the participants, especially since the hearing testing is one more task that has been added to their lists of responsibilities at the TB centre. Participant 5 felt that because of these factors, it may be better for audiologists to do the testing themselves as she noted: *"As a nurse we do it because they say we have to do it but I think it is better if a trained audiologist can do it"* (Lines 67-68). Thus, while there is an overall positive attitude towards performing the testing, there appears to be an underlying frustration that is experienced by the nursing staff, especially with regards to the relationship with audiology.

As a whole the participants had a positive attitude towards the testing machinery, noting that the KUDUwave was user friendly and after proper training, they felt equipped to operate it. Two participants however, felt that the KUDUwave equipment was not sufficiently durable, especially the bone vibrator which Participant 3 described as *"fragile"* (Line 30). Participant 4 described how the bone vibrator was not fastened to the headphones sufficiently and as such,

it often became detached during testing and then would get lost as it was separated from the headphones. In terms of difficult to test patients, while some participants felt that they could benefit from training in order to manage such patients, most of them felt despondent. This was as the participants felt that little could be done to address factors such as language barriers, and lack of concentration due to severe illness or fatigue. This was described by Participant 6: *"The difficult patients, ah I don't know if there's anything that can help. The worst part with those, there's nothing you can do"* (Lines 185-188).

4.3.2. Views on the role of the audiologist

Upon being asked what they thought the role of the audiologist was in TB monitoring, particularly within the ototoxicity monitoring programme at the TB centre, all nurse participants reported relying on the audiologists to interpret and confirm the results of the KUDUwave tests conducted. Furthermore, the nurses reported depending on the audiologists to evaluate whether the results of their testing were accurate or not, as described by Participant 6: *"I can't say because we relied mostly on the audiologist... they say its unreliable then if its unreliable we have to repeat it"* (Lines 156-157). This was also described by Participant 1, who felt that audiologists should inform nursing staff when the testing was not conducted correctly: *"I think it is to tell us when something is wrong. Just to alert us... Isn't it we are doing it, so maybe if we aren't doing it well, they need to tell us"* (Lines 70-73). Furthermore, participants described feeling reassured that the audiologist was there to verify the results that they had obtained, as noted in the following: *"We see the hearing loss but we take the patient to the audiologist and then they confirm by writing... It's okay, I like it. I mean confirmation is the best"* (Participant 1, Lines 203-207).

The participants expressed having a sense of trust and respect towards audiologists, and valued having them as part of the team as they were viewed as experts within the area of hearing testing. This was noted by Participant 5: *"I think it works well because they have experience and they will know what to do. Because they've been trained, they know... they are important"* (Lines 44-46). Aside from audiologists reporting and evaluating the results obtained, participants reported being unsure of what the audiologist actually does, especially in terms of rehabilitation after the diagnosis of a hearing loss. This is evident in the following:

> *Ummm, they just check...I don't know. They just check and they just write down, monitor or maybe the hearing is going down. But, I'm not sure... Because I just go with the paper there and they just do their things. And we bring it back.* (Participant 3, Lines 29-33).

Additionally, participants reported not understanding how the audiologists reached specific conclusions from the results that they as nurses had obtained, especially with respect to medication changes. Participant 3 described this in the following: "*Maybe from audio, maybe they said stop kanamycin. We don't know why, we just say oh okay stop kanamycin. But we don't really know how* [they got to that decision]*"* (Lines 218-219).

Lastly, the nurses in this sample reported referring smear positive patients to audiology when the KUDUwave was unavailable in the clinic, and being told that the audiologists would not see these patients. The nurses were not aware of the lack of infection control infrastructure that led the audiologists to this decision, and as such, the nurses felt negatively towards audiology for not assessing their patients. While the nurses reported relying on the audiologists for the interpretation of results, they appeared hesitant to depend on the audiologists for input regarding the testing procedures. Participant 1 felt less likely to ask the audiologists for

assistance as she felt that she was inconveniencing the audiologists. This was echoed by Participant 4 who noted that now that the head sister had gone, she would most likely ask the doctor who works at the TB centre for assistance if she was struggling with testing procedures.

4.3.3. Training received

The participants were asked to specifically detail the training that they had received in operating the KUDUwave audiometer and in conducting hearing testing. The nurses struggled to describe the precise duration of how long they were trained for, as they considered the training as a continuous learning experience. Each nurse described having one day of training where the head nurse taught them the basic information on how to use the KUDUwave software, how to enter patient details, and how to insert both the foam ear tips as well as place the circum-aural ear cups. If the nurses were trained on the KUDUwave by Emoyo, the formal training occurred over 2 to 3 hours and the training with the head nurse occurred thereafter. Participants, particularly those of an older generation, reported that as they were not computer literate, they struggled the most with learning how to operate the KUDUwave software on the laptop. This was often the portion of training that they felt was the hardest and which was the most time consuming.

As described in the previous chapter, four of the six participants received informal training from the head nurse while two received this in conjunction with formal training from Emoyo. The participants who received the training by Emoyo noted that it was conducted purely from a theoretical perspective, with demonstrations on how to use the software and insert the earphones and foam ear tips. In contrast, when the head nurse trained the participants, it was reported that she taught them the theoretical information but did so in a practical context, when

a patient was physically present for a baseline assessment. This is noted in the following quote by Participant 5: *"She showed theory, then called a patient and showed us on a patient...Ya, that makes a difference" (*Lines 111-114). As Participant 1 described in the following, *"Then we did one patient, two patients, every day."* After the training, the head nurse made sure to give them opportunities to test patients and use their skills while she remained present and watched. Once she felt comfortable with their performance the nurses were allowed to test independently but had the opportunity to consult with her when necessary.

The participants described that this practical training on real patients was more beneficial than theoretical training in isolation. Participant 3 actually noted that she preferred the practical training that the head sister provided instead of the purely theoretical training from the company. This was evidenced in the following quote:

> *Last time he came, and then they just showed us, but not in a proper way. But Sister K always showed us how to do the KUDUwave. They just showed us how to connect the KUDUwave.* [I would've liked something more.] *Like the problem was...there was no patients that time. At least if there was a patient...* (Participant 3, Lines 101-106).

Participants felt that the practical training they received from the head sister taught them how to problem solve, especially in terms of difficult to test patients, an area that was not addressed in the theoretical training they received from the company. This is shown in the response by Participant 1: *"Then she will tell us maybe the patient is lying, he will say I heard the sound and he didn't hear the sound, so she told us we must be careful of this"* (Lines 138-140).

The head nurse also gave the participants memorable mnemonics for things that they may have been struggling with during testing, illustrating that the training was relevant and

individually targeted. This was expressed by Participant 3 who struggled to remember which headphone to place on which ear: *"The one thing I learnt from Sister K when we put the bigger one* [referring to headphones] *the red colour is in the right; R for right. So at least you remember red – right"* (Lines 177-179).Following the training, the nurse participants often relied on the head nurse for support, assistance, and problem solving when they encountered difficulties during testing. They felt comforted by the fact that they could always go back to the head sister to address concerns or any questions that they might have had. This is noted in the following quote by Participant 5: *"But then if there is a problem we will call her to see...so if there is something I don't see she can help me. Because we are having her around always"* (Lines 120-121).

All of the participants felt that the training they had received adequately prepared them for testing in the real world. However, some participants expressed concern that they had not been able to use the machinery consistently, as there has been no laptop for quite some time and prior to this the equipment was not always available at the TB centre. Participants felt that this lack of availability negatively impacted upon their ability to use the machinery effectively as Participant 3 described: *"I remember little bit but its long time. Now we have forgotten how to do the KUDUwave"* (Line 149-150). Participant 1 expressed a similar experience, in the following excerpt, *"She will explain and explain. And then the next time I will have forgotten already. I think to do it frequently is easier"* (Lines 183-184). In this experience, the participant noted that she would ask for assistance in areas that she struggled with, but by the time she tested a patient again thereafter, she had forgotten what she had learnt. The nurses described looking forward to getting new training from Emoyo when the laptop was replaced, so that they could get back into using the KUDUwave regularly.

4.3.4. Patient factors influencing testing

Upon initiation at the clinic, all DR TB patients received counselling, which included that hearing testing would be conducted at each follow-up. The participants reported that all patients were informed regarding the side-effects of the kanamycin injections and were told to look out for symptoms of hearing loss. Most patients were noted as being co-operative and proactive with having their hearing tested, as Participant 1 described patients asking whether their hearing would be screened on that day or not: "*Some will ask, am I not going today* [pointing to the room where hearing testing is conducted] *or am I going?"* (Line 308). However, despite the counselling, some patients were reluctant to have their hearing tested, or didn't take the hearing testing seriously. It must be noted that the participants acknowledged that these patients are in the minority. The participants described that the possible reason for this reluctance was often linked to patient factors such as co-occurring psychological or psychiatric issues, or denial regarding the DR TB diagnosis.

The nurse participants in the study all acknowledged that the KUDUwave testing procedures required significant co-operation from patients. This is as patients are expected to be alert enough to understand and follow instructions as well as be able to sustain concentration for the duration of the testing. As such, the majority of the participants noted that the KUDUwave testing could not be used to assess hearing for all types of patients. Participant 3 went to the extent of suggesting that perhaps another type of audiological evaluation should be used to test such patients. The nurses described being able to recognize which types of patients would struggle with the hearing testing, before even beginning the testing procedures. Participant 4 described this process: *"You know the first thing you can see the patient, like this one is not going to concentrate. Just for the assessment, you can tell this one is not going to do*

it at all" (Lines 77-79). This highlights that the participants were able to judge the level of awareness and state of the patients prior to testing, based on the expectations of the testing environment.

In the experience of participants, patients that struggled the most with the KUDUwave testing included very ill patients, confused patients, patients from the wards, patients that weren't able to sit still and concentrate for the full duration of the test, and elderly patients. Those with pre-existing hearing losses were also difficult to test as they were unable to hear the instructions for testing. The nurses at the TB centre had diverse language backgrounds and used the home language to instruct patients where possible as Participant 5 described: *"We are all speaking different languages. Sometimes you find the patient is speaking isiVenda* [sic] *then we find the nurse that speaks Venda to do the testing"* (Lines 145-147). Despite this diversity, foreign patients posed a significant challenge as they were not able to speak much English and were not familiar with the local South African languages, rendering it difficult for the nurses to instruct them for hearing testing. Participant 4 described this experience: *"...most of the patients are coming from Zimbabwe, only to find that the patient doesn't even know the language this side. Then we don't even know where to start, so it's a problem"* (Lines 99-102). Instructing patients is an important part of the testing as this would be the first time most patients are having a hearing test and thus, they have no prior knowledge to draw from.

The participants noted a trend in that patients tended to perform better on the KUDUwave testing once they were more accustomed to the hearing testing procedures. As a result of this, they explained that some patients tended to perform worse at baseline hearing testing in comparison to follow up tests, as noted by Participant 4: *"The first day they don't even understand, sometimes they don't even want to do it. Then the concentration and the*

understanding gets better" (Lines 347-349). Furthermore, the participants noted that at baseline, when hearing testing was first conducted, patients were often confused by the many medical testing procedures done before medication was initiated and therefore, this may have affected patients' performance in hearing evaluations. This is described in the following:

> *It can happen because by that time* [of the hearing testing] *the patient is confused, the patient might feel confused of doing the ups and downs, the sputums* [sic], *the x rays... But we used to tell the patient to relax* (Participant 6, Lines 74-77).

The nurses noted that patients' reports of their own hearing abilities could not always be trusted and relied upon entirely, as some patients claimed that they had a hearing loss when their hearing was within normal limits. Participant 4 described this phenomenon: *"When you talk to the patient you have to ask them questions. And if the patient tells you their hearing is not well, then don't just write it, ask other questions and you'll see that* [actually] *there's no problem"* (Lines 230-232). Participant 5 also reported this, as she described how the prisoners that she was treating would tell one another that if they report a hearing loss, the doctors would make sure that they don't have to get any more injections. In contrast, Participant 4 further reported that other patients claimed that their hearing was normal despite experiencing symptoms of hearing loss. She expressed this in the following: *"Yes! They say I'm fine, I can hear everything and then when you test, or even when you send upstairs for diagnostic, the audio is not right"* (Lines 237-238). The participant attributed this to the fact that patients were often in a rush to leave the hospital for work or other commitments, and thus, did not report hearing loss as they knew that hearing testing would take much longer.

