Considerations for cochlear implantation in adults with Human Immunodeficiency Virus

by

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LIST OF ABBREVIATIONS

ABR – Auditory Brainstem Response

AIDS – Acquired Immune Deficiency Syndrome

ART – Antiretroviral therapy

ARV – Antiretroviral

CAP – Categories of Auditory Performance

CAPR – Revised version of Categories of Auditory Performance

CI – Cochlear implant

CNS – Central nervous system

CT – Computerized tomography

ENT – Ear-, nose- and throat

HAART – Highly active antiretroviral treatment

HIV – Human Immunodeficiency Virus

HIVpos – HIV-positive

HIVneg – HIV-negative

HL – Hearing loss

HRQoL – Health-related quality of life

JCIC – Johannesburg Cochlear Implant Centre

LMICs - Low- and middle-income countries

MDR-TB – Multidrug-resistant tuberculosis

MRI – Magnetic resonance imaging

OIs – Opportunistic infections

PCIU – Pretoria Cochlear Implant Unit

PLWHA – Persons living with HIV/AIDS

SNHL – Sensorineural hearing loss

TB - Tuberculosis

FORMATTING

APA referencing style was utilized in this dissertation, except in Chapter 3 (article). Chapter 3 was edited according to the editorial specifications of the journal to which the article was submitted, and differs from the editorial style of the rest of this document.

ABSTRACT

Previous observational studies have demonstrated that Human Immunodeficiency Virus (HIV)-positive (HIVpos) cochlear implant (CI) recipients are functional CI users, but have provided limited information regarding HIV-specific preoperative considerations, such as health status, pneumococcal vaccination, CD4+ cell count and viral load status. This study aimed to describe candidacy, audiological and surgical considerations for cochlear implantation in adults with HIV by reviewing data from a larger sample of HIVpos adult CI recipients.

A retrospective chart review was employed for this study. Retrospective data (demographical, hearing loss, CI, medical and surgical data) was captured from the clinical patient files at two South African CI centres, namely the Pretoria Cochlear Implant Unit (PCIU) and the Johannesburg Cochlear Implant Centre (JCIC).

The clinical patient files of 14 post-lingually deafened adult CI recipients (9 females and 5 males, mean age= 42.14 years, SD= 8.08; range= 23-50 years), were reviewed to describe preoperative CI candidacy considerations, cochlear implantation and surgical considerations, as well as postoperative audiological and medical considerations.

Results of this study indicated that all 14 patients performed well with their cochlear implants, including two patients with a history of preoperative meningitis, three patients with less than 100% adherence to the recommended HIV-specific guidelines and one patient with postoperative electrode migration. A comprehensive preoperative audiological and medical test battery, adherence to current South African HIV-specific CI guidelines and a highly individualized surgical and medical risk assessment approach were efficacious in selecting the current PLWHA for CI surgery. HIV-specific considerations for determining CI candidacy

in PLWHA were suggested to ensure functional postoperative outcome after cochlear implantation.

Keywords: cochlear implantation, cochlear implant, HIV/AIDS, disabling hearing loss, persons living with HIV/AIDS.

CHAPTER 1

INTRODUCTION

Aim of chapter: Chapter 1 provides an overview of cochlear implantation in persons living with HIV/AIDS (PLWHA). A rationale for describing considerations for cochlear implantation in PLWHA is also provided.

Cochlear implantation is considered an innovative achievement in the field of medicine and biotechnology. By restoring the sense of hearing, individuals with bilateral severe to profound sensorineural hearing loss (SNHL), and/or single-sided deafness, who receive insufficient benefit from hearing aids, are provided with the possibility to perceive sound and become reintegrated into the hearing world (Al-Muhaimeed et al., 2009; Buchman et al., 2020; Miller et al., 2015). Systematic reviews have confirmed positive cochlear implant (CI) outcomes for postlingually deafened adults in areas such as speech perception abilities, health-related quality of life (HRQoL) , psychosocial well-being and cognition (Boisvert et al., 2020; Buchman et al., 2020). Nowadays, broadening of selection criteria for cochlear implantation allows individuals who were formerly excluded from cochlear implantation e.g. those with more complex medical needs, additional disabilities, co-morbidities, malformed cochleas, single-sided deafness, less severe degrees of hearing loss (HL) and better preoperative open-set speech perception abilities to benefit from CI surgery, including persons living with HIV/AIDS (PLWHA) (Sampaio et al., 2011).

Formerly, cochlear implantation was only limited to individuals meeting specified audiological criteria and without other health related problems, such as individuals with a positive Human Immunodeficiency Virus (HIV) status. This could have been due to past misconceptions regarding cochlear implantation in PLWHA such as stigma towards PLWHA, uncertainty as

to whether surgery may hasten HIV disease progression, increased risks of post-surgical infections, delays in wound healing, skin flap necrosis and implant receiver extrusion (Fatoki, 2016; Jain & Bansal, 2016; Vincenti et al., 2005). Despite numerous efforts targeted at reducing stigma, stigmatization regarding HIV status continues to exist predominantly in poor and low resource settings (Fatoki, 2016). Also in South Africa, PLWHA are at a particularly high risk of experiencing HIV-associated stigma with social, psychological and physiological implications (MacLean & Wetherall, 2021).

For PLWHA specifically, CI surgical criteria have expanded due to the improvements in antiretroviral (ARV) medication and its effects, adapted surgical techniques and enhanced prevention of postoperative infections (Jain & Bansal, 2016). Nowadays, PLWHA must also adhere to HIV-specific preoperative protocols and preparations, enabling them to undergo CI surgery (Sampaio et al., 2011). These include PLWHA being placed on highly active antiretroviral therapy (HAART), be committed to HAART, be clinically healthy and to develop an undetectable/suppressed viral load (<40 copies of HIV per millilitre (cpy/ml) in the blood or <50cpy/ml that is dependent on standard, laboratory-specific, viral load clinical reference values) (Maurice Hockman, M.D. personal communication, 2021; SACIG, 2020b). In addition, PLWHA should preferably have a CD4+ count of 200 cells/mm^3 or close to 350 cells/mm^3 , as most opportunistic infections (OIs) occur when CD4+ counts are less than 200cells/mm^3 (SACIG, 2020b). However, a value of 350cells/mm^3 is patient-dependant and may not always be clinically applicable (SACIG, 2020b). In some PLWHA, the CD4+ counts could gradually increase at the start of HAART, whereas some PLWHA never reach the abovementioned CD4+ requirements (Francois Venter, M.D. personal communication, 2021; Mahomed et al., 2020). Therefore, the viral load is regarded as a more accurate predictor of HAART's effectiveness and the health status in PLWHA's health (Mahomed et al., 2020). Therefore, PLWHA who are clinically healthy and have been compliant on HAART could be regarded as potential CI candidates to avoid delays in CI surgery (Maurice Hockman, M.D.

personal communication, 2021; Hockman & Penfold, 2020). Currently, two weeks before CI surgery, PLWHA should receive a vaccination of Prevnar 13, which is used to protect them from high-risk pneumococcal diseases, such as pneumonia and meningitis (SACIG, 2020b; Yin et al., 2012). In addition, Pneumovax 23 should be given two months after Prevnar 13 (Maurice Hockman, M.D. personal communication, 2021). However, although PLWHA presently have access to CI surgery, a shortage of data exists on how PLWHA may react to CI surgery and benefit from cochlear implantation.

Since its first description and recognition in 1981, HIV/AIDS is no longer viewed as a rare disease, but has become a worldwide burden (Shankar et al., 2005). Without diagnosis and treatment, the immune system gradually deteriorates to the state of an Acquired Immune Deficiency Syndrome (AIDS). This happens when the CD4+ T-cell count is reduced to a level of 200 cells or less per mm^3, resulting in the gradual attack and weakening of the immune system via OIs (WHO, 2018). With more than 32 million lives claimed globally and 1.7 million newly diagnosed HIV individuals in 2019, HIV has become a global health dilemma (UNAIDS, 2020). South Africa is among the low- and middle-income countries (LMICs) with the highest burden of the world's HIV-positive (HIVpos) population, and remains the largest contributor to the HIV pandemic giving rise to 19% of PLWHA, 15% of new infections identified and 11% of AIDS related deaths (UNAIDS, 2018; WHO, 2021). There is an estimated increase from 4,64 million PLWHA in South Africa in 2002 to 7,97 million PLWHA in 2019 (Stats SA, 2019). The lifespan of PLWHA has continued to increase due to improved access to ARV medication and the improved treatment of AIDS-related OIs, altering the mortality rate over time (Stats SA, 2019). HIV/AIDS is no longer viewed as an acute life-threatening disease, but rather a non-life threatening chronic condition, as evidenced in the decline of AIDS-related deaths post-2006 (Stats SA, 2019). As the life expectancy of PLWHA increases, non-life-threatening aspects of HIV/AIDS may negatively influence the HRQoL of PLWHA (van der Westhuizen et al., 2013). Such aspects are

associated with HL, impaired balance (van der Westhuizen et al., 2013), and reduced self-esteem (WHO, 2021).

Hearing loss in PLWHA may either be attributed to damage to the external, middle and /or inner ear structures, resulting in conductive, sensorineural or mixed hearing impairment (Swanepoel & Louw, 2010). PLWHA are at an increased risk of developing HL with reports of HL ranging from 14% to 49% in PLWHA (Luque et al., 2014; Roland et al., 2003; van der Westhuizen et al., 2013; WHO, 2021), particularly due to HIV itself or ototoxic ARV medications (WHO, 2021). PLWHA are also susceptible to frequent auditory and otological complications that could worsen upon disease progression, such as severe SNHL in more advanced stages of HIV (van der Westhuizen et al., 2013).

However, the pathogenesis of HL in PLWHA has not yet been described with certainty. HIV-associated damage to the central and peripheral auditory nervous system can either be attributed to the direct effects of HIV, or indirectly via ototoxic ARV medications, or OIs and the medications used for treatment thereof (Roland et al., 2003). Calles et al., (2010) suggested that the pathological expression of HIV/AIDS is dependent on the struggle between the duplication of the virus and the immune response of the patient. It is well known that PLWHA experience similar immunological suppression and accelerated aging (immunosenescence) as identified in the elderly (de Jong et al., 2019). Immunosenescence could result in damage to the auditory pathways from direct HIV viral action as opposed to ARV medications (de Jong et al., 2019).

Previous studies reported an association between HIV and cochlear dysfunction (Maro et al., 2014; Roland et al., 2003; van der Westhuizen et al., 2013) with decreased cochlear outer hair cell functioning (as measured by distortion product otoacoustic emissions) (van der Westhuizen et al., 2013). Roland and colleagues (2003) explored the pathological

mechanism of HIV-associated HL by determining the efficacy of CIs in PLWHA. Improved speech perception scores in quiet and noisy backgrounds were documented in HIVpos CI recipients, suggesting that HIV-associated damage primarily occurs within the cochlea, as cochlear implantation allows the damaged cochlear structures to be bypassed to a functional auditory nerve. In contrast, damage of the central nervous system (CNS) auditory pathways from HIV itself, OIs or ototoxic ARVs, would not have resulted in such an improved hearing ability (Roland et al., 2003). Another study concluded that HIVpos individuals had reduced distortion product otoacoustic emission signal-to-noise ratio levels compared to HIV-negative (HIVneg) individuals (Maro et al., 2014). The authors concluded that the cochlear dysfunction in the HIVpos group could possibly be attributed to the direct effect of HIV. Whether HIVpos participants were exposed to OIs, or the ototoxic medications thereof, has not been reported (Maro et al., 2014). In a previous study providing support for a direct HIV-induced effect on the cochlea, a temporal bone analysis of deceased PLWHA was conducted for the presence of the HIV-virus within the cochlear duct using electron microscopy (Roland, Healy, Lee, & Cohen, 1997). HIV viral-like particles were identified in the tectorial membrane and surface areas of the stria vascularis in the cochlea. Intracellular HIV-like particles were observed in almost all types of cochlear cells. In addition to the cochlea, the neurotropic nature of HIV also enables viral escalation to surrounding auditory tissue, such as the semicircular canals in the labyrinth (balance system) and auditory nerve (Roland et al., 2003). Other histological temporal bone studies have provided data suggesting HIV-associated damage to the otolith organs, semicircular canals and organ of Corti within the cochlea (Harada et al., 1979; Igarashi et al., 1975; Kwartler et al., 1991).

HIV has also been known to affect the central auditory nervous system, resulting in cognitive deficiencies and neural pathologies along the auditory pathways (Zhan et al., 2018). Gap detection thresholds were analysed in HIVpos participants on and off antiretroviral therapy (ART) (Maro et al., 2014). Peripheral hearing ability (distortion product otoacoustic emissions and hearing thresholds) did not differ between ART-positive and ART-negative groups.