4.3.5. Gaps reported in service provision

The head nurse who left the clinic in mid-August was in possession of the only laptop that was being used at the TB centre to operate the KUDUwave, as previous laptops had been stolen from the hospital. As such, when the nurse departed, the KUDUwave could no longer be used, as there was no laptop to operate the software required for testing. While the head matrons had motivated for a new laptop, patients did not receive KUDUwave tests from mid-August onwards. Fortunately, the majority of patients at this point were already on bedaquiline and had received the latest injectable-free treatment regimen as stipulated by the Department of Health (2018). However, patients on amikacin could not receive ototoxicity monitoring during this time. The nurse participants reported that this was not the first time that the equipment required for the KUDUwave testing had been unavailable at the TB centre.

The participants reported that there was a period of time where patients on kanamycin were not receiving KUDUwave tests as the KUDUwave was stolen. Additionally, as the KUDUwave required the software on a laptop to run, and as the software was loaded on the head nurse's laptop, whenever she was on leave or unavailable, patients who attended the TB centre during that time did not receive baseline or follow-up KUDUwave tests. This was expressed by Participant 3:

> *You see we were using her laptop. So if she is not around, it's a problem for the baseline for the patients. Maybe if we have our own laptop... Then it would be easier to do the baseline to the patient, every patient* (Lines 159-163).

Participant 4 further expressed that the KUDUwave was sometimes inconsistently available in the clinic, as noted in the following: *"It's on and off because maybe 6 months it's not there and then it's there for 3 months or maybe for 2 weeks. Then the person is on leave and then It's not there" (Lines 131-133).*

Nurses reported that for patients that did not receive the baseline test at initiation due to issues as detailed above, they made sure to conduct the KUDUwave testing when the patient returned for the second visit 2 weeks later. Certain patients did not receive testing at 250Hz and 500Hz of the frequency spectrum, as the nurses were selecting the incorrect testing protocol on the KUDUwave software. Other patients did not receive ultra-high frequency testing for this same reason. The participants reported approaching the head nurse who then phoned Emoyo to fix the programme selection on the KUDUwave.

In addition to inconsistent availability of machinery, the nursing staff reported that they were at times at fault for not conducting hearing testing as regularly as they should have been. Participants felt that they could not reprimand their colleagues for not doing the testing when it was supposed to have been done. The excerpt by Participant 4 described this phenomenon:

> *Eish, you know what, the problem sometimes is our problem because we will be seeing the patient and we will see the patient is on kanamycin but we won't do the KUDUwave. We can't always follow people around, like why didn't you do this, things like that. It's like you're annoying* (Lines 318-321).

Participants provided reasons for intentionally not doing the testing, which included understaffing, with too few nurses to conduct all the testing required, including sputum testing,

blood tests, cardiac tests, and hearing tests, for the vast number of patients seen. Participant 4 went as far as to recommend that if there were sufficient staff, one nurse should be allocated to doing KUDUwave tests each day, so that no patients leave without the hearing testing. Additionally, for logistical reasons, sometimes patients did not receive their follow-up hearing tests, as nurses prioritized other tests such as blood and ECG tests for patients who were late so that they could be seen by the doctor before the TB centre closed. The hearing testing was then left for last, by which point patients had already received a pharmacy script and had left the centre instead of waiting for the hearing testing.

Lastly, while the participants provided reasons for the gaps in service delivery, other participants were oblivious to the occurrence that some patients did not receive baselines, others didn't have consistent follow up tests and testing was not always conducted across the full frequency spectrum as prescribed. Participant 1 described being oblivious to the gaps in baseline testing as follows: *"I wouldn't know but I wonder why, because MDR patients are newly diagnosed. They must have a baseline."* This suggested a further gap in service delivery, in that there was no specific clerical system in place to ensure that patients had received all tests. This is especially noteworthy as the patient files had checklists to ensure that all testing was conducted.

4.3.6. Thoughts on future training

4.3.6.1. Information and training needs

All the nurses in the research study noted that they would like further training and information regarding the use of the KUDUwave in the context of ototoxicity monitoring.

The participants described a yearning for knowledge and information, in the area of KUDUwave hearing testing, and some nurses expressed wanting to receive in-service training specifically from audiologists. In addition, participants described going through the motions of testing hearing but not understanding what they were actually doing during testing. This was evidenced in the response by Participant 2: *"This is why I want training. Maybe from audiology... I want to better understand what we are doing and why"* (Lines 80-83). Nurses who felt confident in their testing abilities also held this sentiment, as they still wanted further training. Participant 1 described this: "*Ya, I am good at that but still I will need more training."*

There seemed to be a sense of confusion amongst the participants in relation to the bone conductor, as all nurses who brought the topic up in the interviews, did not seem to understand the use of the bone conductor, and most participants could not remember the name for the bone conductor equipment. As such, the majority of nurses noted that they required further training on how to use the bone conductor, how to place it, how to instruct patients for bone conduction testing, and the purpose behind it. It was further described that patients do not respond well to bone conduction testing, and nurses are unsure of how to help patients as they don't understand the process themselves. This was evident in the response by Participant 5: *"It's this thing, what is this [gesturing to forehead and showing a bone conductor] ya, that. I want more information. You just turn it and then the patient cries, and then I become confused."* (Lines 89-91).

Other areas that participants wanted further training in included, knowing how an audiogram should look, the mechanisms behind hearing loss, recognizing when an ototoxic loss manifests, and strategies on how to problem solve equipment issues without having to call the company. Additionally, participants felt that they required more input on how to deal with difficult to test patients as they found these especially challenging, as noted by Participant 4:

"How to handle the patient during the KUDUwave. Like if the patient cannot concentrate what can I do? Because it's not easy at all" (Lines 275-277). Lastly, participants wanted input on how to monitor whether the KUDUwave was working properly and testing accurately, as nurses despite being trained on the machinery, felt unfamiliar with how it functioned. This was noted in the following: *"I don't know the machine. So the problem is if the machine is not doing well I don't know because I don't know what's going on in that machine. If it's wrong I wouldn't know"* (Participant 4, Lines 205-207). As such, the nurse participants were able to identify the gaps in their knowledge and understanding of the testing procedures, and could clearly stipulate where they required more external input.

4.3.6.2. Training skills

An important question that was posed to participants involved what they would do as nurses, if they found themselves having to train others on the KUDUwave and hearing testing. This was particularly relevant, as the majority of participants in the study received their training from other nurses and not directly from Emoyo. Participant 2 stated that she would not train other nurses as she did not feel that she had the sufficient knowledge in hearing testing and operating the KUDUwave to train other people. She communicated this in the following: *"I would not train other people because I don't feel like I know enough"* (Line 86). This illustrated a sense that nursing staff were able to gauge their level of knowledge and knew that in order to teach others, a solid foundation of pre-existing skills was required. On the whole, the nursing staff admitted that they would not leave anything out when teaching others, as all details were important.

Participants highlighted the importance of communicating the rationale behind the hearing testing, especially for baseline assessments. They noted the importance of teaching people how to counsel their patients beforehand, and stated that they would emphasize the need to take thorough histories from patients and to have tolerance, particularly with difficult to assess populations. The participants further acknowledged that when training others, a combination of both theoretical information and practical training using patients was required. Participant 6 described this as: *"They need both* [practical and theoretical training] *because if you are not there, they need to continue."* (Line 209). As noted in this excerpt, the participants felt that the combination of both theoretical and practical knowledge, facilitated the independent practice of others, as they have experienced themselves having been trained at the TB centre.

4.4. Closing Remarks

The results from the quantitative analysis of patients' hospital files and the qualitative findings obtained from nurse interviews were linked to one another, in that the results from one aspect often confirmed the findings of the other. This link and integration of the findings will be further explored in the following chapter where the results from both phases of the study will be discussed both independently and in relation to one another.

Chapter 5

Discussion

This chapter integrates both the quantitative and qualitative research findings with pre-existing literature in order to provide an overview of the trends in DR TB within a specific ototoxicity monitoring programme, at a tertiary hospital in Gauteng, which was a primary aim of this study. The sub-aims of the study included providing an insight into personal variables of patients attending the DR TB programme, trends in audiological findings amongst patients, and lastly, nurses' experiences of hearing testing within this context. These sub-aims are addressed in this chapter, and the findings have been linked to the theoretical frameworks of this study, which included epidemiology and evidence-based practice with particular emphasis on Bronfrenbrenner's ecosystemic theory and its application within a health context.

The Discussion Chapter highlights that the individual patient factors cannot be addressed without evaluating the individual as a part of wider systems which surround the individual. Furthermore, as the need for ototoxicity monitoring to become more accurate and reliable is increasing, the barriers and enhancing factors within the ototoxicity monitoring programme explored in this chapter, are of particular importance. Preliminary results from this study, particularly from the nurse interviews which explored the further training needs of nurse participants, were shared with Emoyo. This contributed to the next round of training given to the nursing staff, enhancing its contextual relevance, as it was based on some of the findings of this study. This illustrated how the findings of this study contributed to evidence-based practices within this context.

5.1. Personal Variables in DR TB Patients

Personal variables occur at the individual level within the ecosystemic approach, and encompasses variables related directly to patients within their own individual capacity. The majority of patients in this study had contracted DR TB without a previous history of TB treatment. This is consistent with the research findings of Gandhi and colleagues (2006), where more than half of the patient sample was exposed directly to the DR TB strain, without a prior history of failed TB treatment. The findings of the present study further confirm what has long been suspected within the DR TB context in South Africa, that the current pandemic is not driven simply by poor adherence to medication, but by risk factors predisposing patients to acquiring DR TB. This contradicts the Department of Health's statement (2014, pp.74) that the presence of DR TB in the country is based on "man-made" factors such as the poor management of the disease. Additionally, the majority of the patient sample had a DR TB strain that was resistant to the medication rifampicin, and this trend is expected, as statistics have revealed that South Africa has the highest rate of rifampicin resistant DR TB in the world (Department of Health, 2018).

It has been well established in the literature that the risk of acquiring DR TB and the risk of non-compliance with treatment can be liked to a number of factors, both within the individual and within the social and economic landscapes surrounding the individual (Berben et al., 2012; Lie et al., 2016; Marais et al., 2013). Patient compliance and adherence do not simply refer to the intake of medication as indicated, and the arrival for follow-up appointments, but also encompasses the patient's co-operation with hearing testing protocols for ototoxicity monitoring. Nurses in the study reported that some patients, despite being educated and counselled regarding the importance of hearing monitoring, were not motivated to have their hearing checked at each session. This was linked to a number of factors that will

be discussed hereunder. Compliance is a significant determining factor in the successful management of DR TB, as patients who default treatment, are more likely to infect others or to develop further drug resistance (Li et al., 2016). Those who are non-compliant with ototoxicity monitoring protocols are more likely to develop ototoxic hearing loss, or to perform less reliably on testing procedures.

5.2. Ototoxicity Risk Factors

At the individual level, it is important to establish the risk factors for acquiring ototoxicity, as early intervention procedures can be tailored to monitor those most at risk for acquiring this form of hearing loss (Frymark et al., 2010). Furthermore, as bedaquiline has become more widely used in standard practice, these risk factors can be used as a motivation for why patients should remain on bedaquiline, and not receive amikacin. Certain authors have claimed that males are more at risk for developing ototoxic hearing loss (Javadi et al., 2011), while other policies suggest that females have a higher risk of acquiring it (HPCSA, 2018). In the current study, no significant relationship was found between being male or female and developing ototoxic hearing loss.

The exposure to more than one ototoxic drug concurrently, such as ARV's and aminoglycosides, further increases the risk for ototoxicity (HPCSA, 2018). However, despite the high rates of HIV and DR TB co-infection in the current study, the majority of patients were not on consistent ARV treatment due to patients defaulting treatment, patients being unaware of their status or patients having a new diagnosis of HIV. Thus, the effects of ARV's on ototoxicity, could be disregarded in the current study, as most patients did not have consistent exposure to both drugs simultaneously, even if they were newly initiated on ARV's when starting DR TB treatment. Older age did not show a relationship with the development

of ototoxicity in the current study, and this was also the case in earlier studies conducted (Moore et al., 1984, as cited in Sharma et al., 2016). Other risk factors for developing ototoxicity when on aminoglycosides included poor nutrition, low socio-economic status, renal dysfunction, anaemia, and communicable diseases such as diabetes and hypertension which were common in the current study. In this study, a definitive link was noted between these factors and ototoxicity, as patients who did not develop ototoxicity when on kanamycin, did not smoke, drink, or have acute or chronic diseases. While this link is preliminary, the trend does suggest that those with less exposure to these predisposing factors, are less likely to develop ototoxic hearing loss when on aminoglycosides. However, it is very specific to each individual and can be dependent on other factors such as pharmacology and absorption rates of drugs, which are not within the scope of this research study.