However, higher gap detection thresholds were found in the ART-positive group, suggesting possible central auditory nervous system side effects from certain ART regimens (Maro et al., 2014). In addition, electrophysiological testing procedures such as auditory brainstem response (ABR) testing, middle and late latency evoked potential testing, as well as P300 recordings can be used to determine the integrity of the auditory pathway. A cross-sectional study (Matas et al., 2018) reported on delayed absolute and interpeak ABR latencies for HIVpos subjects with and without HAART when compared to an HIVneg control group. P300 latencies were also significantly prolonged for HIVpos subjects with and without HAART, suggesting that HIV and HAART can potentially influence the subcortical and cortical structures of the central auditory nervous system (Matas et al., 2018).

Khoza and Ross, (2002) support the combined direct effect of HIV and the indirect effect of OIs and its medications in the development of HL. Of the 23% of HIVpos individuals who presented with HL, almost all participants presented with a history of OIs, suggesting that HL in PLWHA is attributable to a combination of factors (Khoza & Ross, 2002). HIV-associated hearing loss and auditory processing difficulties are therefore not only attributed to a peripheral or central pathology, but has been known to affect multiple levels of the auditory system (de Jong et al., 2019). Due to the extensive damage caused to several components of the auditory system, it is understandable that HIV is closely affiliated with a potential progressive or sudden SNHL (Harris et al., 2012).

PLWHA are also susceptible to multiple OIs which can negatively affect various structures within the auditory pathway (Tami & Hairston, 2008). Within sub-Saharan Africa, Cryptococcal meningitis, can be viewed as one of the most significant OIs associated with HIV and can lead to severe HL due to 8th cranial nerve compression (de Vedia et al., 2013; Park et al., 2009). Otosyphilis, known for its occurrence in PLWHA, has been associated with cochleovestibular complications resulting in profound SNHL and vestibular dysfunction. HL in patients with otosyphilis will often progress to profound SNHL without treatment

(Pasricha et al., 2010). Multidrug-resistant tuberculosis (MDR-TB) is closely associated with HIV/AIDS and the primary method of treatment involves the use of injectable tuberculocidal drugs such as different types of aminoglycosides (streptomycin and kanamycin) and novel antibiotics, such as capreomycin (Vaamonde et al., 2004). Tuberculocidal drugs are often administered for a period of 18-24 months, increasing the risk of persons with MDR-TB to develop severe to profound aminoglycoside-induced HL (Nathanson et al., 2004). Patients who are placed on MDR-TB regimens are exposed to aminoglycosides for a longer period of time than other tuberculosis (TB) patients, resulting in larger cumulative doses and a higher risk of aminoglycoside-induced damage to the sensory neuroepithelium of the inner ear (Vaamonde et al., 2004). These drugs can have detrimental cochleotoxic and vestibulotoxic effects if overdosed or not monitored well regarding serum levels. In up to 50% of patients, these drugs can cause permanent HL (Seddon et al., 2012; WHO, 2021). In a study of the effect of aminoglycosides on the hearing status in MDR-TB patients, Duggal and Sarkar (2007) found that when amikacin, kanamycin and capreomycin were administered to MDR-TB patients, the hearing loss remained irreversible and permanent. Audiometric follow-ups of the patient population did not indicate any improvement in hearing thresholds after termination of MDR-TB treatment, as aminoglycosides can remain in the auditory system for up to six months following the cessation of therapy. This can result in an increased severity of the HL (Duggal & Sarkar, 2007; Wang et al., 1999). PLWHA with MDR-TB on HAART and MDR-TB treatment are at a four times greater risk of developing ototoxic HL than HIVneg patients with MDR-TB (Harris et al., 2012). Following a single dose of a combination of aminoglycosides, some patients may develop sudden profound SNHL making them candidates for CIs (Harris et al., 2012). The significant prevalence of severe to profound hearing impairment within the population of PLWHA, due to the ototoxic nature of aminoglycosides and HAART is closely linked with poorer HRQoL (Carlsson et al., 2015; Petersen & Rogers, 2015). When hearing deficit progresses beyond the benefit of hearing aids, cochlear implantation can serve as the rehabilitative strategy available for severe to

profoundly hearing-impaired individuals, through direct stimulation of the auditory nerve and central auditory nervous system.

With only a limited number of published studies, there is a dearth of available and recent data in terms of cochlear implantation in PLWHA. Roland et al., (2003) reported positive speech perception outcomes and the absence of wound healing complications in a sample of seven adult HIVpos CI recipients, making a CI the amplification option of choice for PLWHA with severe to profound SNHL (Roland et al., 2003). In this study, pre- and intraoperative universal surgical precautions were undertaken. Clinical files were reviewed indicating an absence of intra- and postoperative complications. A statistically significant difference was found between pre- and postoperative word and sentence recognition scores, with postoperative results being described as “excellent” for all participants, except one with a preoperative history of meningitis. All participants were considered to be active, functional CI users. HIV-specific considerations for CI surgery, such as viral load or CD4+ cell counts were not documented in this study. In spite of the small sample size, it was concluded that PLWHA are excellent candidates for cochlear implantation and have no greater surgical risk than individuals without HIV, provided medical conditions are well managed (Roland et al., 2003).

Similarly, in a single case-study, Vincenti et al. (2005) documented excellent postoperative open-set speech perception outcomes, greater self-reported independence and the ability to converse telephonically six months following CI device activation in a 35-year-old HIVpos CI recipient. The recipient had no family history of HL or history of OIs, and the recipient’s preoperative viral load was not documented. In the 12 months prior to CI surgery, this CI recipient had a preoperative CD4+ cell count of 450cells/mm^3, adhering to the present preferred CD4+ cell count for cochlear implantation (SACIG, 2020b). Preoperative magnetic resonance imaging (MRI) and computerized tomography (CT) indicated an absence of CNS

pathologies and cochleovestibular malformations. In addition, intraoperative trauma, wound healing complications, local and systemic complications and skin flap necrosis were absent. The recipient had obtained stable, functional results and was regarded as an active CI user (Vincenti et al., 2005).

In a more recent report, Jain and Bansal (2016) reported improved postoperative Categories of Auditory Performance (CAP) scores of 6, 7 and 7 at 6, 12 and 24 months respectively, following implantation in a 36-year old adult HIVpos CI recipient, when compared to a preoperative CAP score of 1. The recipient had no family history of HL or the presence of OIs prior to CI surgery. Preoperative CD4+ cell counts, and viral load counts were missing. Preoperative MRI and CT excluded CNS pathologies, cochleovestibular malformations and inner ear abnormalities. Universal surgical precautions were undertaken, and the recipient was medically cleared to undergo CI surgery. Intraoperative surgical complications were absent. There were no wound healing complications at three weeks postoperatively, and after two years, local and systemic complications were still absent (Jain & Bansal, 2016). Medically fit PLWHA with severe to profound SNHL are likely to be ideal candidates for CI surgery, provided that there are no medical contraindications, CNS pathologies and cognitive impairment (Jain & Bansal, 2016).

A study on orthopaedic surgery in PLWHA indicated that if surgical conditions were optimal and without wound contamination, implant surgery could be undertaken in PLWHA as the incidence of wound infection was comparable to that of a healthy HIVneg control group (Harrison et al., 2002). This is in agreement with the previously mentioned studies regarding CI outcomes in PLWHA (Jain & Bansal, 2016; Roland et al., 2003; Vincenti et al., 2005).

Although the above-mentioned studies have documented positive outcomes in HIVpos CI recipients, study samples were small (ranging between 1 and 7 patients), and conclusions and guidelines cannot be drawn based on such limited information.

The few observational studies regarding cochlear implantation in HIVpos CI recipients (Jain & Bansal, 2016; Roland et al., 2003; Vincenti et al., 2005) provide a starting point for future documentation of considerations for cochlear implantation in PLWHA. However, these studies provide limited information regarding HIV-specific considerations (health status, pneumococcal vaccination, CD4+ cell count and viral load status). A systematic analysis of retrospective data regarding considerations for cochlear implantation in a larger sample of PLWHA was therefore destinate and acceptable. This study aimed to contribute to the description of candidacy, audiological and surgical considerations for PLWHA with disabling HL, by reviewing data from a larger sample of HIVpos adult CI recipients. HIV-specific considerations in terms of preoperative CI candidacy considerations, cochlear implantation and surgical considerations as well as post-operative medical and audiological considerations were also suggested to ensure functional postoperative outcome after cochlear implantation.

Therefore, the following research question arose: *What are the candidacy, audiological and surgical considerations for cochlear implantation in adults with HIV?*

CHAPTER 2

METHODOLOGY

Aim of chapter: Chapter 2 describes the main aim of the study and provides an outline of the research process, data collection procedures and data collection materials.

2.1 Research objective

The aim of the study was to describe the candidacy, audiological and surgical considerations for cochlear implantation in adults with HIV.

2.2 Research design

A retrospective cohort study design was used for this study. Retrospective (historical) cohort studies allow researchers to examine pre-existing data of individuals, tracing these individuals from the past to the present in order to determine study outcomes (Klebanoff & Snowden, 2018). This study followed a descriptive research design as it describes an observed phenomenon, establishing relationships between variables, without changing the situation under investigation (Leedy & Ormrod, 2010). Quantitative data was collected and interpreted objectively, excluding verbal or behavioural data (Babbie, 2010).

2.3 Ethical considerations

The *South African Guidelines for Good Practice in the Conduct of Clinical Trials in South Africa (2020), Ethical Guidelines for Good Practice with regard to HIV (2016)* and *Ethics in Health Research (2015)* were adhered to during the course of conducting this study. Adherence to these ethical principles ensured that the study was structured and conducted according to scientific and ethical guidelines formulating the framework for good clinical

practice. Table 2.1 individually lists these ethical principles and describes how they were applied to the current study.

Table 2.1: Ethical principles applied to the formulation of study design, participant selection, consent procedures, data collection and analysis procedures

(du Toit et al., 2015; Health Professions Council of South Africa, 2016; South African Department of Health, 2020)

Ethical principle	Application and relevance to research
Beneficence and non-maleficence Researchers have an ethical and moral obligation to ensure the study design is just and carried out with the necessary competence, maximizing benefit and minimizing harm of participants. Anticipated risks must be reasonable when weighed against anticipated benefits. Although viewed as separate ethical principles, beneficence proscribes intentional infliction of harm on all persons. Non-maleficence refers to an avoidance of harm. Research that does not seek to improve the human condition is viewed as unethical.	The retrospective design of this study ensures that there were no risks involved for participants. Deliberate infliction of harm on participants were avoided, with the research carried out in a sound and ethical manner.
Fair selection of participants Inclusion and exclusion criteria for prospective participants were based on scientific, moral and ethical principles. Potential participants are not to be unfairly excluded on the basis of unlawful grounds for discrimination: sex, age, race, culture, religious belief, sexual orientation, education, income status, disability, marital status, language and ethnic beliefs. Similarly, participants are not to be targeted for research based on one or more of these discriminatory grounds.	Adult (>18 years) CI recipients with a diagnosis of HIV prior to cochlear implantation was included in this study. The grounds for exclusion are based on participants not adhering to the aforementioned criteria.
Ethical clearance All organisations, health agencies, health establishments and institutions conducting medical and medical-related research involving human participants are to be registered to a Human Research Ethics Committee (REC) in order to undergo an independent ethical review.	Ethical clearance was obtained from the *Research Ethics Committee of the Faculty of Humanities* at the University of Pretoria (Appendix A) prior to the commencement of data collection. The researcher also signed a plagiarism declaration form, confirming that all research is the original work of the researcher.
Informed consent	

Participation in research remains voluntary and is based on informed decisions by the participant. Voluntariness and informed decisions are established during the informed consent process, prior to the commencement of data collection for the purpose of research.	The CI team coordinators of the two participating CI centres received an information letter detailing the nature of the study and what would be expected of them in order to participate in the study (Appendix B). Permission to conduct this study and to access participant records was obtained from the CI team coordinators of both the Pretoria Cochlear Implant Unit (PCIU) (Appendix C) and Johannesburg Cochlear Implant Centre (JCIC) (Appendix D). Clinical data/patient files were not accessed without informed consent of potential participants. The retrospective nature of the study required no active participation from adult (>18 years) CI recipients diagnosed with HIV prior to cochlear implantation. A standard procedure at PCIU and JCIC is that all adult CI patients are requested to complete a consent form in which permission is asked that medical, audiological and psychological records may be accessed, and that this information may be used for research purposes. Consent is given that this information may be used for the purpose of research, publication in scientific literature, and to share with the appropriate bodies concerned with the performance of the CI (Appendix E). Only CI recipients who gave consent for access and copying rights to their medical, audiological and psychological records, were included in the study sample.
<u>Continuous respect for enrolled participants through privacy and confidentiality</u> Privacy refers to who has access to personal information and health care data found within participant records. Confidentiality concerns itself with implementing appropriate measures set out to prevent unauthorized disclosure of sensitive patient information during the research process.	Since patient privacy should be maintained at all times, no identifying information was utilized for the purpose of this study. Accordingly, each CI recipient was allocated a unique alphanumeric code in order to ensure confidentiality. The identities of all participants remained only known to the researcher, study supervisor and study collaborators. The right to privacy and