5.3. Risk factors for DR TB

The socio-economic and environmental factors to which patients are exposed, impact upon the acquisition of DR TB and compounds the risk for developing ototoxicity when patients are exposed to aminoglycoside antibiotics. Thus, due to the complex interactions between surrounding health systems, individual factors, economical influences as well as the social environment wherein patients are located, an ecosystemic model has been used. This is to better understand the impact of these factors on both DR TB and ototoxicity, in order to enhance patient management. Such an understanding of DR TB factors has been endorsed and recommended by the World Health Organization (WHO), to optimize patient management (Borg et al., 2012). Figure 5.1 is an adapted version of the model suggested by the WHO.

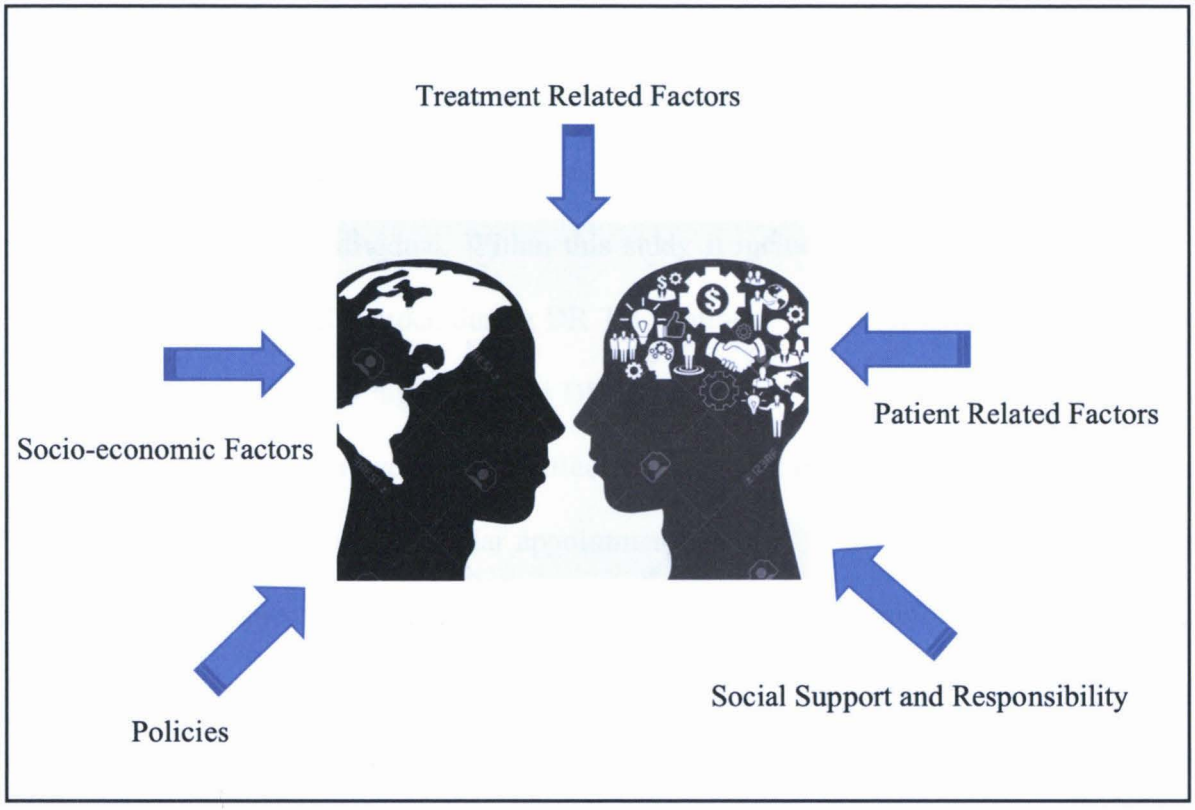

Figure 5.1. Ecological Determinants of Health in the Current Study.

Note. Created for this dissertation from images available on www.123RF.com

The results of this research study revealed that patients were exposed to a multitude of influences which not only affected them individually, but predisposed them to developing DR TB. Such factors often hindered the compliance and successful treatment of patients, and has impacted upon the overall well-being of patients, an effect that has been long established within literature (Hollander, 2018). Some of these factors will be discussed individually in further detail.

5.3.1. Treatment related factors

As part of the microsystem, treatment related factors refer to the dynamics of medical treatment, and its impact upon the patient, as the processes of medical treatment can have a profound effect on the individual. Within this study it included the complexity of DR TB treatment and the high pill burden during DR TB treatment. The increased burden of disease in the population as well as high HIV and DR TB co-infection rates, were also classified as treatment related factors, however, these affected the patient on an individual level. Once on DR TB treatment, patients had regular appointments at the TB centre monthly, and at local clinics weekly for injectable DR TB treatment which patients were subjected to before July of 2018. The injections are often painful and unpleasant and generally the treatment protocols are complex, long-term, and have side-effects including nausea and ototoxicity. This negatively impacts upon patients physically, emotionally, and in terms of day-to-day functioning. It further affects patients' compliance with treatment regimens as well as their attitudes towards treatment, and research has shown that patients who experience ototoxicity as a side-effect of medication, are less likely to be compliant with treatment (Berben et al., 2012).

The second highest number of referrals to the TB centre were from the medical wards at the hospital, and this confirms that the DR TB patient load is in fact high amongst hospital-in patients treated for other medical related disorders (Marais et al., 2013). This further links to the high burden of disease amongst DR TB patients, who often suffer from co-occurring chronic and acute diseases. One can conclude that the presence of these diseases have predisposed individuals to acquiring DR TB (Seegert et al., 2017). Most patients in the current sample, had concomitant acute and chronic diseases, and a high pill burden, as they were on

treatment for DR TB as well as other disorders such as diabetes, cholesterol, anaemia and organ failure.

The most common acute disease was kidney failure, as a result of TB treatment, and it must be noted that impaired renal function can increase the risk for ototoxicity (HPCSA, 2018). Acute diseases as a result of opportunistic infections was rather common in the patient population, and these included thrush, genital herpes, shingles, and hepatitis. This confirms findings from other research studies which stated that DR TB patients have an increased likelihood of developing opportunistic infections (Marais et al., 2013). Many people who had acute diseases in the sample, had concomitant chronic diseases, and there was a high prevalence of chronic non-communicable diseases amongst the DR TB population. Furthermore, large numbers of patients within the sample, required referrals to other medical professionals and specialists, to manage co-occurring diseases. Three patients from the sample experienced dysphagia, yet none of them were referred to a speech therapist for further management, despite speech therapy services being available in the hospital. Research has established a link between non-communicable diseases and DR TB as hypertension, anaemia and diabetes impair the immune response to disease, thus rendering patients vulnerable to DR TB (Seegert et al., 2017).

While diabetes was shown to be highly prevalent in DR TB studies in other countries, a small proportion of patients in the current study had diabetes. This links to the trend that in Africa, most patients with diabetes are from urban areas. In this study, a large proportion of patients were from informal settlements and non-urban areas, and thus, diabetes was less likely to be prevalent amongst patients who originated from these contexts (Marais et al., 2013). The overlap between DR TB which is a communicable disease, with non-communicable diseases and acute disorders has resulted in a high burden of disease amongst the DR TB patient

population. Not only do these factors increase the complexity of successful treatment, but they place increased levels of stress on patients who need to attend multiple appointments with different specialists while ingesting various medications daily. It further places strain on an already over-burdened healthcare system, especially in the South African context, where health systems are not always well equipped to deal with overlapping burdens of disease.

The high co-infection rates between HIV and DR TB noted in the current study, further compounded the burden on healthcare, especially as South Africa has one of the highest global rates of co-infection between DR TB and HIV (Department of Health, 2014). In this study, patients were often first diagnosed with HIV at the TB centre, when initiated on DR TB treatment, and this is a common trend in the South African context (Department of Health, 2014). Thus, patients have to come to terms not only with their DR TB diagnosis, but with the diagnosis of HIV, a disease which has a life-long impact upon the individual. It further results in the same healthcare workers who are responsible for the DR TB treatment of patients, being responsible for the HIV management of these patients. This illustrates the reason behind the TB centre referring many patients to the HIV Clinic at the hospital, as patients required counselling and support to manage their HIV while on DR TB treatment. In this study it was beneficial that the majority of nurses working at The TB centre, had prior experience working within the context of HIV, as it aided the nurses in managing and counselling patients effectively. The WHO suggests that no DR TB management programme can be successful without the simultaneous management of HIV, as the two diseases cannot be separated (WHO, 2018).

5.3.2. Socio-economic factors

At the macrosystem level of the current study, were the socio-economic determinants of health, which included lack of food security, financial burden on patients, unemployment, poor living conditions, and social risk factors, which predisposed patients to DR TB. The majority of patients in the study had no food security and required referrals to dieticians as they were underweight. Not only does malnutrition increase the risk for DR TB, but it further increases the likelihood that patients will experience more side-effects of medication, resulting in decreased compliance with treatment regimens (Marais et al., 2013). Most of these patients required referrals to social workers so that grants could be provided, for patients to purchase food and cover the travel costs to commute to the hospital for appointments.

For those who defaulted treatment due to insufficient funds, ambulance services were organized to transport DR TB patients to The TB centre from the local clinic. Some patients with no food security, were foreigners, and as such, could not qualify for South African grants, due to a lack of identification documents. Other patients were South African citizens, but, did not have identification documents, as they were prisoners. As such, these patients were then referred by the social workers to receive food parcels at local clinics, and Appendix N is the form that was filled out for this purpose.

Related to the high levels of food insecurity amongst patients in the sample, was the high rates of unemployment. Unemployment has a strong correlation with the development of DR TB (Duarte et al., 2018) and further exacerbates the effects of DR TB and the impact of social risk factors upon the individual patient. While the majority of patients were unemployed before developing DR TB, two patients in the sample lost their jobs because of their DR TB diagnosis.

A further patient was not given leave from her employer to attend the TB centre for appointments, and as such, defaulted her treatment and developed ototoxicity during the time she was not monitored. When patients defaulted treatment, the TB centre made an effort to follow-up with these patients, and the necessary information pertaining to this process is shown in Appendix O, which is the document that was filled out during this process.

The majority of DR TB patients within the sample lived either in informal settlements or in township areas and this relates to studies conducted globally, which found DR TB to be more prevalent in impoverished areas and in the outskirt areas of cities (Kolifarhood et al., 2015). Living in overcrowded informal settlements, with multiple people sharing the same house and with poor living conditions including inadequate ventilation and sanitation, has been shown to further perpetuate the risk for DR TB (Department of Health, 2013; Marais et al., 2013). These living conditions were common amongst patients within this study, who lived far distances away from healthcare services and local clinics. Studies have shown that a larger distance away from clinics and healthcare services has been related to patients defaulting in treatment, as well as delays in accessing healthcare services (Kolifarhood et al., 2017).

The highest rate of referrals in the current study, originated from local clinics in the areas wherein patients resided. Up until July of 2018, bedaquiline was not available in any of the local clinics, and as such, patients had to travel either to the TB centre for bedaquiline treatment or be admitted to a specialized tropical disease hospital. Thus, despite there being clinics near informal settlements, patients had to travel far distances to access DR TB care, creating an increased burden on patient finances. Currently, the South African Department of health is in the process of distributing bedaquiline to local clinics, however, it is not yet widely available at present. Thus, patients still travel to the specialized DR TB centre at the hospital.