Research participants have the right to privacy, confidentiality and should be informed as to how these rights will be protected and ensured during the research process. Test results and HIV-status of PLWHA should be treated with the highest level of confidentiality and should not be disclosed to other health practitioners without prior consent from the patient. Researchers are ethically obligated to ensure that appropriate measures are taken to ensure confidentiality and privacy of patient records and data.	confidentiality was also confirmed in the consent form signed by adult CI recipients of the PCIU and JCIC (Appendix E).
Autonomy and dignity This principle ensures that all participants capable of informed decisions are treated with the necessary respect and freedom to exercise self-determination, ensuring that the well-being, dignity and safety interests of research participants remain first priority.	The retrospective nature of the study required no active participation, maintaining the well-being, dignity and safety of all prospective participants.
Relevance and value Research should remain relevant, responsive and sensitive to the needs of the South African population and, ideally, explaining how the proposal will contribute to knowledge generation and the translation of findings into processes, services and interventions to improve the living conditions and well-being of all South-Africans.	The research objective was carefully constructed to deliver reliable, objective data about candidacy, audiological and surgical considerations for cochlear implantation in adults with HIV.
Storage of data	Upon completion of the study, all relevant data will be stored electronically at the Department of Speech-Language Pathology and Audiology at the University of Pretoria for a period of fifteen years (Appendix F). In addition, data will also be uploaded onto the University of Pretoria's Research Data Repository.
Release of findings	A research article was compiled with the purpose to publish research findings in an international, accredited journal and to make it available to the scientific community. The research dissertation will be made available online and stored in hard copy at the University of Pretoria's library.

2.4 Research setting

At present, there are 12 independent CI programs/ centres in South Africa, and all are affiliated with the South African Cochlear Implant Group (SACIG). Participants for this study were recruited from two of these CI programs/ centres, namely the PCIU and JCIC. Demographic, HL, CI related data, surgical and medical data were captured from clinical patient files at the PCIU and JCIC.

2.5 Participants

The study included adult (>18 years) CI recipients diagnosed with HIV prior to cochlear implantation. A non-probability, purposive sampling technique was used for the study. Non-probability (non-random) sampling refers to a sampling technique utilized in a large population in which participants of the population are not provided with equal chances of being selected (Etikan et al., 2016). Although subjective in nature, non-probability sampling was used to create generalizations pertaining to the population (Etikan et al., 2016). Purposive (judgement) sampling was used as the researcher made a deliberate choice of the participants due to certain qualities the participants possessed (Etikan et al., 2016).

Twenty-four adult CI recipients adhered to the inclusion criteria. The inclusion criteria specified for the adult CI recipients are described and justified in Table 2.2. Consent to access and utilize patients' recorded data (Appendix E) was not obtained for seven CI recipients. Medical records were inaccessible for another three patients. The final study sample included 14 postlingually deafened adult CI recipients (9 females and 5 males), with a total of 16 ears implanted (2 bilateral CIs). Five HIVpos CI recipients were recruited from the PCIU and nine HIVpos CI recipients from the JCIC. Participants were aged between 14 and 48 years at the time of the first cochlear implantation with a mean age of 36 years (SD = 8,40 years). The mean estimated duration of deafness (severe to profound SNHL) prior to CI

surgery was 2.36 years (SD= 1,52 years). The youngest participant at the time of the first cochlear implantation (14 years) had become 23 years of age at the time of retrospective data collection in 2020, and had adhered to this study's age requirement as specified in Table 2.2. The age at the time of data collection ranged between 23 to 50 years (M= 42,1 years). For the purpose of this study, only data for the first cochlear implantation after HIV diagnosis was included for the two bilateral CI recipients. Sample population characteristics are shown in Table 2.3.

Table 2.2: Inclusion criteria for adult cochlear implant (CI) recipients

Inclusion criteria	Justification and relevance to research
Participants should be 18 years of age or older at the time of data collection (retrospective record review).	According to the Constitution of the Republic of South Africa, someone under the age of 18 years is classified as a child and requires special legal protection (du Toit et al., 2015). Participants aged 18 years and older have the capacity to act independently and is capable of understanding the nature and purpose of the research in which they are involved in (du Toit et al., 2015).
Participants should have been diagnosed with HIV prior to cochlear implantation.	Ear-, Nose- and Throat (ENT) surgeons require potential CI recipients to disclose their HIV status and the date on which HIV/AIDS testing was conducted prior to undergoing CI surgery. All patients undergoing not only CI surgery, but surgery in general should undergo HIV testing (Smit, 2010). An HIVpos diagnosis warrants present HIV antibodies in the blood. Thereafter, the ENT surgeon will require a complete blood count in which the white blood cell, red blood cell and platelet level is analysed (AIDS Institute, 2011). CD4 cells are a type of white blood cell that is destroyed by HIV. A CD4 cell count of 350-500 cells/mm^3 is regarded as minor symptomatic. A CD4 count of 200-350 cells/mm^3 places PLWHA at risk of OIs. CD4 counts <200 cells/mm^3 is diagnosed as AIDS (AIDS Institute, 2011). Viral load counts must be done routinely (every 3-4 months) to provide information on the state of the CD4 count and whether the treatment regimen has stopped working (AIDS Institute, 2011). Preoperative blood tests and viral load tests are routinely filed within medical patient files. Surgical data was only disclosed to the researcher by the surgeon if the participant has given consent that medical files can be accessed, and medical data be utilized for research purposes (Appendix E).
Participants should have provided informed consent allowing the researcher the right to use their information for the purpose of research.	Only adult CI recipients who have provided written consent that their information may be used for the purpose of research, publication in scientific literature, and to share with the appropriate bodies concerned with the performance of the CI (Appendix E) were included as participants in the study.
Participants should be CI recipients (unilaterally or bilaterally implanted) and receiving CI device programming and aural rehabilitation services from either the PCIU or JCIC.	Only two CI centres participated in this study. Patient files/clinical data were only made available at these two centres, as participants were patients of either the PCIU or JCIC.

Table 2.3: Characteristics of sample population

Adult cochlear implant (CI) recipient	Mode of amplification at time of study	Etiological factors	Rapidity of hearing loss onset	Duration of deafness prior to CI surgery[1]	Preop CT scan	Preop MRI	Age at first CI (years)	Cochlear implant	Preop CAP^{R} score	Postop CAP^{R} score[2]
Patient 1	Bilateral CI	Noise exposure[3]	P	*	N	*	41	Cochlear CI 24 RE (CA) Perimodiolar	4	8
Patient 2	Unilateral CI	ART, unspecified TB (unknown TB med)	P	2 yr 5 mo 6 d	N	N	35	Cochlear CI 512 Perimodiolar	5	7
Patient 3	Bimodal	ART, unspecified TB (unknown TB med)	P	2 yr 4 mo 11 d	N	N	34	Cochlear CI 24 RE (CA) Perimodiolar	4	8
Patient 4	Bimodal	ART, MDR-TB (unknown TB med)	P	2 yr 8 mo 23 d	N	N	48	MED-EL Synchrony ST Lateral wall	4	8
Patient 5	Bimodal	ART, meningitis	S	3 mo 11 d	A[4]	A[5]	40	Cochlear CI 24 RE (CA) Perimodiolar	2	6
Patient 6	Bilateral CI	ART, Pneumonia	S[6]	2 yr 8 mo 24 d[6]	N[6]	*	39[6]	Cochlear CI512 Perimodiolar	1[6]	8[7]
Patient 7	Unilateral CI	ART, MDR-TB (Kanamycin, Streptomycin)	S	4 yr 8 mo	N	*	39	Cochlear CI512 Perimodiolar	0	8
Patient 8	Unilateral CI	ART, meningitis	S	1 yr 1 mo 24 d	N	*	14	Cochlear CI24RE(CA) Perimodiolar	3	8
Patient 9	Unilateral CI	ART, MDR-TB (Kanamycin)	S	1 yr 4 mo 19 d	N	*	36	Cochlear CI24RE(CA) Perimodiolar	2	8
Patient 10	Unilateral CI	ART	P	1 yr 7 mo 8 d	N	*	23	Cochlear CI512 Perimodiolar	2	7
Patient 11	Unilateral CI	ART, MDR-TB (Kanamycin)	P	3 yr 9 mo 17 d	N	*	42	Cochlear CI512 Perimodiolar	0	7
Patient 12	Unilateral CI	ART, MDR-TB (Kanamycin)	P	5 yr 5 mo 13 d	N	N	40	Cochlear CI512 Perimodiolar	0	7
Patient 13	Unilateral CI	ART, MDR-TB (Kanamycin)	P	1 yr 7 mo 7 d	N	N	38	Cochlear CI24RE(CA) Perimodiolar	1	8
Patient 14	Unilateral CI	ART, MDR-TB (Kanamycin, Streptomycin, Rifampicin)	S	8 mo 10 d	N	*	37	Cochlear CI24RE(CA) Perimodiolar	0	6

** = Missing data from clinical patient files; Bimodal = Cochlear implant and hearing aid amplification; MDR-TB = Multidrug-resistant tuberculosis; med = Medication; ART= Antiretroviral therapy; P = Progressive; S = Sudden; yr= Year, mo= Months, d= Days, N = Normal; A = Abnormal; CA = Contour advanced*

[1] Duration of deafness prior to CI surgery is estimated using the first date that a diagnosis of severe to profound SNHL was obtained. Deafness could have occurred before diagnosis of severe to profound SNHL.
[2] Postoperative CAPR scores were assigned to all 14 patients at the time of data collection, with varying durations of CI usage.
[3] Data on preoperative ART was not documented in clinical patient files for Patient 1.
[4] Bilateral asymmetric labyrinthine ossificans on CT.
[5] Segmental fluid signal loss and labyrinthine ossification on MRI.
[6] Data is before CI device failure and CI reimplantation.
[7] Data is after CI reimplantation.

2.6 Data collection materials

For the purpose of the study, retrospective data (demographical, HL, medical, CI and surgical data) was captured from the clinical patient files of eligible participants from the PCIU and JCIC.

2.6.1 Data collection sheet

An electronic database was developed for the capturing of the retrospective data. Retrospective data (demographic data, HL, medical, surgical and CI related data) from pre-, intra- and postoperative periods were captured and systematically organized on an Excel spreadsheet (Microsoft, version 16) to prepare for data analysis. The datasheet was designed to ensure that data could be captured consistently and uniformly, with fixed response categories (selection options) for most variables (except continuous variables). Frequent data entry spot checks were performed, and the datasheet was checked meticulously for any data capturing errors by the researcher, study supervisors and study collaborators. A summary of the data categories and related variables (data fields), together with response categories (where applicable) are presented in Table 2.4.

2.6.2 Revised version of Categories of Auditory Performance (CAPR)

Participants' auditory performance was retrospectively rated (pre- and postoperatively) by the managing audiologists at the PCIU and JCIC by means of the revised version of the Categories of Auditory Performance (CAPR) (Archbold et al., 1995; Stacey et al., 2006) (Appendix G). The CAP's rating scale has been used worldwide as a global functional outcome measure in cochlear implantation across a wide range of age groups, providing an indication of auditory receptive abilities with good inter-observer reliability that is well-understood by non-professionals (Archbold et al., 1998). This has contributed to the CAP's robustness (Archbold et al., 1998). The CAPR has nine categories ranging from 0 to 8. The lowest level (0) describes no awareness or detection of environmental sounds, with the

highest level (8) representing the ability to converse telephonically with an unknown speaker. Retrospective pre- and postoperative CAPR scores were assigned to all participants based on their managing audiologist's subjective opinion, accurate recall of pre- and postoperative auditory performance and the revision of the available communication assessment reports in clinical patient files.

Table 2.4: Summary of data collection categories and related variables with response categories

Demographical data [8]	Hearing loss (HL) data [8]	Cochlear implant (CI) data [8]	Surgical data [8]	Medical data [8]
Gender Male Female **Preoperative employment** Employed Full-time Employed Part-time Unemployed Current educational (training setting) Retired **Preoperative communication mode** Oral (spoken communication) Sign Language Total (mixed) communication Bilingual-Bicultural **Most-recent postoperative communication mode** Oral (spoken communication) Sign Language Total (mixed) communication Bilingual-Bicultural **Home Language** Afrikaans English Ndebele Northern Sotho Sotho Swazi Tswana Tsonga Venda Xhosa	**Etiological factors for HL** Noise exposure Tuberculosis (TB) medication Combination of ARV and TB medication Antiretroviral therapy (ARV) Other **Onset of hearing loss** Post-lingual Pre-lingual **Rapidity of onset** Congenital Progressive Sudden Unknown **Bilateral/Unilateral preoperative HL** Bilateral Unilateral **Preoperative type of HL** Sensorineural Mixed Conductive Auditory Neuropathy Spectrum Disorder (ANSD) **Preoperative degree of HL (L&R)** PTA (500Hz,1000Hz, 2000Hz) Left ear >90dB – Profound >71-90dB - Severe (Stach, 2010) Right ear >90dB – Profound >71-90dB – Severe	**Mode of amplification at study** Bilateral implant Bimodal amplification (CI + HA) Unilateral implant **Age at implantation (years)** Mean, range, standard deviation (SD) **CI funding** Private funding (no medical aid) Medical aid complete Medical aid and private funding Donations only Sponsor(s) Donations and medical aid Donations and private funding Donations, medical aid, private funding Public: government funding Other **Duration of severe to profound deafness prior to first CI** Mean, range, standard deviation (SD) **CI manufacturer** Med-el Cochlear Advanced Bionics **Electrode type** Perimodiolar Double array Lateral wall	**Preoperative blood count** Viral count <40cpy/ml or <50cpy/ml[9] No indication Haemoglobin count 12.0-15.0 g/dl No indication CD4 count 358-1259 cells/mm^3 No indication Leukocyte count Within reference No indication **Preoperative vaccinations** Prevnar 13 Pneumovax 23 Prevnar 13 and Pneumovax 23 **Preoperative imaging** CT scan Normal Abnormal No indication MRI scan Normal Abnormal No indication **Postoperative imaging** Type of imaging Stenver X-ray CT scan **Intraoperative cochlear ossification**	**Family history of illnesses/disabilities/deafness** **Additional illnesses/disabilities** Visual problems Epilepsy Other None **Preoperative treatment/antibiotics** Antiretroviral Therapy (ART) Tuberculosis (TB) medication Combination of ART and TB medication None No indication Other **Presence of OIs following HIV diagnosis prior to first CI** Tuberculosis (TB) Cryptococcal meningitis (CM) Toxoplasmosis Kaposi's sarcoma Oesophageal candidiasis Cytomegalovirus (CMV) Herpes simplex viruses No indication Other **Medication used to treat OIs** TB medication CM medication Aminoglycosides No indication Other

[8] Data collection categories, and related variables with response categories are only applicable to the first CI after HIV diagnosis prior to CI surgery.
[9] Viral load requirements of <40cpy/ml or <50cpy/ml are both regarded as undetectable/suppressed and is dependent upon the standard clinical reference values that are used by the laboratories where blood results are processed.

Zulu Other **Health sector** Private Public	**Preoperative unaided pure tone thresholds (dBHL)** AC: 125Hz-8000Hz (L&R) BC: 250Hz-4000Hz (L&R) **Preoperative unaided speech perception scores (L&R)** NU6 words & CID-sentences Testing conducted in Afrikaans/English Pre-recorded/live-voice stimuli Presentation level (dBHL) Score/percentage (%) Noise/quiet testing environment With/without visual cues **Postoperative aided pure tone thresholds (L&R) at first follow-up (F/U)** AC: 250Hz-6000Hz **Postoperative aided speech perception scores (L&R) at first follow-up** NU6 words & CID-sentences Pre-recorded/live-voice stimuli Presentation level (dBHL) Score/percentage (%) With/without visual cues **Postoperative aided pure tone thresholds (L&R) at most recent F/U** AC: 250Hz-6000Hz **Postoperative aided speech perception scores (L&R) at most recent F/U** NU6 words & CID-sentences Pre-recorded/live-voice stimuli Presentation level (dBHL) Score/percentage (%) With/without visual cues **Postoperative impedances at most recent F/U** Normal Open circuit (>30kOhms) Short circuit (<1kOhm)	**Type of speech processor at the time of initial stimulation** **First audiological F/U** Number of active electrodes Data logging **Most-recent audiological F/U** Number of active electrodes Data logging	Present Absent No indication **Intraoperative complications** Anaesthesia related Medically related No indication None **Intraoperative trauma to auditory structures** Basilar membrane External auditory canal Annulus Chorda Tympanic membrane Facial nerve Gusher No indication **Complete/partial insertion** Complete Partial **Scala tympani/vestibuli** insertion Vestibuli Tympani **Insertion technique** Cochleostomy Round Window membrane approach No indication **Duration of CI surgery** **First surgical F/U** Time following CI surgery Presence/absence of hematoma Local/systemic complications present **Most-recent surgical F/U** Time following CI surgery Local complications present	

2.7 Data collection procedures

The CI team coordinators at the PCIU and JCIC were contacted and provided with an information letter outlining the purpose, procedures and what was expected of them in order to participate in the study (Appendix B). Both CI team coordinators provided written consent for participation, allowing the researcher access to data of the HIVpos CI recipients at the PCIU (Appendix C) and JCIC (Appendix D) who adhered to the study's inclusion criteria. A standard procedure at PCIU and JCIC is that all adult CI patients are requested to complete a consent form in which permission is asked that medical, audiological and psychological records may be accessed, and that this information may be used for research purposes (Appendix E). Only adult CI recipients who adhered to the inclusion criteria and who signed the PCIU/JCIC consent slip indicating that they give permission to PCIU and JCIC to have access and copying rights to their medical, audiological and psychological records (Appendix E), were included. Audiologists and surgeons managing the included participants assisted the researcher with retrospective data capturing from clinical patient files. Retrospective data from the clinical patient files of 14 adult CI recipients were captured and systematically organized on a Microsoft Excel data spreadsheet. Frequent data entry spot checks and clarification of data queries were performed by the researcher, study leaders and study collaborators. The development of a single data spread sheet enabled uniform data to be captured in a consistent format from both CI centres and to simplify data analysis. Due to this study's retrospective design, patient files were not complete for every investigated variable. Study results are therefore based on the available data for each variable at the preoperative, first postoperative and most recent postoperative time period.

2.8 Data analysis

Descriptive statistics were utilized to define the study population in terms of demographic, CI, HL, surgical and medical related characteristics. Data analysis was performed with Excel for Windows (version 16) and descriptive measures were employed to describe the central

tendency and normal distribution of recorded variables in terms of frequencies, means and standard deviations. Due to this study's retrospective design, the investigated variables in clinical patient files were not always complete. Thus, study results are based on the available data for each variable at the preoperative, first postoperative and most recent postoperative time period.

2.9 Reliability and validity

Continuous measurements of validity and reliability enables researchers to maintain and enhance quality throughout the research process (Heale & Twycross, 2015). Validity refers to the extent to which an intended construct and all related aspects are accurately measured and that it measures what it is intended to measure. Reliability refers to the accuracy of a research tool and the extent to which the same conclusion is reached on repeated occasions (Heale & Twycross, 2015).

The study warranted reliability and validity in the following ways:

- A pilot study was conducted, allowing the researcher to assess the validity and reliability of the data capturing tool as well as the data collection procedures. The aim of the pilot study was to evaluate the feasibility of the study protocol, allowing the researcher to identify weaknesses and to test the appropriateness of the data collection tools and procedures (Hassan et al., 2006). Consent to access the clinical patient files of three adult CI recipients from the PCIU was obtained and these three clinical patient files were reviewed. The pilot study had enabled the researcher to determine the quality and functionality of the data collection sheet, based on the availability of data and the format in which data were captured for different variables. The pilot study was used to reconsider variables that seemed to be absent in patient files for all pilot study participants. Adaptations of data collection procedures were implemented to overcome

potential obstacles to data collection, to ensure efficient data capturing procedures. Confidentiality of data was maintained and all necessary changes were made to the data capturing tool and procedures, enhancing validity and reliability.

- The descriptive, retrospective nature of the study allows the researcher to accurately report findings. Data obtained from patient files/clinical records are objective and constant. The retrospective nature of the study required no active patient participation that may have influenced study outcomes, contributing to both reliability and validity.
- The use of non-identifying data guaranteed confidentiality and the elimination of tester bias and error. This further enhanced validity.
- A single data spread sheet enabled intended and uniform data to be captured in an accurate and consistent format from both CI centres. The retrospective data was captured with a consistent data collection tool that succeeded to measure demographics, HL, medical, surgical and CI related data. It is considered to be valid.
- Frequent data entry spot checks of the data capturing tool by the researcher and study supervisors ensured that data was captured accurately and correctly interpreted. Data queries were also regularly clarified by the researcher, study supervisors and study collaborators. This further enhanced reliability.

CHAPTER 3

RESEARCH ARTICLE

CONSIDERATIONS FOR COCHLEAR IMPLANTATION IN ADULTS WITH HUMAN IMMUNODEFICIENCY VIRUS (HIV) - A CHART REVIEW FROM TWO SOUTH AFRICAN COCHLEAR IMPLANT CENTRES

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3.1 Abstract

Objective

To describe candidacy, audiological and surgical considerations for cochlear implantation in adults with Human Immunodeficiency Virus (HIV).

Study Design

A retrospective chart review was conducted at two South African cochlear implant centres to describe preoperative CI candidacy considerations, surgical considerations and cochlear implantation as well as postoperative audiological and medical considerations of cochlear implant recipients with HIV. The clinical patient files of fourteen postlingually deafened HIV-positive adult cochlear implant (CI) recipients (9 females and 5 males), aged between 23 and 50 years (M= 42,1 years) at the time of the study, were reviewed.

Results

As a group, all 14 patients performed well with their cochlear implants, including two patients who presented with a history of preoperative meningitis, three patients with less than 100% adherence to the recommended HIV-specific guidelines and one patient with postoperative electrode migration. The limited medical and surgical complications that occurred did not relate to HIV as such.

Conclusions

CI surgery is an effective treatment strategy to treat severe to profound sensorineural hearing loss in persons living with HIV/AIDS (PLWHA), provided that they are medically cleared and accepted for the procedure with standard surgical risk assessments prior to surgery. HIV-specific considerations to determine CI candidacy for PLWHA are proposed to

ensure optimal functional postoperative outcomes. Adherence to universal HIV-specific CI guidelines will corroborate CI benefit without increased surgical risk.

3.2 Introduction

Restoring the sense of hearing by cochlear implantation has provided individuals with bilateral severe to profound sensorineural hearing loss (SNHL) the possibility to escape disabling hearing loss (HL) and become reintegrated into the hearing world [1–3]. Systematic reviews have confirmed positive cochlear implant (CI) outcomes for postlingually deafened adult CI recipients in areas such as speech perception abilities, health-related quality of life, psychosocial well-being and cognition [2,4]. Nowadays, individuals who were formerly excluded from cochlear implantation, e.g. those with complex medical needs, additional disabilities and co-morbidities, including persons living with HIV/AIDS (PLWHA) can now be considered for cochlear implantation [5]. For PLWHA specifically, this is due to improvements in antiretroviral (ARV) medications, adjusted surgical techniques and enhanced prevention of postoperative infections [6].

The neurotropic nature of the Human Immunodeficiency Virus (HIV) enables extensive damage to the auditory system, and is therefore closely affiliated with potential progressive or sudden SNHL [7,8]. Histological temporal bone studies have suggested HIV-associated damage to the otolith organs, semicircular canals and the organ of Corti [9–11]. Reports of severe HL in PLWHA in more advanced stages of HIV ranges from 14% to 49% [8,12–14], particularly due to HIV itself or ototoxic ARV medications [14].

PLWHA are also susceptible to multiple opportunistic infections (OIs), such as Cryptococcal meningitis that can lead to severe HL due to 8th cranial nerve compression [15,16].

Otosyphilis, known for its occurrence in PLWHA, has been associated with cochleovestibular complications resulting in vestibular dysfunction and profound SNHL [17]. Multidrug-resistant tuberculosis (MDR-TB) is also closely associated with HIV. The treatment of MDR-TB includes injectable tuberculocidal drugs such as different types of aminoglycosides (streptomycin and kanamycin) and novel antibiotics, e.g. capreomycin [18]. In up to 50% of patients, these ototoxic drugs can cause permanent HL [14,19]. Following a single dose of a combination of aminoglycosides, some patients may develop irreversible, profound SNHL [7]. A South African study showed that 57% of MDR-TB patients developed permanent high frequency hearing loss due to ototoxicity within three months after being treated with injectable aminoglycosides [14]. The significant prevalence of severe to profound HL within the population of PLWHA should allow these patients to be considered candidates for CI surgery. Ordinary CI candidacy provides that PLWHA are medically fit and without medical contraindications, such as central nervous system (CNS) pathologies or cognitive impairment [6,8,20], but additional considerations for cochlear implantation in PLWHA should be explored.