While authors have stated that high rates of DR TB in a given society are a measure of the prevalence of poor socio-economic factors within the population (Marais et al., 2013), this is far too wide a generalization. While the current study did show that there were higher rates of DR TB in patients who were unemployed, had no food security, and who lived in townships and informal settlements, DR TB was also present amongst patients who were from urban areas, with permanent employment and a tertiary level of education. As South Africa is so uniquely diverse with pockets of poverty and privilege existing within the same society, this research study has given valuable insights into factors affecting DR TB and its management. One cannot simply generalize that DR TB is a disease of poverty, as it has many determining and predisposing factors, rendering it complex in nature, and difficult to treat if viewed in a one-dimensional manner.

5.3.3. Policies

Located at the level of the chronosystem, were policy guidelines, and within the South African context, this referred largely to policies on bedaquiline administration during DR TB treatment. The vast majority of patients in the study, despite being initiated on kanamycin, were switched to bedaquiline in the early stages of treatment, as a result of ototoxicity or other medical complications. In seven cases, bedaquiline was not prescribed to patients when the audiologist recommended it, as the decision was not supported by medical doctors. A possible reason for this is that due to the lack of guidelines on what constitutes the presence of ototoxicity, doctors grapple with whether shifts are truly significant or not, thus, affecting service provision (Hollander, 2018). This finding further illustrates the lack of communication between professionals, and highlights the importance of team discussions and collaborative decision

making processes, so that professionals are afforded the opportunity to problem-solve conjointly.

While bedaquiline was largely available in South Africa, prior to July 2018, patients had to await approval for the drug before it could be administered. This resulted in there being time delays between when the audiologists recommended bedaquiline, and when the patient was actually initiated on the medication. While PAS, a non-ototoxic drug, was provided to most patients in the interim, these policies resulted in bedaquiline not being easily accessible during DR TB treatment, as it could not be administered immediately when ototoxicity was detected. As such, the latest bedaquiline expansion plan policy has made bedaquiline available country-wide to all patients immediately when the drug is required, in order to combat this problem (Department of Health, 2018). Thus, unlike the patients in this study, future patients will be able to receive bedaquiline before developing ototoxic shifts in hearing. If patients are on amikacin, the proposal is that regular ototoxicity monitoring will detect any shifts immediately, so that alternative drugs can be explored.

5.3.4. Social support and responsibility

Social support systems, which are located at the level of the microsystem, have long been proven to affect medical treatment, as having a good social support system during DR TB treatment, can enhance treatment outcomes and encourage patient compliance (Li et al., 2016). Approximately half of the sample in the current study were either married or in a relationship and depended on their partners for emotional support during treatment. Married and unemployed female patients often depended on their spouses for financial support. A large proportion of patients in the study had children, often of a young age, that resided with them.

Young children are at increased risk for DR TB, and thus, the TB centre ensured that the children of patients were screened for the disease. Aside from this, having children meant that patients had child rearing responsibilities within their social contexts.

While patient experiences of treatment and of DR TB were not the focus of the study, it was documented in one patient's file that she experienced stigma from family members due to her DR TB diagnosis. She was forced to move out of the family home, as her sister-in-law refused to live with a TB patient. This supports previous literature which has indicated that DR TB has a social impact upon patients living with the disease (Hollander, 2018). During the period of relocation, the patient defaulted her DR TB appointments at the TB centre, and ototoxicity monitoring could not be performed. As such, the social context wherein patients live, further impact upon their healthcare and well-being.

5.3.5. Patient related factors

At the level of the individual, the last determinant of health pertinent to this study included patient related factors, such as social risk factors for DR TB, level of education of patients, the knowledge and attitude of patients towards healthcare, and the acceptance of the DR TB diagnosis. Compliance with hearing testing, the awareness and state of arousal of patients, and psychiatric health were also considered. Patients within the current study displayed many social risk factors for DR TB, which included exposure to alcohol and smoking, as well as a history of incarceration, contact with others who had previously been diagnosed with TB and low levels of education.

Smoking and the consumption of alcohol increases the risk for developing DR TB as well as ototoxicity, and heavier drinkers are known to have poorer outcomes in terms of DR TB management (Seegert et al., 2017). Thus, it is not unusual that many of the patients in the study smoked, and others were classified as heavy drinkers, as this is on par with global trends. Incarceration played a role in the current study, as patients sometimes defaulted DR TB treatment, as they had been imprisoned during treatment. Others had a previous history of imprisonment or were currently imprisoned during DR TB treatment. One participant had shared a cell with someone who had been previously treated for TB. This confirms that living in close quarters with others, especially those previously exposed to the disease, increases the risk of developing DR TB for patients a factor that was evident in previous literature (Marais et al., 2013).

A few patients in the sample were foreign nationals from neighboring African countries such as Zimbabwe and this posed a particular challenge within the current context, as patients often travelled up and down between South Africa and their home countries. During these periods of travel, foreign patients defaulted on DR TB treatment, placing other people at risk for contracting the disease. Furthermore, foreign patients in this study were more likely to have concomitant health issues including HIV, thus, placing further load on the South African healthcare system. Aside from the treatment challenges, nursing staff reported difficulties in instructing these patients for KUDUwave hearing testing, as they had limited English and did not speak the local South African languages that the nurses were fluent in. This resulted in poor performance on the KUDUwave tests and thus, unreliable results, which placed a strain on time and resources, as nursing staff spent more time assessing such patients. This had a negative impact on time management and resource allocation at the TB centre, which was already over-burdened with high numbers of referrals from local clinics and hospitals. While the health

system cannot ethically deny foreign patients treatment, it is challenging when the treatment of foreign patients compromises the quality of health care that patients who are citizens, receive. As such, procedures may need to be put in place, to ensure that ototoxicity monitoring and treatment practices are further developed in neighbouring African countries.

The majority of patients in the sample had received secondary education, at high school level. However, there were patients in the sample that did not receive any formal education or only had primary school education. Not only are low levels of education related to an increased risk of developing DR TB (Department of Health, 2013), but it further hampers how well patients understand the treatment process, thus, affecting compliance with treatment regimens and with hearing testing. These findings provide audiologists and healthcare professionals with valuable information regarding how patient instructions and counselling can be tailored to cater towards the capabilities of patients accessing DR TB care. High numbers of referrals from local clinics, means that pamphlets and fliers with information on DR TB and ototoxicity need to be made available in these contexts, and in a manner that caters to the varied levels of education and literacy present amongst this population.

Research by Berben and colleagues (2012), revealed that patients with a positive attitude towards health and who assume an active role in their treatment, are less likely to default or have treatment failure. Patients who experience fewer negative side-effects are more likely to view treatment favorably, and those who experience side-effects including ototoxicity, are more likely to have a negative attitude towards treatment (Berben et al., 2012). DR TB treatment at the TB centre aimed to empower patients with knowledge to ensure that they were able to take responsibility for their own healthcare. This was achieved by counselling and informing patients at initiation, on factors such as ototoxicity and its associated symptoms. In

turn, patients were then aware of the symptoms of ototoxic hearing loss, and could attend the TB centre if these manifested, despite not being booked for an appointment. During the interviews, nursing staff reported that the counselling had a positive effect on patients, as some assumed an active role in their treatment, and enquired when their hearing tests were going to take place.

In contrast, patients who experience denial regarding their DR TB status, are more likely to have negative attitudes towards treatment and as a result, become less compliant. Nursing staff noted this in their interviews, as they explained that some patients did not want to have hearing tests and co-operate with KUDUwave testing, because they were often unconvinced that they had DR TB. Other patients who were less willing to have their hearing tested included patients with concomitant psychiatric issues. The state of arousal and awareness of patients impacted upon how well they could follow instructions and respond to testing. Patients who were more ill, confused, lethargic, or drowsy often struggled with KUDUwave hearing testing, and nursing staff noted that such patients were most challenging. Furthermore, the nurses felt ill-equipped to deal with these difficult to test populations of patients and described that they would have liked support and assistance to ensure that these patients were tested accurately.

Some nurse participants went as far as to suggest that other testing methods be put in place to evaluate such patients. This is where audiologists have a role to play within the current context, as in-service training for nurses should target strategies on how to assess these types of patients. Where possible, audiologists should be available to aid in this process, by conducting objective hearing assessments that require less patient involvement. This should include DPOAE's, which do not require the patient to respond in order to obtain results. Furthermore, audiologists can inculcate modifications to the assessment protocol, such that

only the important frequencies required for ototoxicity monitoring are tested, to decrease the length of tests for patients who struggle. Thus, the testing of higher frequencies should be prioritized, ranging from 4000 Hz to 12 000 Hz. The lower frequencies can then be omitted for difficult to test populations, and this is in line with what is recommended by the HPCSA (2018).

Within the South African context, the public sector experiences the highest burden on healthcare, as the majority of the population accesses treatment at this level. However, the services in the public health sector are not always well equipped to deal with the large patient load and diverse needs of the population. The current study has illustrated that DR TB is not simply a by-product of human error as originally defined by the South African Department of Health (2014). Instead it is a result of a multitude of diverse and interacting variables, which have resulted in the marked presence of the disease within the South African context. Thus, the current study proves that an ecosystemic model of healthcare is applicable to the context of DR TB, due to the high burden of disease and other co-occurring factors which patients experience when accessing treatment. The strength of this model is in its consideration of the context of patients, and its emphasis on collaborative practice between health care professionals, for the purpose of resource conservation and better patient management. Aspects of collaboration are present in the current study, where referrals are made to social workers, dieticians and other health care professionals. This shows that the foundations for the implementation of collaborative practice are in place, but further work is needed to enhance the current structures of service delivery.

5.4. Audiological Findings Using the KUDUwave

While the hospital has an audiology department, there are not enough staff members and equipment to service the needs of both the hospital as well as the TB centre where ototoxicity

monitoring takes place. Furthermore, there are difficulties in assessing patients within a sound proof booth when they are contagious, as DR TB patients need to be treated in spaces with good infection control and ventilation. As such, the KUDUwave audiometer which does not necessitate a sound-proof booth, and the ability of trained nurses to operate the KUDUwave at the TB centre, has been beneficial in meeting the needs of patients within this context. Despite the changes in bedaquiline policies, ototoxicity monitoring is still a vital part of successful DR TB treatment. Thus, the hearing test results obtained, and the methods used to do so, need to be as accurate and reliable as possible (HPCSA, 2018).

By far the most significant result of this study, was that a relationship existed between ototoxic hearing loss detected on a KUDUwave audiometer and ototoxic hearing loss detected on a standard GSI audiometer. This relationship indicated that when the KUDUwave revealed that ototoxicity was present, the same conclusion was reached using a standard GSI audiometer, illustrating that the KUDUwave was able to detect the presence of ototoxicity. Although the use of the KUDUwave in this context has not been researched before, a previous study revealed that the KUDUwave was reliable when used to test for a specific type of hearing loss (Brennan-Jones et al., 2017), which ties in with the current research findings.

The results from this study are significant, as no previous research has assessed whether the KUDUwave is suitable for ototoxicity monitoring, and whether results at the ultra-high frequency range could be relied upon (Adjekum, 2014; Storey et al., 2014). This finding is also significant as the equipment used in ototoxicity monitoring needs to be sensitive enough to detect ototoxicity to render a DR TB monitoring programme efficient (HPCSA, 2018). Unfortunately, hearing testing results obtained from a KUDUwave audiometer could not be directly compared to results obtained from a GSI audiometer, as patients only received

diagnostic evaluations on a GSI when discharged from the DR TB programme. There was a large gap in days between the last KUDUwave assessment and the diagnostic audiological evaluation. As such, results not conducted on the same day or at the same sitting, could not be compared, especially since ototoxic changes occurred within the interim.

In terms of the audiological results measured during KUDUwave testing, it was noted that patients had hearing thresholds that were worse at baseline, in comparison to their thresholds at follow-up sessions. This was noted particularly in the lower frequency region, where a mild hearing loss was present at baseline, followed by thresholds returning to the within normal limits range, at the next testing session. This was not in keeping with what is expected during ototoxicity monitoring, as patients generally enter programmes with better hearing, and as they are exposed to ototoxic drugs, hearing thresholds decline over time (Human et al., 2014). Furthermore, when the audiologists reported on the results obtained by the KUDUwave, it was more frequently reported that results were unreliable at the baseline sessions, in comparison to the other testing sessions.