Nowadays, PLWHA must adhere to HIV-specific preoperative protocols [5]. These include being placed on highly active antiretroviral therapy (HAART), be clinically healthy, committed to HAART and to reach an undetectable/suppressed viral load (<40 copies of HIV per millilitre (cpy/ml) in the blood or <50cpy/ml depending on laboratory-specific, standard, viral load reference values) (Maurice Hockman, M.D, personal communication) [21]. In addition, PLWHA should preferably have a higher CD4+ count than 200 cells/mm^3 or close to 350 cells/mm^3, as most OIs occur when CD4+ counts are less than 200cells/mm^3 [21]. However, a value of 350cells/mm^3 is patient-dependant and may not always be clinically reachable [21]. In some PLWHA the CD4+ counts could gradually increase at the start of HAART, whereas some PLWHA never reach the abovementioned CD4+ requirements (Francois Venter, M.D. personal communication, 2021) [22]. Therefore, the viral load is regarded as a

more accurate predictor of HAART's effectiveness and the health status in PLWHA, than the CD4+ cell counts [22]. PLWHA who are clinically healthy and have been compliant on HAART could be regarded as potential CI candidates to avoid delays in CI surgery (Maurice Hockman, M.D. personal communication) [23]. Study results about preoperative viral loads and CD4+ cell counts have been inconclusive in predicting intraoperative morbidity and mortality [24]. Currently, two weeks before CI surgery, PLWHA should receive a vaccination of Prevnar 13, which is used to protect them from high-risk pneumococcal diseases, such as pneumonia and meningitis [21,25]. In addition, Pneumovax 23 should be given two months after Prevnar 13 (Maurice Hockman, M.D. personal communication) [21].

Although PLWHA presently have access to CI surgery, a shortage of data exists on how PLWHA respond to CI surgery and benefit from cochlear implantation. To the authors' knowledge, only a few observational studies, limited to nine patients in total, have been published on cochlear implantation in PLWHA [6,8,20]. These studies provide insufficient information regarding HIV-specific preoperative considerations (health status, pneumococcal vaccination, CD4+ cell count and viral load status). Conclusions cannot be drawn based only on these observational studies with small sample sizes ranging between 1-7 patients [6,8,20]. This study therefore aims to contribute to the description of candidacy, audiological and surgical considerations for cochlear implantation in PLWHA with disabling HL, reviewing data from a larger sample of HIV-positive (HIVpos) adult CI recipients.

3.3 Approval and methods

The study institution's Institutional Review Board at the University of Pretoria, South Africa, approved of this study (Institutional IRB number: HUM007/1219).

3.3.1 Study population

Two CI centres in South Africa, the Pretoria Cochlear Implant Unit (PCIU) and the Johannesburg Cochlear Implant Centre (JCIC), contributed data for this retrospective study (conducted from February 2020 to April 2021). Patients were implanted between April 2011 and October 2019 (n=14). Potential participants were adult (>18 years) CI recipients at the time of the study, implanted either unilaterally or bilaterally, with an HIVpos diagnosis confirmed prior to CI surgery, and managed at either the PCIU or JCIC. A total number of 24 adult CI recipients adhered to the study's inclusion criteria. Permission to access and utilize patients' recorded data could not be obtained for 7 CI recipients and patient records were inaccessible for another 3 patients. The final study population thus included 14 postlingually deafened adult CI recipients (9 females, 5 males), with a total of 16 ears implanted (2 bilateral CIs). The mean age at the time of data collection was 42,1 years and ranged between 23 to 50 years (n=14). Participants were aged between 14 and 48 years at the time of the first cochlear implantation with a mean age of 36 years (SD = 8,40 years). The youngest participant at the time of the first cochlear implantation (14 years) had become 23 years of age at the time of retrospective data collection in 2020, and thus adhered to this study's age requirement for inclusion. For the purpose of this study, only data for the first cochlear implantation after HIV diagnosis was included for the two bilateral CI recipients.

3.3.2 Data collection

A retrospective chart review of HIVpos adult CI recipients was employed to establish HIV-specific considerations. Retrospective data (demographical, HL, CI, medical and surgical) were captured on an electronic datasheet. Auditory performance was retrospectively rated (pre- and postoperatively) by the managing CI audiologists by means of the revised version of the Categories of Auditory Performance (CAPR) [26,27]. Auditory receptive abilities were categorized on this hierarchal scale (CAPR), that ranged from 0 (unaware of environmental

sounds) to 8 (telephone usage with an unfamiliar person) [27]. All retrospective data from preoperative, intraoperative and postoperative periods were captured on an Excel spreadsheet (Microsoft, version 16) and prepared for statistical analysis. Audiologists and surgeons managing the included patients assisted with retrospective data capturing from clinical patient files. Postoperative patient data had been recorded at varying time periods and was not consistently available for fixed postoperative periods. Hence, available data at the first and most recent postoperative follow up appointments were used to describe postoperative audiological and medical considerations.

3.3.3 Statistical analysis

Data analysis was conducted with Excel for Windows, version 16. Central tendency and normal distribution of recorded variables were described by means of descriptive statistics in terms of standard deviations (SD), means and frequencies. Due to this study's retrospective design, the investigated variables in clinical patient files were not always complete. Thus, study results are based on the available data for each variable at the preoperative, first postoperative and most recent postoperative time period.

3.4 Results

3.4.1 Preoperative CI candidacy considerations

All patients used only spoken language preoperatively (n=13), except one patient who used a combination of spoken language, lip-reading and gestures (n=1). Preoperative tinnitus and dizziness/vertigo were present in 46% (n=6/13) and 23% (n=3/13) of the patients, respectively. Most patients were public health care patients (57%), compared to 43% in private health care. Sample population characteristics are described in Table 3.1. All patients were fitted with hearings aids and underwent standard preoperative audiological assessment

(unaided and aided pure tone and speech perception testing) [28]. Calculation of pure-tone-averages (PTA) (over 0.5kHz, 1kHz, 2kHz) [29] showed all patients to have bilateral severe to profound SNHL (Severe: PTA >71dBHL to 90dBHL; Profound: PTA >90dBHL) [29]. The exceptions were one patient with a profound mixed hearing loss in the second implanted ear and one patient with a moderately severe SNHL (PTA >56dBHL to 70dBHL) in the non-implanted ear. The mean preoperative PTA in the first implanted ear was 97dBHL (n=14/14; SD= 12.33; range= 71,7dBHL-110dBHL). Preoperative aided pure tone and aided speech perception results revealed limited hearing aid benefit for all patients (n=14). The mean preoperative CAPR score was 2 (identification of some environmental sounds; SD= 1.75; range= 0-5).

Routine preoperative medical examinations and preoperative temporal bone CT imaging were undertaken in all patients (n=14). Preoperative CT excluded inner ear anomalies and labyrinthitis ossificans for all patients (n=13/14, 93%), except one (Patient 5). Magnetic resonance imaging (MRI) of the cochlea, internal meatus, CNS and inner ears was conducted in six patients (n=6/14, 43%). MRI excluded cochlear abnormalities in five out of six patients (n=5/6, 83%). For Patient 5, a compromised basal turn of the cochlea and a segmental fluid loss suggested bilateral asymmetric labyrinthine ossification on the CT and MRI, respectively. In the twelve patients with a history of OIs, records showed causes to be TB (n=9/12, 75%), meningitis (n=2/12, 17%), and pneumonia (n=1/12, 8%). Seven patients (78%) had a history of MDR-TB with six patients who had received tuberculocidal drugs (Table 3.1). Pulmonary x-rays and pulmonary CT scans were undertaken for two TB patients (n=2/9, 22%) as part of the preoperative CI workup, both rendering normal results.

Table 3.1: Characteristics of sample population

Adult cochlear implant (CI) recipient	Mode of amplification at time of study	Etiological factors	Rapidity of hearing loss onset	Duration of deafness prior to CI surgery[11]	Preop CT scan	Preop MRI	Age at first CI (years)	Cochlear implant	Preop CAP^{R} score	Postop CAP^{R} score[12]
Patient 1	Bilateral CI	Noise exposure[13]	P	*	N	*	41	Cochlear CI 24 RE (CA) Perimodiolar	4	8
Patient 2	Unilateral CI	ART, unspecified TB (unknown TB med)	P	2 yr 5 mo 6 d	N	N	35	Cochlear CI 512 Perimodiolar	5	7
Patient 3	Bimodal	ART, unspecified TB (unknown TB med)	P	2 yr 4 mo 11 d	N	N	34	Cochlear CI 24 RE (CA) Perimodiolar	4	8
Patient 4	Bimodal	ART, MDR-TB (unknown TB med)	P	2 yr 8 mo 23 d	N	N	48	MED-EL Synchrony ST Lateral wall	4	8
Patient 5	Bimodal	ART, meningitis	S	3 mo 11 d	A[14]	A[15]	40	Cochlear CI 24 RE (CA) Perimodiolar	2	6
Patient 6	Bilateral CI	ART, Pneumonia	S[16]	2 yr 8 mo 24 d[16]	N[16]	*	39[16]	Cochlear CI512 Perimodiolar	1[16]	8[17]
Patient 7	Unilateral CI	ART, MDR-TB (Kanamycin, Streptomycin)	S	4 yr 8 mo	N	*	39	Cochlear CI512 Perimodiolar	0	8
Patient 8	Unilateral CI	ART, meningitis	S	1 yr 1 mo 24 d	N	*	14	Cochlear CI24RE(CA) Perimodiolar	3	8
Patient 9	Unilateral CI	ART, MDR-TB (Kanamycin)	S	1 yr 4 mo 19 d	N	*	36	Cochlear CI24RE(CA) Perimodiolar	2	8
Patient 10	Unilateral CI	ART	P	1 yr 7 mo 8 d	N	*	23	Cochlear CI512 Perimodiolar	2	7
Patient 11	Unilateral CI	ART, MDR-TB (Kanamycin)	P	3 yr 9 mo 17 d	N	*	42	Cochlear CI512 Perimodiolar	0	7
Patient 12	Unilateral CI	ART, MDR-TB (Kanamycin)	P	5 yr 5 mo 13 d	N	N	40	Cochlear CI512 Perimodiolar	0	7
Patient 13	Unilateral CI	ART, MDR-TB (Kanamycin)	P	1 yr 7 mo 7 d	N	N	38	Cochlear CI24RE(CA) Perimodiolar	1	8
Patient 14	Unilateral CI	ART, MDR-TB (Kanamycin, Streptomycin, Rifampicin)	S	8 mo 10 d	N	*	37	Cochlear CI24RE(CA) Perimodiolar	0	6

** = Missing data from clinical patient files; Bimodal = Cochlear implant and hearing aid amplification; MDR-TB = Multidrug-resistant tuberculosis; med = Medication; ART = Antiretroviral therapy; P = Progressive; S = Sudden; yr= Year, mo= Months, d= Days, N = Normal; A = Abnormal; CA = Contour advanced*

[11] Duration of deafness prior to CI surgery is estimated using the first date that a diagnosis of severe to profound SNHL was obtained. Deafness could have occurred before diagnosis of severe to profound SNHL.
[12] Postoperative CAPR scores were assigned to all 14 patients at the time of data collection, with varying durations of CI usage.
[13] Data on preoperative ART was not documented in clinical patient files for Patient 1.
[14] Bilateral asymmetric labyrinthine ossificans on CT.
[15] Segmental fluid signal loss and labyrinthine ossification on MRI.
[16] Data is before CI device failure and CI reimplantation.
[17] Data is after CI reimplantation.

3.4.2 Cochlear implantation and surgical considerations

The majority of patients (n=11/13, 85%) achieved an undetectable/suppressed viral load and had a CD4+ count of >200 cells/mm^3 (n=12/13, 92%) before CI surgery. Patient 1 had no recent preoperative viral load counts available, but initial blood tests confirmed HIV, with 21991 HIV-1 RNA copies/ml in the blood. For the purpose of this study, the standard clinical reference value for a suppressed/undetectable viral load at the laboratories that were used by the PCIU and JCIC for blood analyses was <40cpy/ml. Details of HIV relevant preoperative blood counts are shown in Table 3.2. All patients (n=14) received preoperative pneumococcal vaccinations in the form of Prevnar 13 (36%), Pneumovax 23 (21%) or a combination of both (43%). All patients (n=14) were considered medically fit to undergo CI surgery. Additionally, intraoperative HIV surgical precautions were undertaken in all HIVpos patients (n=14) with emphasis on the use of double-gloving, protective eyewear, water-impermeable gowns and the avoidance of hand-to-hand passage of sharp objects to decrease the risk of injuries. Patients were implanted with either Cochlear CI24RE (CA) (n=7/14; 50%), Cochlear CI512; (n=6/14; 43%) or MED-EL Synchrony ST (n=1/14; 7%) devices. Patient 6 was unilaterally implanted and underwent CI re-implantation of the first ear after 1.3 years, due to failure of the original CI device. The majority of patients (91%) received routine peri-operative, systemic antibiotics (Augmentin®, Rocephin®) and one patient (9%) had Augmentin® and the viscosurgical device, hyaluronan (Healon®), applied locally to the opened cochlea. Patients underwent cochlear implantation in the right (43%) and left (57%) ears by means of a transmastoid facial recess approach (n=14). From the start of surgical incision, CI surgery on average lasted 183 minutes (n=10/14; SD= 28 minutes; range= 140-225 minutes). No intraoperative complications were reported for nine patients with available data (n=9/10, 90%). For Patient 5, intraoperative Stenver X-ray confirmed cochlear sclerosis with non-optimal electrode positioning and suspected intraoperative trauma to the basilar membrane. All 14 patients had normal intraoperative impedance telemetry confirming the absence of short/open circuits for all electrodes.

Intraoperative electrically-evoked compound action potential (ECAP) measurements were present at all electrodes for 11 patients (n=11/14, 79%) but could not be obtained at ten electrodes (in Patient 5), two electrodes (in Patient 13) and at one electrode (in Patient 4).

Table 3.2: HIV-relevant preoperative blood counts (n=14)

Adult cochlear implant (CI) recipient	Viral count (copy/ml) R: <40cpy/ml	CD4 count (cells/µl)/mm^3 R: 358-1259	Leukocyte count (10^9/1) R: 3.92-9.88
Patient 1	*	441 cells/µl	*
Patient 2	<40 copy/ml	315 cells/µl	3.96
Patient 3	<40 copy/ml	734 cells/µl	6.5
Patient 4	<40 copy/ml	157 cells/µl	*
Patient 5	<40 copy/ml	454 cells/µl	7.54
Patient 6	<40 copy/ml	560 cells/µl	*
Patient 7	>40 copy/ml	263 cells/µl	*
Patient 8	<40 copy/ml	488 cells/µl	*
Patient 9	<40 copy/ml	750 cells/µl	*
Patient 10	<40 copy/ml	230 cells/µl	3.82
Patient 11	<40 copy/ml	250 cells/µl	*
Patient 12	<40 copy/ml	572 cells/µl	*
Patient 13	>40 copy/ml	*	*
Patient 14	<40 copy/ml	656 cells/µl	*

** = Missing data from clinical patient files; R = Standard clinical reference values*

3.4.3 Postoperative audiological and medical considerations

3.4.3.1 Audiological outcomes

Postoperative aided pure tone and speech perception results were captured. CI initial stimulation took place on average 35 days after CI surgery (n= 13/14, SD= 18 days; range= 10 days to 77 days). At the first (M= 2 months, 9 days post CI initial stimulation, SD=26 days) and most recent (M= 41 months, 12 days post CI initial stimulation; SD= 30 months) audiological follow up appointments, patients demonstrated a mean postoperative aided (with CI) PTA of 23dBHL (SD= 4.20; range= 18.3dBHL-30dBHL) and 22dBHL (SD= 4.16; range= 18.3dBHL-30dBHL), respectively (n=14). Aided speech perception scores (for word

and sentence stimuli) were determined at 40dBHL without visual clues (Table 3.3). All patients (n=14) demonstrated improved pure tone thresholds and speech perception scores when compared to preoperative performance (Table 3.3). The mean postoperative CAP***R*** score was 7 (Usage of telephone with a familiar person; SD= 0.76; range= 6-8). Data logging at the most recent audiological follow up, was only available for eight patients (57%) and indicated consistent CI device usage (M= 13.9 hours a day; SD= 1.35; range= 12-15.3 hours a day). At the time of retrospective data collection, the managing CI audiologists confirmed that all 14 patients were functional CI users and oral communicators.

Table 3.3: Postoperative audiological outcomes (n=14)

Adult cochlear implant (CI) recipient	First audiological follow up				Most recent audiological follow up						
	Duration of CI use[18]	Aided PTA (dBHL)	Aided speech perception scores at 40dBHL without visual clues		Duration of CI use[18]	Aided audiological testing			Cochlear implant measurements		
						Aided PTA (dBHL)	Aided speech perception scores at 40dBHL without visual clues		Number of active intracochlear electrodes	CI impedance telemetry	Data logging[19]
			Mono-syllable word score (%)	Sentence score (%)			Mono-syllable word score (%)	Sentence score (%)			
Patient 1	132 d	21.7	92%	*	1601 d *(2324 d)*[20]	26.7	*	*	22[21]	N	*
Patient 2	83 d	18.3	*	*	978 d *(1432 d)*[20]	18.3	20%	*	18[22]	N	*
Patient 3	36 d	21.7	*	82%[23]	92 d *(2654 d)*[20]	18.3	*	84%[23]	22[21]	N	*
Patient 4	71 d[24]	30	*	42%	71 d[24] *(97 d)*[20]	30	*	42%	12[25]	N	12.3h
Patient 5	63 d	26.7	60%	50%	755 d	20	80%[23]	*	22[21]	A[26]	*
Patient 6	43 d	21.7	80%	*	3204 d[27]	25	*	*	22[21]	N	15.3h
Patient 7	98 d	21.7	64%	*	465 d	20	72%	88%	22[21]	N	12h
Patient 8	80 d	20	100%	*	2933 d	20	97%	*	22[21]	N	*
Patient 9	35 d	25	71%	*	1525 d (1613 d)[20]	21.7	92%	96%	22[21]	N	14h
Patient 10	59 d	25	*	*	755 d	20	56%	85%	22[21]	N	12.7h
Patient 11	49 d	26.7	34%	41%	1657 d	21.7	91%	64%	22[21]	N	14.4h
Patient 12	71 d	20	30%	60%	1082 d	25	80%	92%	22[21]	N	15h
Patient 13	57 d	25	90%	*	1104 d	20	92%	96%	22[21]	N	*
Patient 14	77 d	25	*	*	1405 d	25	*	92%	22[21]	N	15.2h

* = Missing data from clinical patient files; N= Normal impedances were measured at all electrodes; A= Abnormal impedances that were absent at some electrodes

[18] Duration of HA use calculated from date of CI initial stimulation to first and most recent audiological follow up date.
[19] Data logging is referred to as "time on air" and is calculated as daily average in hours. Data logging at the most recent audiological follow up ranges from 1 year and 98 days to 8 years and 276 days after CI initial stimulation.
[20] Most recent audiological follow ups for CI measurements (electrodes, impedances, data logging measurements) took place on a different date than aided audiological testing (PTA, speech perception). Unless otherwise indicated, CI measurements and audiological testing took place on the same day. Number of days in brackets indicates duration of CI usage until date of most recent CI measurements.
[21] Total of 24 electrodes (22 intracochlear electrodes,2 extracochlear electrodes - Cochlear).
[22] Electrodes 1-4 disabled. Total of 24 electrodes (22 intracochlear electrodes,2 extracochlear electrodes - Cochlear).
[23] With or without visual cues is not specified in clinical patient files.
[24] At the time of this study, the most recent audiological follow up for Patient 4 had not yet taken place due to Covid-19 restrictions. Therefore, the first audiological follow up is also regarded as the most recent audiological follow up.
[25] Total of 12 electrodes (Med-el).
[26] Impedances revealed short circuits (<1 kOhm) of electrodes 21 & 22 in common ground (CG) mode.
[27] Duration of CI use is estimated based on date of 1st CI initial stimulation excluding an unknown period of device malfunctioning and reimplantation.

3.4.3.2 Medical considerations

Postoperative medical considerations at first (M= 9 days post CI surgery, SD= 7days) and most recent follow up (M=1 year, 4 months post CI surgery; SD= 11 months) periods are described in Table 3.4. Postoperative Stenver X-rays confirmed complete electrode insertion in scala tympani for seven patients (n= 7/8, 87,5%). One patient (Patient 2, n=1/8, 12,5%) had four electrodes outside of the cochlea. Local and systemic complications were absent for all patients at the first medical follow up (n=11/12, 92%), except for Patient 3 (n=1/12, 8%) who exhibited with blood in the middle ear (hemotympanum), 6 days after CI surgery. To date, at their most recent medical follow up appointments, local and systemic complications still remain absent in the four patients (Patients 2, 4, 5 and 9) for whom such data are available.

3.5 Adherence to HIV-specific considerations and guidelines

The recommended HIV-specific guidelines to determine CI candidacy for PLWHA are summarized in Figure 1, together with an indication of adherence to these guidelines for the HIVpos CI recipients in this study.

Table 3.4: Postoperative medical considerations at first and most recent follow up periods (n=14)

Adult cochlear implant recipient	Postoperative intravenous antibiotics	Discharged on oral antibiotics	Postoperative imaging	Duration of hospital stay[28]	Health condition at discharge[29]	First medical follow up		Most recent medical follow up	
						Time following CI surgery (days)	Complications[30]	Time following CI surgery (days)	Complications[30]
Patient 1	*	*	*	*	*	8 d	None	*	*
Patient 2	Augmentin 1.2gm IVI	Augmentin SR 2bd (7 d)	A - Stenver X-ray[31]	12h	Excellent	15 d	None	890 d	None
Patient 3	*	*	*	*	*	6 d	Local (hemotympanum)	*	*
Patient 4	None	*	*	*	Good	31 d[32]	None	31 d[32]	None
Patient 5	*	*	CT [33]	24h	*	8 d	None	559 d	None
Patient 6	Augmentin 1.2gm IVI	Augmentin SR 2bd (7 d)	N - Stenver X-ray	24h	Good	8 d[34]	None	*	*
Patient 7	*	*	*	*	*	*	*	*	*
Patient 8	Augmentin 1.2gm IVI	Augmentin SR 2bd (7 d)	N - Stenver X-ray	24h	Good	7 d	None	*	*
Patient 9	Augmentin 1.2gm IVI	Augmentin SR 2bd (7 d)	N - Stenver X-ray	24h	Good	7 d	None	505 d	None
Patient 10	Augmentin 1.2gm IVI	Augmentin SR 2bd (7 d)	N - Stenver X-ray	24h	Good	1 d	None	*	*
Patient 11	Augmentin 1.2gm IVI	Augmentin SR 2bd (7 d)	N - Stenver X-ray	24h	Good	7 d	None	*	*
Patient 12	Augmentin 1.2gm IVI	Augmentin SR 2bd	N - Stenver X-ray	24h	Good	8 d	None	*	*
Patient 13	None	Augmentin SR 2bd	*	48h	Good	*	*	*	*
Patient 14	Unspecified antibiotics	Augmentin SR 2bd (5 d)	N - Stenver X-ray	24h	Good	10 d	None	*	*

** = Missing data from clinical patient files; IVI = Intravenous injection SR= Sustained release; d= Day; bd = Twice a day; N = Normal; A= Abnormal; h= Hours*

[28] Duration of hospital stay calculated from after CI surgery to hospital discharge. Hospitals/clinics where CI surgery was performed included Chris Hani Baragwanath Hospital, Muelmed Mediclinic, Netcare Linksfield, Union Hospital and Zuid-Afrikaans Hospital.
[29] Health condition at discharge described by surgeon in clinical patient files.
[30] Postoperative complications refer to the presence/absence of hematoma formation, local/systemic complications, skin flap necrosis and implant receiver extrusions.
[31] Postoperative Stenver X-ray imaging was conducted 10 hours after CI surgery and confirmed four electrodes outside of the cochlea.
[32] At the time of this study, Patient 4's most recent medical follow had not yet taken place due to Covid-19 restrictions. Therefore, the first medical follow up is also regarded as most recent medical follow up.
[33] Straight curvature of electrode array.
[34] First surgical follow-up took place 8 days after CI re-implantation in Patient 6.