Aside from machinery related factors, possible reasons for these patterns within the current study, may be related to the placement of the KUDUwave insert earphones, and patient factors during testing. During the interviews, nurses reported that they often struggled with the foam tip placement of the insert headphones and were afraid of placing it too deeply into patients' ears and causing them discomfort. As such, nursing staff reportedly asked the patients to place the insert foam tips into their own ears themselves. As patients are not familiar with such a procedure, and often have no knowledge of foam tip placement, it is possible that the insert earphones were not placed appropriately or deeply enough, thus, causing inaccurate results, especially in the lower frequencies. Difficulty with foam tip placement amongst nurses appears

to be a common problem, as noted by Hollander (2018). The literature suggests that despite the KUDUwave having double attenuation, if the insert earphones are not placed deeply enough, noise may not be sufficiently attenuated at the lower frequencies (Clark & Roeser 1988, as cited in Swanepoel et al., 2015). This then results in inaccurate, lowered thresholds, within the low frequency spectrum (Swanepoel et al., 2015).

The nursing staff also reported that patients were overwhelmed by all the testing procedures at baseline, including blood tests, sputum tests and chest x-rays, and that by the time their hearing was tested, they had often fatigued. Nurses further stated that patients often struggled to understand instructions for the hearing testing procedures, particularly at baseline as this was the first testing session. However, with frequency and familiarity, patients became used to the testing and were able to respond to the test appropriately. Thus, such patient factors may be linked to poorer performance and therefore, worse hearing thresholds at the first session, as patients struggled the most at this point. Results then improved at follow-up sessions, when patients were more familiar with testing procedures. As noted by authors in the literature, more research is required in KUDUwave testing of difficult to test populations, as there is a paucity of research in this area (Adjekum, 2014). In most cases, information regarding the patient's report of hearing functioning, was not recorded on the KUDUwave test results, thus, resulting in missing case history information. This is not ideal, as at times, patients experience symptoms of ototoxicity such as tinnitus, before it manifests clinically on an audiogram. Therefore, the omission of this information may have resulted in a delayed diagnosis of ototoxicity.

While some authors relied on patients' reports of their own hearing in order to gauge whether hearing loss was present during ototoxicity monitoring (Human et al., 2010), the

findings of the current study demonstrate that the patient report is not always reliable, and this has been supported by previous research (Borg, 1998). The majority of patients both at baseline and follow-up sessions reported that their hearing was within normal limits. However, hearing testing revealed that hearing loss affecting frequencies in the speech spectrum, was often present in these cases. Nursing staff reported on this phenomenon, and noted that the patient report of hearing could not always be trusted, as certain patients would claim that their hearing was normal despite having difficulties. This was done by patients who were in a rush and wanted to reduce the length of their appointments by avoiding KUDUwave testing. Thus, patients perhaps did not understand the implications of not reporting hearing loss during ototoxicity monitoring. Furthermore, the nursing staff were tasked with the responsibility to ascertain whether patients truly experienced hearing loss, or had no difficulties.

Overall, the mean hearing thresholds for the KUDUwave assessments revealed that hearing was initially within the normal range. However, at follow-up appointments hearing was most commonly described as affecting the ultra-high frequencies or frequencies within the speech spectrum, indicative that patients had developed ototoxic hearing loss. Thus, as time progressed, patients were exposed to kanamycin and then developed signs of ototoxicity. The configuration of hearing loss was sloping at both follow-up sessions, confirming previous studies which described that in ototoxicity, a decline in hearing begins at the high frequencies before affecting the low and mid frequencies (Adeyemo et al., 2016; Appana et al., 2016; Human et al., 2010). While hearing was symmetrical between ears, hearing loss was slightly more prevalent in the left ear. This relates to the ototoxicity findings within the current study, which revealed that amongst patients where one ear was affected by ototoxicity before the other, ototoxicity more commonly affected the left ear. This confirms previous findings by

Modongo and colleagues (2014), who also found ototoxicity to be more prevalent in the left ears of patients.

Within the current sample, ototoxicity manifested early on in DR TB treatment, as it was often detected at the first follow-up session conducted on average, 41 days into treatment. This was in comparison to the findings by Appana and colleagues (2016), where patients only manifested ototoxic shifts nearing the end of treatment, and to the findings by Modongo and colleagues (2014) where ototoxicity was detected 170 days into treatment. This indicated that not only was the KUDUwave successful in detecting ototoxicity within the current sample, but it was able to do so in a timeous manner, thus enhancing the efficiency of the ototoxicity monitoring programme.

A large number of KUDUwave tests were not sent up to audiology for reporting. This is problematic, as without the input of an audiologist, hearing tests cannot be interpreted. Furthermore, the rationale behind hearing testing at follow-up sessions is to detect ototoxic shifts and adjust medications accordingly. Without an audiologist assessing the results for reliability and ototoxicity, conducting hearing testing is fruitless. As previously mentioned, the audiologists often reported hearing tests to be unreliable and they came to this conclusion by evaluating how the audiogram looked. They did not use the data printed on the KUDUwave such as the false positive and false negative rates, to determine reliability. There should be an integration of the two, whereby the statistics recorded by the KUDUwave are also taken into account as they provide quantifiable proof of the reliability of testing.

Aside from the audiologists providing a brief interpretation of the KUDUwave results that were sent upstairs to the department, there was little involvement from audiology within the

ototoxicity monitoring programme as a whole. While the nurse participants described feeling a sense of trust towards audiologists and a sense of comfort knowing that they would be double checking their results, the audiologists did not interact much with the nursing staff who performed the testing. Audiologists within this context should be spear-heading the ototoxicity monitoring programme, as stipulated by their scope of practice, and should assume a collaborative consultation approach to support the delivery of audiological services. They have a responsibility to establish, monitor, and supervise ototoxicity programmes and should be responsible for tailoring guidelines to suit the needs of the health setting (HPCSA, 2018). Furthermore, for any service provision using teleaudiology as a means of hearing monitoring, collaboration with the necessary stakeholders and professionals is required to render it a success (Hollander, 2018).

Results from the interviews revealed that nursing staff had very limited knowledge of what audiologists did, and how audiologists made decisions based on the hearing test results. This was despite the fact that audiologists and nurses were expected to work collaboratively with one another in this context. Audiologists play a vital role in rehabilitation once ototoxic hearing loss has been detected, as they facilitate the dispensing of hearing aids and the counselling of patients regarding the diagnosis (HPCSA, 2018). However, none of the nursing staff at the TB centre were aware that audiologists could further manage hearing loss, and simply saw them as experts within the field of hearing testing and ototoxicity detection. As such, 16 patients were not referred to audiology for diagnostic hearing testing, despite having hearing loss upon initiation on treatment. This illustrated the negative impact that a gap in knowledge can have, particularly in contexts where multi-disciplinary work, and cross-referrals are necessary for effective service provision. These patients should have received hearing aids or further audiological management, but were lost to the system due to breakdowns in communication.

The nursing staff described wanting to receive in-service training from the audiologists directly, to better understand the KUDUwave testing. They also wanted more training from audiologists to understand why results were deemed unreliable and how to modify their protocols when re-testing patients. Five patients were re-tested either at baseline or at follow-up sessions, based on the recommendations by the audiologist. When the repeated test results were reviewed, it showed no change in hearing thresholds between the two tests, yet it was evident that the test results were inaccurate. The nursing staff reported that when asked to repeat testing, they simply re-did the test as they had done it before, with little to no modifications in their techniques. Furthermore, nurses reported not knowing how to judge the reliability of test results and feelings of frustration when asked to repeat tests which they had previously thought were accurate. Nursing staff were often left to independently problem solve regarding what had gone wrong during testing, and the nurses relied on one another in a group setting to aid in this process, as no external support was given to them. This highlights the need for audiological support and intervention, as nurses should be provided with information as to why the results were deemed to be unreliable. Nurses should be further trained in this area so that they are better equipped to accommodate difficult to test patients. Such interventions would save time and resources, as nurses would perform tests more reliably, and thus, not have to spend time re-testing patients.

In this context, it is the responsibility of the audiology department to ensure that there are open channels of communication between the department, the doctors, and the nursing staff who are conducting testing. Some nurse participants claimed that now that the head nurse had left, they would rely on the doctor at the TB centre to assist them with hearing testing issues. Instead, measures should be put in place so that nurses can rely on audiologists to provide this

support, as they are the experts within this field and are best equipped to provide input on improving the reliability of test results and testing difficult patient populations.

The results of the current study which revealed that nurses both wanted and needed support from audiology during KUDUwave assessments, stands in contrast to what Smith and colleagues (2018) have recommended. The authors stated that the KUDUwave can be operated in hospitals providing ototoxicity monitoring programmes, where on-site audiologists are not present and available. However, this research study provides evidence for why such services cannot be provided without the input of audiologists, especially since ototoxicity is such a specialized field, and requires the integration of a number of factors. These include but are not limited to case history information, hearing test results and previous hearing thresholds. It is unlikely that nurses would have been trained for this as part of their higher education curriculums (Keating, 2006; Nelson & Welch, 2006; South African Nursing Council, 2019) and thus, the training that they receive at work, would not sufficiently prepare them for such decision-making processes. This study also provides insights into the consequences when nursing staff are not aware of audiological services, as patients with pre-existing hearing losses, who require specialized audiological intervention are not detected and referred onwards. Thus, instead of eliminating the use of audiologists, effective team collaboration between audiologists and those performing KUDUwave testing is required to improve service delivery in contexts where professional resources are scarce.

From the total sample of 120 patients, very few received baseline hearing assessments, before initiation on DR TB drugs. Almost all of the patients in the sample received a hearing test at the second session. This shows that despite the policy documents by the World Health Organization (Seddon et al., 2012), Department of Health (2015), and HPCSA (2018), stating

that hearing evaluations must be done prior to initiation on treatment, or within 72 hours of receiving treatment, in practice this is not always the case. Additionally, patients did not receive consistent hearing testing at each follow-up appointment, and this is reflected in the decreasing number of KUDUwave assessments conducted at follow-up sessions. For the shortest treatment regimen, patients should have had an average of 9 to 12 KUDUwave assessments at minimum, during the course of treatment, however, this was not the case for any of the patients treated. Merely 58 patients received a third follow-up test, and 34 patients had a fourth follow-up KUDUwave test.

The interviews conducted with nursing staff revealed that they were all well aware of the hearing testing protocols at the TB centre, and all the nurses emphasized the importance of hearing testing for ototoxicity detection, both at baseline and at follow-up sessions. They seemed to understand that aminoglycosides caused ototoxicity, and thus, knew the rationale behind performing regular testing, to ensure that no shifts in hearing were present. The ototoxicity monitoring protocols were further displayed on the walls of the nurse consultation rooms at the TB centre and were clearly visible to all staff. Thus, the reasons behind the omission of follow-up tests was not due to a lack of knowledge on the part of the nursing staff.

During interviews, the nurses provided some reasons for why baseline tests and regular follow-up sessions were not conducted. This included that the laptop used to operate the KUDUwave software was the personal property of the head nurse at the TB centre, as the pervious hospital laptops were stolen. When she was not at work, her laptop was unavailable and the KUDUwave could not be operated. Therefore, patients initiated on treatment or returning for follow-up tests on these days, were not able to receive KUDUwave testing and ototoxicity monitoring. If the laptop was unavailable when patients were initiated, the nurses

made sure to test the hearing of these patients at the first follow-up session. This explains why the number of patients who received a KUDUwave assessment at the first follow-up session, was much higher than at baseline or at any other testing session.

Another reason for the gap in testing included that patients sometimes arrived late for their appointments at the TB centre, and thus, the priority tests such as blood and sputum were done first, so that the doctor could see the patients before leaving. The hearing testing was left until last, at which point, patients were in a rush and left the clinic before having the hearing test. However, some nurses reported that at times, they were to blame for not conducting testing at every session, despite knowing that patients were on kanamycin. They deliberately omitted testing when they were short-staffed or over-burdened with work and did this to prioritize the treatment of other patients. Nurses felt that they could not reprimand their colleagues for practicing in this manner, as they understood the reasoning behind it. Thus, these findings highlight that the gaps in regular hearing monitoring are not due to a lack in knowledge of the importance of testing, but rather due to resource constraints and logistical issues. This is not surprising within the South African context, as previous research within the field of ototoxicity monitoring revealed that discrepancies between policies and practice are largely due to shortages of staff and limited availability of equipment (Govender & Paken, 2015).