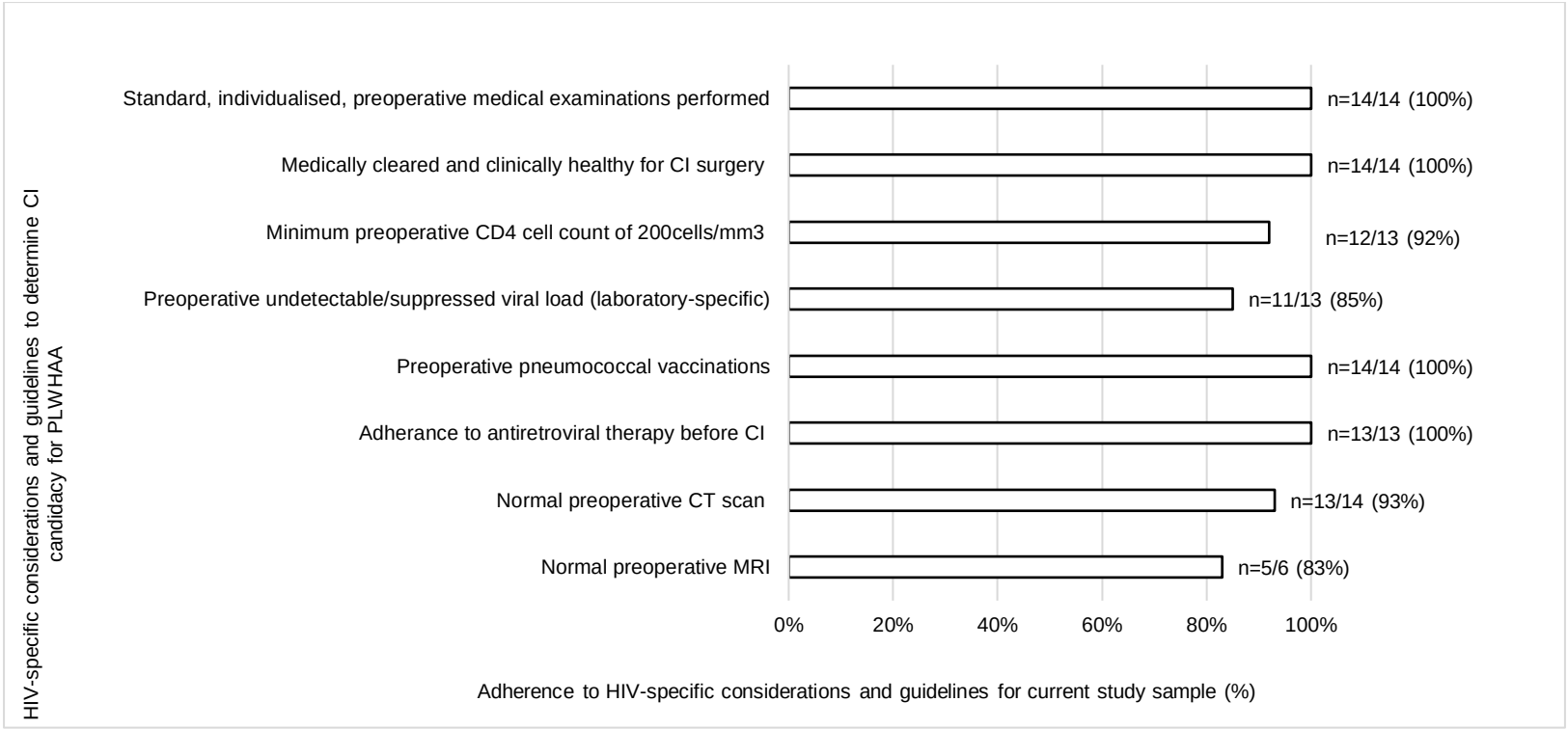

Fig 1. Study sample adherence to the recommended HIV-specific CI considerations and guidelines for PLWHA

3.6 Discussion

Previous observational studies have demonstrated that HIVpos CI recipients are active and functional CI users [6,8,20]. All our patients were also regarded as functional CI users by the managing CI audiologists at the time of the study. To date, the largest series of cochlear implantations in PLWHA was described in 2003, with a sample size of seven participants [8]. Authors reported positive speech perception outcomes and no wound healing complications in the seven PLWHA, suggesting them to be excellent recipients for cochlear implantation, having no greater surgical risk than individuals without HIV, provided medical conditions were well managed [8]. Similarly, in a single case-study, Vincenti et al. [20] documented excellent postoperative open-set speech perception outcomes and greater self-reported independence in a 35-year-old HIVpos CI recipient [20]. In 2016, Jain and Bansal documented no wound healing complications and no local or systemic complications in a 36-year old adult HIVpos CI recipient between three weeks to 2 years post CI surgery [6]. A study on orthopaedic surgery in PLWHA, indicated that if surgical conditions were optimal and without wound contamination, implant surgery could be undertaken in PLWHA [30]. Our chart review shows a more or less identical surgical result for all patients, with no wound healing complications, postoperative infections, skin flap necrosis, systemic complications or CI receiver extrusion. There is a variety of factors that may have contributed to these positive outcomes, as CI outcomes vary and are influenced by different interacting factors [4].

There is a dearth of published data on HIV-specific preoperative considerations that PLWHA should adhere to before CI surgery. Within the existing literature on CI surgery in PLWHA [6,8,20], reference is made to a combination of preoperative CI candidacy assessments for PLWHA, such as MRI [6,20], CT [6,8,20], vestibular testing [20], electrical auditory brainstem response testing [20], patient counselling [6,20], audiological testing [6,8], medical

assessments [6,8] and neuropsychological testing [6,26]. Even though previous literature [6,8,20] reported functional outcomes for all HIVpos CI recipients, the studies were small and inconclusive in providing HIV-specific CI considerations, possibly due to previous uncertainties regarding cochlear implantation in PLWHA. These uncertainties included stigma, ambiguity as to whether surgery may hasten HIV progression and if there was an increased risk of post-surgical infections, delay in wound healing, skin flap necrosis or implant receiver extrusion [6,20,31]. Our study, in conjunction with previous limited observational studies [6,8,20] confirms that there are positive CI outcomes for HIVpos CI recipients, provided that additional considerations/guidelines are taken into account prior to PLWHA undergoing CI surgery. HIV-specific considerations in the form of preoperative CI candidacy, CI and surgical considerations as well as postoperative audiological and medical considerations are described for PLWHA in the current study.

Preoperative considerations for CI surgery in PLWHA include etiological factors for HL in PLWHA and those are attributed to HIV-associated OIs, such as meningitis, or the ototoxic side effects of OIs and TB-related medications as well as ARV medications [32]. In this study, 64% and 14% of the sample, respectively, had TB medication and meningitis that could have contributed to the development of disabling HL. Particularly in low- and middle-income countries (LMICs), like South Africa, it is anticipated that the majority of the current HIVpos CI recipients could have had a history of TB, as South Africa is among the countries with the highest HIV and TB burden globally [14]. The use of ototoxic TB drugs by the HIVpos CI recipients in the current study, such as Rifampicin and Kanamycin are well-known to cause irreversible, profound SNHL [7,14]. Particularly in South Africa, TB continues to be one of the leading causes of death, with more affordable aminoglycosides such as Streptomycin and Kanamycin primarily administered during the injectable phase of TB treatment [33,34]. Recent developments in the treatment of drug-resistant tuberculosis

specify the use of non-ototoxic TB-regimens, such as bedaquiline, to prevent the risk of ototoxic hearing loss associated with injectable aminoglycosides [19,34].

In the current study, the high incidence of preoperative tinnitus and dizziness/vertigo at 46% and 23%, respectively, was anticipated, as pre-and postoperative tinnitus and dizziness are common symptoms in CI recipients [35]. In their study on cochlear implantation in HIVneg CI recipients, Mikkelsen and colleagues [35] reported the presence of preoperative tinnitus in all patients with preoperative dizziness. Similarly to the current study, all HIVpos CI recipients with preoperative dizziness also experienced preoperative tinnitus, regardless of HIV-status [35].

Preoperative CT and MRI are complementary imaging modalities used for CI surgery [36]. CT scans are used to detect cochlear malformations and MRIs are useful in determining the fluid content of the membranous labyrinth and to visualize the integrity of the auditory nerve [36]. Abnormalities in these findings could negatively affect CI surgery and potentially influence CI outcomes [36]. In the current study, preoperative CT was undertaken in 100% of patients, whereas MRI in only 43% of patients. The deficiency of preoperative MRI scans in the current study could possibly be explained by different CI protocols being followed at the time of CI surgery at the different hospitals. Therefore, CT scans were possibly considered to be the minimum requirement for CI surgery, especially if CT indicated an absence of noticeable cochlear malformations, as CT is considered more preferable than MRI during preoperative planning [37]. For a given patient and clinical situation, the operating surgeon at the time of CI surgery determines if no further MRI analysis is required based on the absence of noticeable cochlear malformations upon CT. The optimal approach to decide on an imaging strategy for the evaluation of a given patient is to determine what information is needed and then to balance it against the available imaging modality's limitations [38]. In addition, in South Africa, the deficiency of MRI scans could be explained by funding constraints, as health and medical procedures are among the most expensive in the world, with MRI scans being the most costly when compared to the price in nine other countries

[39]. Although cochlear ossification can typically be observed on CT, MRI is more sensitive to detect early fibrosis, which may remain undetected on CT [40]. Cochlear ossification in Patient 5 was observed on CT and MRI due to the history of meningitis, as meningitis has a high prevalence in PLWHA and is known to cause cochlear ossification [25,41]. A greater insertion force of the electrode array, possibly due to ossification could explain the trauma to the basilar membrane suspected in Patient 5.

In South Africa, the general surgical/intraoperative considerations for CI candidacy, regardless of HIV-status, as outlined by the South African Cochlear Implant Group (SACIG), require the cochlear nerve to be present, the cochlea to have sufficient patency for electrode insertion and surgery to result in minimal trauma to the inner ear [42]. In comparison to CI surgery in HIVneg individuals, surgical considerations for PLWHA require additional intraoperative HIV precautions as body fluids and needlestick injuries are potentially infectious [24]. Furthermore, when CI surgery is undertaken in PLWHA, the "*Protocols for management of HIV in cochlear implant candidates and users*" as outlined in the SACIG guidelines, including health status, pneumococcal vaccination, CD4+ cell count and viral load, should be adhered to [21]. The HIV-specific considerations and guidelines that were adhered to and documented for our patients were developed and based on SACIG's guidelines [21] as well as additional supportive documents (Figure 2). In this study, one patient was 14 years of age at the time of the first cochlear implantation. SACIG's HIV-specific guidelines [21] provide no age-specific HIV considerations, except for CD4+ cell requirements in adults and children (from one to five years of age). It is therefore assumed that this adolescent patient at the time of the first CI surgery, had adhered to SACIG's HIV-specific adult requirements, and was also found medically fit for CI surgery. Our results demonstrate that all patients with available data, adhered to HIV-specific surgical considerations except two, with viral load counts >40 copies/ml and one patient with a CD4+ cell count of 157 cells/mm$^{3.}$ The surgical risk assessment should remain highly individualized

for PLWHA and clinical assessments should be performed for healthy PLWHA with CD4+ cell counts < 200cells/mm^3 to determine CI candidacy (Francois Venter, M.D. personal communication) [43]. Furthermore, all aspects of the patient's medical profile should be critically evaluated preoperatively, as neither the CD4+ cell count or viral load should be solely used as a predictor for peri-operative risk and surgical outcomes [43]. The decision to proceed with CI surgery in our three patients not adhering to special surgical considerations, could have been due to normal CT results along with prompt TB intervention and the absence of additional comorbidities; as well as an individualized, surgical risk assessment approach, in which a multidisciplinary CI team weighed the potential benefits of CI surgery against the risks [24].

Retrospective pneumococcal vaccination data revealed that some patients formerly received vaccinations that were different from the current guidelines, possibly due to some patients receiving only Pneumovax 23 before Prevnar 13 was available. Irrespective of this, it is important to note that all our patients were vaccinated for high-risk pneumococcal disease prior to CI surgery.

Notably, the recommended average duration of 2-4 hours for CI surgery, was adhered to for all our patients and was comparable to that of HIVneg CI recipients [44]. We found that a comprehensive preoperative audiological and medical test battery, adherence to HIV-specific CI guidelines [21], and a highly individualized surgical and medical risk assessment approach, was efficacious in selecting PLWHA for CI surgery, as evidenced in all patients who performed well with their cochlear implants.