The low frequencies of 250 Hz and 500 Hz were often omitted during KUDUwave testing, and this was noted in baseline tests as well as in follow-up assessments. This is strange as the Department of Health (2015) guidelines and the HPCSA (2018) guidelines both stipulate that ototoxicity monitoring should involve the full frequency spectrum, from 250 Hz to 16 000 Hz bilaterally. The omission of these frequencies may have possibly resulted in poor identification

of conductive pathologies which affect the lower frequencies, especially since bone conduction testing was not performed during KUDUwave testing.

Other patients did not receive extended high frequency audiometry beyond 8000 Hz, despite being monitored for ototoxicity which generally occurs in the ultra-high frequencies, beyond 8000 Hz (Human et al., 2010). Previous studies wherein the ultra-high frequencies were not tested during ototoxicity monitoring, revealed that ototoxicity was missed, as the hearing in the standard frequency spectrum was normal, while changes had occurred at the higher frequencies (Duggal & Sarkar, 2007; Modongo et al., 2016; Sharma et al., 2016). Thus, ototoxicity monitoring is unsuccessful without the assessment of the extended high frequency range. If the ultra-high frequencies are not tested, when the next assessment is conducted, audiologists have no previous results to compare the findings to and thus the detection of ototoxic shifts is affected. In the current study, when the ultra-high frequencies were omitted, the audiologists commented on the results, noting that frequencies were omitted and should be tested. As such, less patients had the ultra-high frequencies omitted at follow-up test sessions, revealing that the audiologist's recommendations were adhered to by the nursing staff.

The nurse participants reported that the audiologists were unhappy when frequencies were missing on KUDUwave testing, and the nurses did not understand why this was the case. This displayed the lack of communication between both sets of professionals, a common occurrence within DR TB management (Hollander, 2018). On further investigation by the nursing staff, the reason for the omission of the low and ultra-high frequencies was due to the fact that they were selecting the incorrect testing protocol on the KUDUwave software. The KUDUwave technicians were called in by the head nurse to resolve the matter. The majority of nurses who performed the test reported not realizing that frequencies were absent, and only noted it when

the audiologists' pointed it out in their written report of the KUDUwave audiograms. Furthermore, the nurses reported that they performed KUDUwave testing robotically, without having an understanding of what they were doing. This was evident in the test results, as nurses displayed that they did not have the necessary experience to problem solve and identify errors in testing procedures.

Bone conduction results during KUDUwave testing were not available for the majority of patients. While bone conduction testing runs automatically, it does require the nursing staff to place the bone conductor appropriately and instruct the patient for testing. Every nurse in the sample did not feel confident with bone conduction testing; some nurses did not remember the term bone conductor, and others admitted that they did not know the purpose of bone conduction, how to place the transducer and how to instruct the patients for this section of testing. Some nurses described that patients struggled with bone conduction testing, and the nurses themselves were unable to help them, as they were unsure of what was being tested and how it functioned. All the nurses in the study noted that they required further training in what bone conduction is, how to place the bone conductor and how to instruct patients for this portion of testing. This is perhaps why bone conduction results were unavailable for most patients who were tested in this study, as the nurse operators were not confident in this area and thus, were not able to perform the testing.

5.5. Audiological Findings at Exit from the Programme

The South African guidelines stipulate that all patients exposed to aminoglycosides should have a full exit audiological evaluation, including otoscopic and tympanometric evaluations, puretone audiometry with ultra-high frequency testing, as well as speech testing (HPCSA, 2018). However, out of the total sample of 120 patients, very few received an exit diagnostic

audiological evaluation, despite the staff being aware that this was the protocol. The nurses who were interviewed reported not knowing why patients needed an exit audiological evaluation, and perhaps the lack of knowledge regarding the rationale behind testing, has resulted in decreased compliance with booking patients for diagnostic evaluations.

The majority of patients who were tested at exit received otoscopic and tympanometric testing, however, a large number of patients did not receive ultra-high frequency testing, despite having had a history of exposure to ototoxic medications. This is particularly concerning, as patients within the sample who had displayed ototoxicity during KUDUwave follow-up tests, did not have this range of the frequency spectrum assessed. Furthermore, not all patients received bone conduction testing, which meant that the type of hearing loss could not be established, and speech audiometry was rarely done at diagnostic testing sessions. Not only is this in contravention of the South African guidelines (HPCSA, 2018), but it is expected that qualified audiologists within this context, are aware that patients exposed to ototoxicity, who are at high risk for hearing loss, should receive thorough diagnostic testing. Those who did have ultra-high frequency testing, had threshold results for frequencies including 11 200 Hz and 12 500 Hz. While this is unconventional, research shows that these frequencies are particularly sensitive to ototoxic shifts (Hollander, 2018), and these were the set frequencies pre-programmed on the GSI audiometer that was used.

The omission of bone conduction audiometry has an implication for the identification of conductive pathology, which was present in the current patient population. At diagnostic evaluation, certain patients required referrals to the ENT (Ear, Nose and Throat) surgeons due to symptoms of middle ear pathology, hearing loss and abnormal tympanometric results. This trend is on par with what is expected, as conductive pathology is common amongst the DR

TB population, particularly in those co-infected with HIV. This is as HIV compromises the immune system, placing patients at an increased risk for opportunistic infections such as otitis media (Konrad-Martin et al., 2005). This finding not only highlighted the need for multi-disciplinary work within this patient population, but emphasized that thorough patient assessment is necessary due to the overlap of disorders. It further displayed that gaps in service delivery within the current context, were not limited to the practice of nursing staff alone, but included audiologists.

During diagnostic evaluations, it was noted that the patient report of hearing functioning did not match the quantitative hearing test results. Most patients reported their hearing to be within normal limits, however, upon assessment, these patients were found to have a hearing loss, affecting the speech spectrum of frequencies between 250 Hz and 8000 Hz. Literature suggests that the reason for this discrepancy may be based on patient's perceptions of functioning and the demands placed on them by their own environments (Borg, 1988; Berben et al., 2018). A patient who is more functional, and interacts within a multitude of dynamic conversational environments, might experience a hearing loss more severely than someone who is unemployed or spends large amounts of time in solitude. As such, one cannot assume that the objective test results from hearing assessments are the most accurate reflection of patients' needs and levels of functioning. Thus, audiological intervention for patients should be tailored to the individual requirements of patients, particularly with respect to the provision of intervention services.

The majority of patients in the sample presented with a hearing loss that was sloping in configuration. However, in comparison to the KUDUwave tests where hearing loss was most common in the ultra-high frequencies, hearing loss at diagnostic assessments was present in

the speech spectrum from 3000 Hz onwards. Bedaquiline was available to patients within the current sample, and patients were mostly taken off kanamycin immediately when ototoxicity was detected.

In some cases within the current study, the doctors did not agree with the audiologist's recommendations to switch patients to bedaquiline, and thus, these patients continued with kanamycin. Therefore, better communication and collaboration is required in this area, so that professionals are on the same page regarding patient management. Despite these oversights, generally the relevant precautions were taken to reduce ototoxicity. Yet, patients still developed ototoxic hearing loss that affected the speech spectrum. This illustrates that to effectively reduce ototoxicity, patients should not receive ototoxic drugs, as ototoxicity monitoring practices are not sufficient enough. As such, the new South African and WHO guidelines which recommend bedaquiline for all patients aside from those requiring amikacin, is a step in the right direction in reducing the burden of ototoxic related hearing loss. It reveals that caution should be taken when making the decision to place patients on amikacin which is ototoxic (Duggal & Sarkar, 2007) as monitoring procedures are not always effective.

In terms of outcomes, most patients had hearing loss that could not be remediated with hearing aids, as the hearing loss occurred at frequencies beyond the amplification range of hearing aid devices. As such, most patients were counselled regarding their hearing status, given compensatory strategies to improve communication, and informed to be vigilant for symptoms of hearing loss, should their hearing status worsen. While it is recommended that patients be monitored for 6 months following discharge from TB treatment (HPCSA, 2018) this is not feasible for staff or for patients who are often not within a close radius of the hospital.

Thus, appropriate counselling ensures that patients are equipped to identify the symptoms of hearing loss and are able to access hearing services when necessary.

5.6. Nurses in Hearing Testing

It is the responsibility of nurses to educate, train, and supervise their fellow colleagues, particularly in areas of service provision that are unfamiliar or specialized in nature (Tompkins, 2001). Furthermore, tertiary education equips nurses with the basic skills required for healthcare, while it is the responsibility of institutions to ensure that nurses are trained in the more specialized services which they require their nurses to provide (Keating, 2006). In this case, this includes hearing screening, and as such, the TB centre is in line with these guidelines, as nurses were not expected to have prior knowledge in hearing screening, and were trained on the KUDUwave during the period of their employment. The implication of this is that both pre-existing knowledge as well as gaps in knowledge can be attributed to the training opportunities afforded to nursing staff within the hospital context.

The majority of nurses within the study, had received training from the head nurse and not directly from Emoyo who services KUDUwave. This trend highlights the importance of having nurses who are well trained and experienced within ototoxicity monitoring and KUDUwave testing, so that these individuals can train others, up-skilling and developing more professionals to meet the needs of the many patients accessing healthcare. This is especially the case since it has been acknowledged that nurses are required to facilitate the learning and development of their colleagues, in unfamiliar or challenging settings (Tompkins, 2001). The formal Emoyo training focused largely on the technical and theoretical aspects of hearing testing, using the KUDUwave audiometer. The head nurse taught nurses these skills, but also allowed the nurses to observe her during testing and afforded them the opportunity to assess patients while she

supervised. All of the nurses, especially those trained by both Emoyo and the head nurse, highlighted the positive effect that this practical training had on their performance when testing patients independently. Those who were trained by both entities, claimed to prefer the head nurse's training over the formal training from Emoyo, as they did not simply learn the theoretical aspects of testing such as software and earphone placement, but acquired skills and knowledge experientially.

The nurses reported that observing the assessment of patients equipped them with practical skills that they needed for testing, including how to problem solve as well as how to determine whether patients were concentrating during testing or not. These findings provide valuable information for how future KUDUwave training should be conducted, in that while theoretical information should be included, an emphasis on practical training is necessary. This form of training is especially important in unfavourable contexts where nurses need to problem solve independently, in the event that no senior staff or audiological support is available.

A trend in the current study revealed that nurses who were older in age required more training on the KUDUwave than younger nurses, as they were not computer literate, and thus, struggled with the KUDUwave software. This is an interesting finding to consider when training nursing staff, as the focus is often placed on the practical aspects of testing such as earphone placement. Little thought is given to the technological factors that influence the ease through which nurses understand how to operate such machinery. This ties in with literature which emphasizes how medicine has been revolutionized by technology, yet nursing staff are not always well equipped to understand and operate machinery, especially in contexts where technology has transformed the manner in which services were typically provided (Nelson & Welch, 2006; Tompkins, 2001). Thus, having to assume the new role of someone who performs

hearing screening, as well as being expected to operate the KUDUwave, are two areas for which nurses were not previously trained or prepared. Instead, they are expected to adapt and learn dynamically, within the context that they work, and such an expectation has become common place within the 21st century of nursing practice (Tompkins, 2001).

The inconsistent availability of the KUDUwave machinery in the current context, did not only negatively impact upon patient care as regular follow-up assessments were not conducted, but it also negatively impacted upon the nursing staff. Nurses lost out on the opportunity to use the machinery and practice their skills on a daily basis, and some nurses admitted to having forgotten how to use the KUDUwave in the months that it was not present at the clinic. The loss of the head nurse at the TB centre has had a marked effect on the nursing staff. Not only has her absence meant that the laptop was no longer available for KUDUwave testing, but nurses have lost a vital member of their team, whom they relied upon especially when having difficulty during KUDUwave assessments. While the nursing staff will rely more upon one another, this study has highlighted that audiologists need to assume a more active role in some capacity to assist the nursing staff; even if this support occurs periodically and on an ad hoc basis. This is in line with what is recommended by the HPCSA (2018), with regards to the role audiologists should play in supporting and developing ototoxicity monitoring programmes.

The nurses emphasized the importance of instructing patients adequately during testing, and made every effort to accommodate patients, including adapting the language to best instruct patients for hearing testing. Nursing staff who are able to relate to both the linguistic and cultural backgrounds of patients, are better equipped to cater towards the needs of patients, especially in terms of environmental and contextual factors (Keating, 2006). The nurses felt that the KUDUwave was user friendly and easy to operate, but not sufficiently durable enough,

especially with regards to the mobile bone conductor, which often broke or was displaced. Such a finding is noteworthy, as no other studies have looked into the views of people who have used the KUDUwave audiometer for assessment, particularly in busy contexts where the machinery is relied upon daily.

On the whole, the nursing staff had a positive attitude towards performing hearing tests. They felt a sense of empowerment and joy from performing the testing, and further described a sense of responsibility to conduct the testing accurately, as they were aware of the implications that hearing results had on DR TB management. However, the nurses expressed frustrations with audiologists, especially when they declined to test the infectious smear positive patients in the booths, or when they marked hearing test results as unreliable, with no further explanations. Nurses further felt frustrated that they were required to do hearing testing, especially on busy days when they had many other responsibilities and a high work load at the TB centre. One nurse described being unhappy that she had to take time out of her day to take KUDUwave results upstairs to audiology, which was both time consuming and stressful. The buy-in from nursing staff is both important as well as necessary to ensure that the DR TB monitoring programme works smoothly within this context, as staff attitudes towards patients can further affect patient outcomes (Li et al., 2016). Therefore, there is a need to recognize nurses as important members of the team within this context and to communicate openly with them, such that their morale is kept high and they are provided with a sense of mastery, allowing them to feel equipped to function within this context.

The nurses in this study had high levels of self-awareness and were able to identify the areas in which they required further training and skills development. Such a quality is important, as in the changing landscape of healthcare nurses are expected to assume new roles

and responsibilities to achieve success in the workplace. Considering this, nurses need to be critical of their own knowledge and capabilities to enhance professional development (Tompkins, 2001). Nurses described wanting more information on what ototoxicity looked like, the use of the KUDUwave, bone conduction audiometry, the theory behind ototoxicity monitoring, and how to determine the accuracy of KUDUwave results. These points were communicated to the Emoyo DR TB co-ordinator who came in December of 2018 to re-train the nursing staff on how to operate the KUDUwave audiometer, as it had not been in use for half of the year. This illustrated how some of the findings of this study have provided valuable information for future training and intervention procedures. Not only does this indicate that nurse operators of the KUDUwave are well aware of their capabilities and limitations, it also provides a window of opportunity to tailor training programmes to the specific needs of nurses, so that testing procedures can be refined, and future resources conserved.

As many nurses in this study were trained by other nurses, an important question that was posed in the interviews, involved how prepared nurses felt to train other nurses on the use of the KUDUwave. While most highlighted that they would include practical training and emphasize the importance of patient instruction and counselling, one nurse admitted that she would not train others as she was not confident in her own ability to use the machinery. This is significant, as within the context of teleaudiology and public health, we should not simply be training staff to be competent within a given context, but equipping them with dynamic skills that will foster the growth of themselves as well as other professionals, in any diverse context in which they are placed.

5.7. Remarks

The findings of this study have brought to light the value of analyzing factors that exist beyond the individual, to gain a better understanding of what DR TB patients experience both personally, socially, environmentally, and as active members of their own societies. The various levels of Bronfrenbrenner's ecosystemic model are relevant to the findings of this study, and aid in establishing specific determining and interacting factors, and the relation of these to individual patients. Figure 5.2 displays how the findings of this study have been integrated with Bronfrenbrenner's ecosystemic theory, such that the tiers of the chronosystem, macrosystem, mesosystem, microsystem and individual have been detailed according to the research findings.

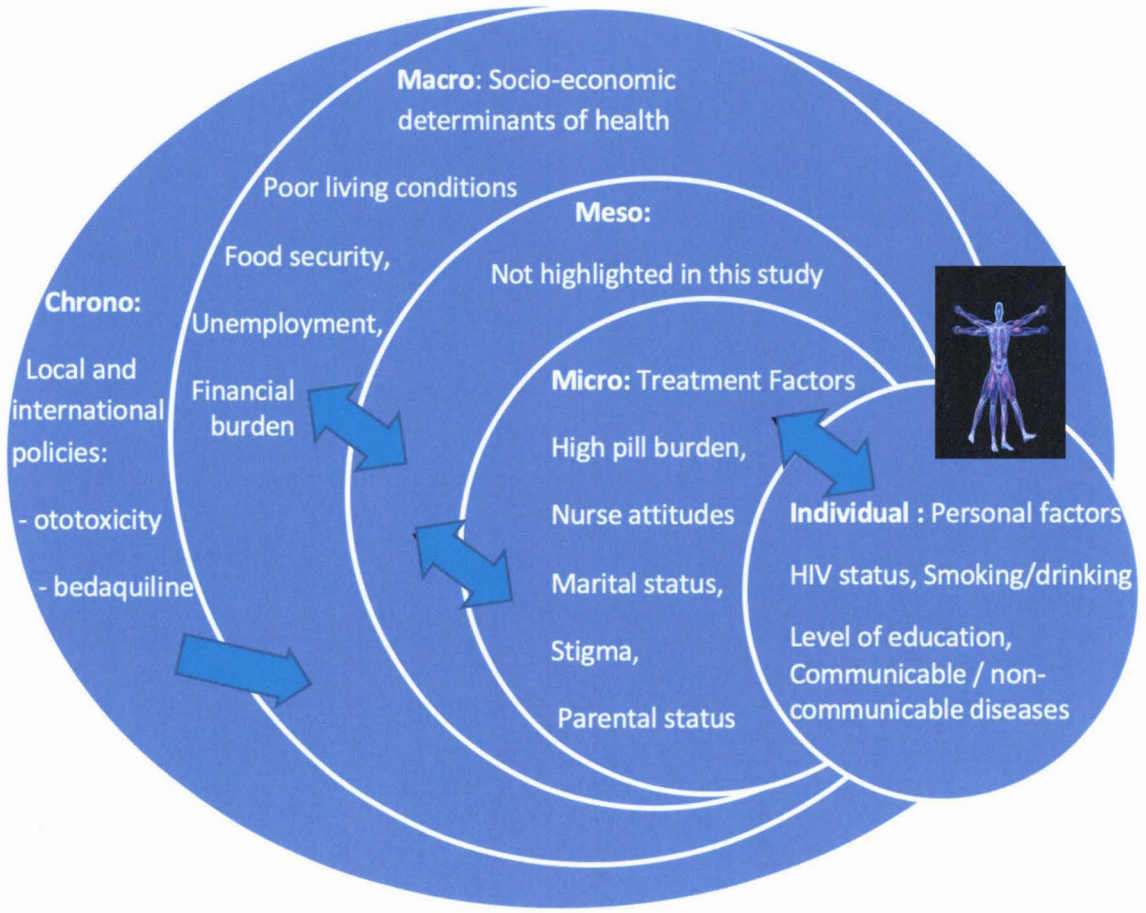

Figure 5.2. Application of the Ecosystemic Theory to the Current Study.

Note. Image of the human retrieved from: voronamassagetherapy.com

As illustrated, this holistic perspective has the potential to equip medical professionals with the necessary knowledge and skill-set to better manage and treat patients within the DR TB context, while providing intervention that is sensitive to the needs of patients at various levels of their reality. Viewing patients in this manner enhances collaborative practice between professionals, especially since this study has highlighted the important role nurses have to play in such a context. Nurses require on-going support and training to ensure the successful implementation of teleaudiology within the DR TB context. Thus, the ecosystemic model in conjunction with quantitative epidemiological findings can be used to inform evidence-based practice within the public health care setting.

Chapter 6

Conclusion and Recommendations

6.1. Summary of Findings

This study which explored an audiological protocol in ototoxicity monitoring within the context of DR TB in a tertiary hospital in Gauteng, brought to light an array of factors associated with DR TB, ototoxic hearing loss, and the monitoring thereof. The use of an ecosystemic approach, revealed that patients should not only be evaluated based on individual factors such as medical criteria and diagnosis, as such a viewpoint is reductive in nature, and disregards many of the other system factors which influence the health and functioning of patients. While the findings of this study revealed that patients within the DR TB population had a high burden of disease, with large co-infection rates between HIV and DR TB, and a high prevalence of acute, chronic, and opportunistic diseases, the results also brought forward many environmental and social factors that affected patients with DR TB. Patients displayed high rates of unemployment, low food security, and other trying circumstances which predisposed them to DR TB, affected their compliance with hearing testing and treatment, and rendered them vulnerable to the acquisition of ototoxicity. While many of the personal factors explored in the current study are endemic to the context of patients living in South Africa, such issues are present in societies all over the world, and as such, these considerations and this model, can be utilized in multiple and diverse contexts.

The study further emphasized the need for multi-disciplinary intervention between healthcare professionals, as patients experienced a host of factors which required cross-referrals between professionals, as well as the diverse expertise of more than one practitioner. In the present context, nursing staff are important stakeholders within the ototoxicity monitoring team, as those who are equipped to perform KUDUwave hearing tests are an asset

to the system. This is as it decreases the burden on audiologists and allows for resources to be distributed appropriately. However, better collaboration and communication is required to support the nursing staff who, themselves are understaffed and over-burdened. Audiological support and collaboration at this level would enhance patient management and reduce the wastage of both time and resources.

The overall findings revealed that despite the availability of bedaquiline and audiological services, patients still developed ototoxic hearing loss, which affected frequencies within the speech spectrum. This was as patients did not always receive bedaquiline when they required it. Furthermore, the findings of this study highlighted that patients did not receive regular follow-up hearing tests and at times, were initiated on aminoglycosides without having received a baseline hearing assessment. The majority of patients were not referred to audiology for an exit audiogram, and some patients who required audiological services were lost to the system. These gaps in service delivery did not only occur at the level of nursing staff operating the KUDUwave, but were also detected in diagnostic services provided by audiologists as ultra-high frequency testing was not always included within the test battery.

A significant outcome of the study was that there was a correlation between the KUDUwave detecting ototoxicity and the standard GSI audiometer detecting ototoxicity, indicating that the KUDUwave was able to detect ototoxicity effectively. In comparison to other research studies, ototoxicity was detected faster in the current study, revealing that the KUDUwave was efficient in ototoxicity detection. While the KUDUwave was able to detect ototoxic hearing loss, the manner in which nurses operated the machinery had an effect on the accuracy of the hearing thresholds obtained. The overall KUDUwave results revealed that the thresholds of patients particularly in the lower frequencies, were negatively affected by

incorrect insert earphone placement. Patients performed worse on baseline assessments than at follow-up sessions due to fatigue and unfamiliarity with testing procedures.

During KUDUwave monitoring, patients developed ototoxic hearing loss affecting the ultra-high frequencies while receiving kanamycin treatment, and this ototoxicity was present when patients were switched to bedaquiline. However, upon exit from the programme, the diagnostic tests revealed that hearing loss affected frequencies within the speech spectrum, indicating that despite monitoring, ototoxic medication still had an effect on patients' hearing. Staff shortages and inconsistent availability of machinery resulted in patients not receiving baseline and follow-up tests as per the South African guidelines. While South African policies dictate that every patient receives diagnostic audiological assessments upon exit from the DR TB programme, merely 28 patients from the sample of 120 in this study, received exit diagnostic audiograms. These gaps in service delivery were related to a lack of knowledge regarding the role of the audiologist and lack of staff and resources at the TB centre at the chosen hospital. There appeared to be a lack of involvement of audiologists when nurses performed KUDUwave testing in the current study, yet insights from the nurse interviews highlighted the difficulties that nursing staff experienced within this context, and the vast need for audiological support within this area.

6.2. Implications

The preliminary findings of this study have been shared with the necessary stakeholders at the TB centre of the hospital, to ensure improved service delivery and appropriate training for the nursing staff. This was done when the DR TB co-ordinator from Emoyo came to train the nursing staff on the KUDUwave and the new laptop. Further training and collaboration between the audiology department and the TB centre should be encouraged to facilitate the

optimal functioning of the DR TB ototoxicity monitoring programme and to enhance the referral process. These modifications will be specifically applicable to those on amikacin, who require more stringent ototoxicity monitoring.

Firstly, this study has highlighted that ecosystemic approaches should be considered in hearing healthcare as the focus needs to be shifted from practical processes, systems, and individual factors, to a holistic understanding of the contextual factors which influence both policy and practice. The dynamic interactions between patients and their contextual factors requires particular consideration. As such, healthcare planning, service provision, and preventative medicine needs to focus on the human aspect of intervention, considering the end users who access healthcare services, in order to render healthcare that is contextually relevant for any given society. Thus, the use of this approach in DR TB transforms the lens through which patients are viewed, moving towards the consideration of external environmental aspects of patients' lives, which in turn, has strong implications for both policy and practice.

An important implication of this study is that it is the institution's responsibility to train and prepare nurses for the duties that they are expected to perform, especially in terms of the assessment and management of ototoxicity in DR TB. This is since nursing staff have very little to no prior knowledge in this area as tertiary level education does not focus on this avenue of service provision. While nurses are required to learn how to operate technology and advanced equipment such as the KUDUwave in a health care setting, audiologists have an important role to play in this respect, as nurses should not and cannot be expected to perform their role in ototoxicity monitoring unsupported. If they do not receive the necessary support, inaccuracies in KUDUwave testing and gaps in service provision occur, as has been demonstrated in this study. Therefore, audiologists should collaborate with nursing staff, and

support should be given through in-service training, and consultation if and when necessary, so that audiologists are completing their duty towards preparing nurses for the role which they are required to assume.

Considering that globally, kanamycin is still readily used in DR TB treatment, this study highlights the need for bedaquiline to replace kanamycin, as a first-line drug of choice in countries other than South Africa. This is as ototoxicity monitoring procedures alone cannot successfully prevent ototoxicity as it occurs, especially due to logistical barriers within healthcare settings. This was illustrated in this study, as patients still developed ototoxic hearing loss affecting the speech spectrum, despite receiving ototoxicity monitoring and despite the presence of teleaudiology equipment and an audiology department at the hospital. Patients were lost to the system, and did not have access to hearing testing regularly at every follow-up, despite this being legislated in policy documents. Therefore, logistically, bedaquiline reduces audiology patient numbers significantly, as patients do not require hearing testing as frequently as before, thus reducing the burden on audiology departments. This is significant for developing countries such as South Africa, where the patient load far exceeds the number of trained audiologists available. As such, the inclusion of bedaquiline, allows audiologists to focus more specifically on hearing screening for DR TB patients who most require it, such as those on amikacin.

The patient factors explored within this study have highlighted that DR TB patients experience complex comorbidities and, conditions which require multi-disciplinary intervention from a number of professionals in order to achieve positive treatment outcomes. The contextual backgrounds of patients were explored, and this provided indications for the types of factors that healthcare professionals need to take into account when treating such

patients. The high numbers of foreign patients in the study emphasized that the DR TB phenomenon is not unique to South Africa. There is a need for global cross-collaboration to ensure that DR TB treatment programmes are well established in neighbouring African countries, which may further assist with reducing the burden of disease within South African hospitals. Research and practices from ototoxicity monitoring programmes locally can be used to benchmark service development in other neighbouring countries, building up on their existing resources.

As logistical barriers such as not having consistent access to a laptop affected the service provision at the TB centre, the findings highlighted the need to ensure that tertiary health services, particularly those experiencing high volumes of patients, are provided with the necessary resources and equipment. When these equipment are not available, contingency plans should be put into place so that patient services do not come to a halt. The buy-in from nursing staff is crucial when running an ototoxicity monitoring programme, especially if nursing staff are expected to perform hearing testing using equipment such as the KUDUwave. Thus, nurses should be counselled regarding the reality of the situation, where hearing testing may add to their work load, but is fundamental for patient care and management. Through collaborative practice and better communication, nurses would understand the role of audiologists both in assessment, intervention, and rehabilitation, and this would then enhance the referral process.

When exploring the topic of nurse training, which should ideally be done by audiologists, provision should be made to teach nurses in the manner in which they best respond to, in order to improve the response to training. The findings highlighted that nurses learn best when given practical exposure and as such, when trained, they should be given the opportunity to test one

another, therefore reinforcing various aspects of training. Areas wherein nurses particularly required input within this ototoxicity monitoring programme included how to manage difficult to assess patients, and how to identify inaccurate testing results. The process of positioning insert earphones needs to be taught to nurses, so that they feel confident doing it, and are not reliant on patients for foam tip placement. This may improve the reliability of the results obtained. A broader understanding of how the KUDUwave functions and the implications of hearing monitoring on ototoxicity needs to be established. While these areas were specifically brought up by the nurses at this research site, these findings provide a brief outline for the areas in which training for nurses would be beneficial.

The findings of this study have highlighted that patients who are difficult to assess are a common occurrence in the DR TB sample, and subjective assessment measures requiring co-operation from patients, are not always appropriate. Therefore, there is a need to modify ototoxicity assessment procedures in order to accommodate such patients. This can be done by prioritising the testing of the ultra-high frequencies over the other frequencies, and utilizing objective measures such as DPOAE's in assessment protocols. An audiologist would need to be present for such modifications to occur and thus, this further illustrates the team collaboration that needs to occur within this context. Specific guidelines for ototoxicity monitoring within health institutions should be drawn up by audiologists and the health team, to avoid miscommunications between professionals.

6.3. Limitations

The audiological results from the baseline and the first two follow-up KUDUwave sessions were used, without the inclusion of the other follow-up tests as the sample displayed attrition from the third follow-up test onwards. This was as fewer patients received follow-up tests as

time progressed, which was an important finding within the study. However, the use of fewer follow-up sessions affected the robustness of the data presented, and was not a thorough reflection of hearing decline over time as fewer testing sessions were examined. Furthermore, exit diagnostic testing and KUDUwave testing were not conducted on the same day and as such, the hearing thresholds obtained by each audiometer could not be directly compared to one another. Thus, conclusions on how accurate the hearing thresholds were between the two types of machinery could not be ascertained. Despite the fact that 120 patients files were reviewed, very few patients in the sample presented with certain characteristics such as diabetes, rendering it challenging to perform more complex inferential statistics. Lastly, as only six nurses met the inclusion criteria for the qualitative phase of the study, the interview schedule could not be piloted prior to data collection. While changes to the interview schedule were not necessary within the current study, the piloting of research instruments aids in maintaining rigor within a qualitative study.

6.4. Suggestions for Future Research

6.4.1. Patient compliance

Future research could explore the factors determining patient compliance with treatment and with hearing testing procedures. Interviews should be done with patients to ascertain what affects non-adherence to medication regimens and ototoxicity monitoring protocols, so that these can be taken into account by healthcare professionals. Furthermore, patients' attitudes and views towards hearing testing should be investigated, especially amongst those on lengthier treatment regimens. This may provide insight as to which factors impede upon patients' willingness to actively participate in hearing monitoring practices.

6.4.2. KUDUwave testing

As this research study was unable to directly compare KUDUwave results to puretone audiometric results, more research comparing these two audiometers when measuring thresholds within the ultra-high frequency range and within the context of ototoxicity, is necessary. This will provide further information into the accuracy of the KUDUwave within the context of DR TB.

6.4.3. The effects of training

A follow-on study should be conducted wherein nurses are formally trained on the KUDUwave and how to operate it using a standard protocol. The accuracy of results and measures of nurse performance during testing should be assessed both pre- and post- training, to ascertain the affect that training by an audiologist has had on nurses' performance.

6.4.4. Further mixed methods research

Lastly, it is recommended that future studies within the field of audiology include a qualitative aspect to data analysis, as was done in the current study using a mixed methods approach. Qualitative data augments the quantitative findings and provides a rich and insightful glimpse into the context of the research study, which would not be possible if quantitative analysis were to be used in isolation. Furthermore, from an ecosystemic approach, the mixed methods aspect allows for the analysis of factors affecting the patient that exist beyond the realm of the individual, including circumstances in the immediate environment and larger society as a whole. While this study has explored the ecosystemic approach in relation to patients being

tested for ototoxicity in DR TB, further research could delve into the systems surrounding nursing staff, and how this affects their testing practices and ability to learn how to operate the KUDUwave. Other aspects of ototoxicity such as ototoxicity monitoring in renal dysfunction or in chemotherapy, could be explored by examining the various ecosystemic factors which impact upon audiological service delivery within these areas.

6.5. Concluding Remarks

The findings of this study highlighted the importance of a mixed methods design in conjunction with an ecosystemic framework of analysis, which together addressed the predisposing and exacerbating factors which occurred beyond the level of the individual. Not only does this provide a rich understanding of the context of DR TB patients in the population, but provides researchers and healthcare professionals with invaluable information regarding the experiences of such patients, and how best to tailor services to address diverse life experiences. Understanding the context of patients can provide beneficial information which can effect change both at a micro level as well as a macro level of service provision, where communities and societies are equipped to deal with health, social, and contextual issues.

South Africa has made the bold decision to transform DR TB treatment by eliminating injectable aminoglycosides such as kanamycin, from the standard treatment protocol. This is advantageous as the current study proves that not all patients were receiving accurate and regular ototoxicity monitoring services. However, the ototoxic drug amikacin, still exists within the treatment regimen, and while it is not standardly prescribed, the WHO (2018) and the Department of Health (2018) have suggested that hearing monitoring for ototoxicity continues for all patients, despite the prescription of bedaquiline. This is as patients may need to start amikacin during treatment if the outcomes during drug therapy are not favourable. As

such, baseline hearing upon entry into DR TB programmes is still necessary. Therefore, despite the presence of bedaquiline, ototoxicity monitoring is still paramount and should be conducted as accurately as possible. The presence of bedaquiline has changed the face of ototoxicity monitoring not by eliminating its necessity, but by reducing the burden of patients accessing the ototoxicity monitoring system. This is as patients now need to be monitored less frequently, yet more precisely. This then leads to the outcomes of this study and how they can be implemented within DR TB monitoring programmes.

While the findings of this study revealed that the KUDUwave was able to detect ototoxicity, it was noted that the manner in which the nurse operators used the KUDUwave equipment, had a marked effect on the accuracy of results. Results revealed that the nurses required further training and continued support, particularly from audiologists, in order to operate the machinery accurately and efficiently. Thus, the changes in bedaquiline laws have been opportune in that nurses will have fewer patients to test each month, affording them the opportunity to refine their skills and receive hands-on intervention from audiologists in the areas in which training is most required. The aim of this is to reduce the rate of re-testing and promote time-saving and resource conservation practices. As these laws apply to all provinces nationally, this strategy is not applicable to the TB centre alone, and can be used in other hospitals and clinics nationwide.

Multi-disciplinary teamwork is fundamental within this context and can only enhance and contribute towards the development of the individual. Health professionals need to work together to successfully provide services that are clinically and contextually appropriate for the patients accessing public health services, while bearing in mind that collaborative practice further contributes to the development of other health professionals, health institutions and

wider society. South Africa has paved the way for injectable free DR TB treatment regimens which will make a vast difference in the successful management of patients and the promotion of healthy lifestyles.

This study has provided areas wherein ototoxicity monitoring procedures can be refined to meet the holistic needs of patients both clinically as well as socially, emotionally, and economically. While the current study examined a specific protocol at one tertiary hospital in Gauteng, the data obtained was representative of broader issues affecting patients with DR TB, which were not specific to one hospital, one city or one province. In fact, some of the findings confirmed assumptions made by international authors, who observed similar trends amongst DR TB patients in countries across the globe. Aside from the patient factors present amongst those accessing services at a particular hospital, this study examined the use of the KUDUwave as part of teleaudiology in this ototoxicity management protocol.

The KUDUwave was not explored in terms of reliability and validity, but within a larger system which was affected by both facilitators and inhibitors to success. The consideration of a multitude of factors affecting both patients and the nursing staff who perform the KUDUwave testing, creates a bird's eye-view of the entire ototoxicity monitoring system within DR TB in this setting. Insight was provided into the professionals working in ototoxicity within this context, the patients who had DR TB and received ototoxicity monitoring and the contexts and societies from which patients originated. Insights into the policies governing DR TB treatment, and ototoxicity in South Africa were explored, both of which have a profound capacity to influence every aspect of patient management.

Therefore, with a view of all these diverse and unique influences, audiological care and overall healthcare management should assume a renewed perspective when treating ototoxicity in DR TB. This perspective is crucial as there is great potential for South Africa's healthcare system to drastically shift towards service provision that provides ototoxicity intervention at the various levels of influence, thus, empowering both healthcare workers and patients alike.

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