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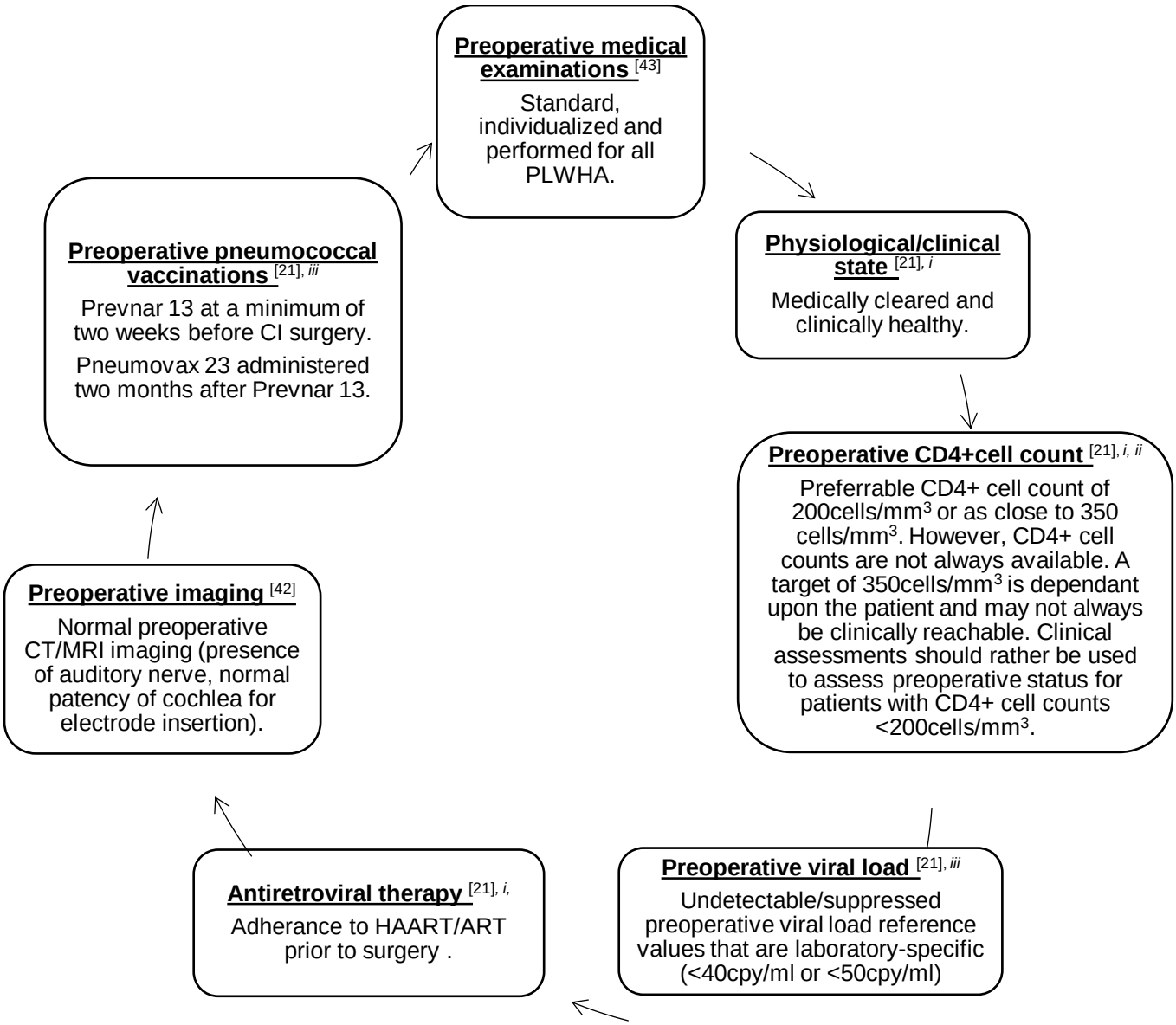

FIG. 2. "Proposed HIV-specific guidelines and considerations to determine CI candidacy for PLWHA.

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i Maurice Hockman, M.D, personal communication, February 9, 2021.

ii Francois W.D. Venter, M.D, personal communication, February 9, 2021, and June 18, 2021.

iii Maurice Hockman, M.D, personal communication, May 11, 2021.

Postoperative audiological CI considerations indicated improved postoperative speech perception abilities and auditory performance for all our patients. Postoperative medical considerations in the form of a postoperative hemotympanum was documented in one patient (Patient 3). However, this did not affect this patient's CI performance, as postoperative hemotympanum is common in CI recipients and will resolve spontaneously [45] . Postoperative modified Stenver X-ray showed four electrodes outside of the cochlea in Patient 2, after complete electrode array insertion had been documented intraoperatively. It is possible that early electrode migration had occurred from the cochlea directly after CI surgery, explaining why four electrodes were disabled at subsequent audiological follow ups (Table 3.3). Notably, there were no cases of postoperative pneumonia or meningitis in our chart review, possibly due the majority of patients receiving intravenous antibiotics (Augmentin®) postoperatively and orally after discharge. The absence of severe postoperative infections possibly improved functional outcomes in our patients. In our review, the two patients with preoperative meningitis, the three patients with less than 100% adherence to the recommended HIV-specific guidelines [21] and the one patient with postoperative electrode migration, were still regarded as functional CI users, and performed well post-surgery in spite of the factors mentioned. The limited medical and surgical complications that occurred in this study sample did not relate to HIV as such.

Study limitations

As with all retrospective studies, our results were limited by data availability and the inconsistent and heterogeneous documentation of data in patient files. Given the small size of this cohort, our findings should not be seen as a representation for all HIVpos CI recipients in South Africa. During the retrospective study period, preoperative and postoperative CI audiological and surgical assessment protocols were altered, and data was not always documented at fixed time periods. This made it difficult to draw conclusions about outcomes and compare outcomes over time. After CI initial stimulation, it is recommended

that adult CI recipients attend audiological follow up appointments at 3, 6 and 12 months postoperatively, and then annually thereafter [28]. However, in LMICs like South Africa, access to healthcare services are often limited by barriers such as transport, travel costs and poor service delivery in rural settings [46,47]. These barriers can also restrict the routine attendance of medical and audiological follow up appointments. Linguistically appropriate, culturally fair and contextually relevant speech audiometry material is critical to assess pre- and postoperative CI speech perception performance [42,48]. The absence of standardized speech audiometry material for each of the 11 official languages of South Africa, accompanied by a culturally and linguistically diverse patient population, complicate the evaluation of speech perception abilities in languages other than English [48,49]. As a result, not all patients in this study were tested in their respective home language, but rather in a second language in which they were proficient. Speech perception outcomes should therefore be interpreted with caution.

3.7 Conclusion

This study shows that a comprehensive preoperative audiological and medical test battery, adherence to current HIV-specific CI guidelines and a highly individualized surgical and medical risk assessment approach is efficacious in selecting PLWHA for CI surgery. The study is hitherto the largest in its kind and supports previous findings in limited observational studies. Our review suggests detailed HIV-specific considerations/guidelines for determining CI candidacy in PLWHA to ensure functional postoperative outcomes after cochlear implantation.

Acknowledgements

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CHAPTER 4

DISCUSSION AND CONCLUSION

Aim of chapter: This chapter provides a summative discussion of the study results that were obtained and critically evaluates the strengths and limitations of the research that was conducted.

4.1 Summative discussion of results

Previous observational studies have demonstrated that HIVpos CI recipients are functional CI users, as evidenced by improved postoperative speech perception scores (Roland et al., 2003; Vincenti et al., 2005), absence of wound healing complications (Jain & Bansal, 2016; Roland et al., 2003), and improved self-reported patient benefit (Vincenti et al., 2005). This led authors to conclude that cochlear implantation is the intervention option of choice for PLWHA with severe to profound SNHL (Jain & Bansal, 2016; Roland et al., 2003; Vincenti et al., 2005). The involved CI professionals in the current study concluded that all followed-up patients in the dataset were to be regarded as active, functional CI users. There are a variety of factors that may have contributed to positive CI outcomes, as CI outcomes vary and may have been influenced by different interacting factors (Boisvert et al., 2020).

Recommendations regarding future research in HIVpos CI recipients are made in the current study. Given the lack of universal CI candidacy guidelines in general on an international basis (Buchman et al., 2020), but also specifically for PLWHA, the current study in a larger sample of HIVpos adult CI recipients in South Africa, suggests HIV-specific considerations for determining CI candidacy in PLWHA. This is done by describing preoperative CI candidacy considerations, cochlear implantation and surgical considerations, as well as postoperative audiological and medical considerations. HIV-specific guidelines are also

proposed to determine CI candidacy and to possibly contribute to the functional postoperative outcomes for HIVpos CI recipients.

Preoperative cochlear implant considerations

Etiological factors for HL in PLWHA are attributed to HIV-associated OIs, such as meningitis, or the ototoxic side effects of OI and TB-related medications as well as ARV medications (Maro et al., 2014). In this study sample, 64% and 14% of the patients respectively had TB medication and meningitis contribute to the development of disabling HL. The majority of patients in this study sample had a history of TB. This is in line with a recent report confirming that South Africa is among the countries with the highest HIV and TB burden globally (WHO, 2021). Ototoxic drugs such as Rifampicin as well as a combination of Kanamycin and Streptomycin could have contributed to etiological factors for TB-related HL in some of our study's patients, as these drugs are primarily used to treat MDR-TB and are well-known for causing irreversible, profound SNHL (Harris et al., 2012; WHO, 2021). In a South African study it was revealed that 57% of patients developed permanent high frequency ototoxic HL within three months of being treated with injectable aminoglycosides (WHO, 2021). This is due to the use of more affordable aminoglycosides, such as Streptomycin and Kanamycin which are used to treat MDR-TB during the injectable phase of TB treatment (WHO, 2019). Recent developments in the treatment of drug-resistant tuberculosis specify the use of non-ototoxic TB-regimens, such as bedaquiline, to prevent the risk of ototoxic hearing loss associated with injectable aminoglycosides (Seddon et al., 2012; WHO, 2019). The major health concerns associated with TB and HIV, particularly within a highly prevalent HIVpos and TB-positive South African population, necessitates the assessment of the preoperative physiological status of the patient to determine the operative risk for mortality and morbidity prior to surgery (Smit, 2010). Two patients from this study were subjected to pulmonary TB assessments which rendered normal investigations for both.

The high incidence of preoperative tinnitus and dizziness/vertigo at 46% and 23%, respectively was anticipated, as pre-and postoperative tinnitus and dizziness are common symptoms in CI recipients, regardless of HIV-status (Mikkelsen et al., 2017). In this study by Mikkelsen and colleagues (2017) on cochlear implantation in HIVneg adults, preoperative dizziness and tinnitus were significantly related, as all HIVneg CI recipients with preoperative dizziness also had preoperative tinnitus. Similarly in the current study, all patients with preoperative dizziness, experienced preoperative tinnitus.

Preoperative imaging in the form of CT and MRI is important in the preoperative evaluation of potential CI patients (Alleman, 2020). CT is useful in detecting cochlear malformations such as cochlear aplasia, vestibular aqueduct and cochlear hypoplasia, whereas MRI scans are used to determine the fluid content of the membranous labyrinth and to visualize the integrity of the auditory nerve (Widmann et al., 2020). The patency of the cochlea for electrode insertion, the presence of inner ear anomalies and labyrinthitis ossificans, as well as the status of the auditory nerve should be assessed preoperatively (SACIG, 2020a), as negative findings in these assessments could potentially influence postoperative CI outcomes (Widmann et al., 2020). Preoperative considerations in the form of CT imaging of the auditory nerve, cochlea and temporal bone were also undertaken for all patients in the current study. Preoperative MRI scans were only undertaken in 43% (n=6/14) of the current study's patients. The deficiency of preoperative MRI scans in the current study could possibly be explained by different CI protocols being followed at the time of CI surgery at the different hospitals. Therefore, CT scans were possibly considered to be the minimum requirement for CI surgery, as CT is considered more preferable than MRI during preoperative planning (Angtuaco et al., 2017). The optimal approach to decide on an imaging strategy for the evaluation of a given patient is to determine what information is needed and then to balance it against the available imaging modality's limitations (Alleman, 2020). Particularly in South Africa, a deficiency of MRI scans could further be explained by

health and medical procedures being among the most expensive in the world, with MRI scans regarded as the most expensive when compared to nine other countries (Mediclinic, 2014). However, preoperative MRI and CT imaging are useful and play an important role in assessing CI candidacy as CI surgeons need to be informed about structural abnormalities that could negatively affect surgery and potentially influence CI outcomes (Widmann et al., 2020).

Cochlear implantation and surgical considerations

Although positive functional outcomes were reported for all patients in previous observational studies, universal HIV-specific surgical considerations have been inconsistently described (Jain & Bansal, 2016; Roland et al., 2003; Vincenti et al., 2005). The South African Cochlear Implant Group's (SACIG) general CI surgical criteria, specifying a present and intact cochlear nerve, sufficient patency of the cochlea for electrode insertion and surgery to result in minimal trauma to the inner ear and the patient (SACIG, 2020a), should be adhered to for all individuals undergoing CI surgery, regardless of HIV status. In addition, PLWHA should adhere to SACIG's additional "*Protocols for management of HIV in cochlear implant candidates and users*", including health status, pneumococcal vaccination, CD4+ cell count and viral load, prior to CI surgery (SACIG, 2020b). The development of an undetectable preoperative viral load over time is particularly important in determining PLWHA's overall health and HAART's effectiveness (Mahomed et al., 2020).

Based on SACIG's HIV-specific considerations for PLWHA that were published in South Africa (SACIG, 2020b), all CI recipients in this study sample received pneumococcal vaccinations and were regarded as clinically healthy, with the majority of them developing an undetectable/suppressed viral load, and having a preferable minimum CD4+ count of 200 cells/mm^3 prior to CI surgery (SACIG, 2020b). The surgical risk assessment for all PLWHA

who undergo surgery, should also be highly individualized (Madiba et al., 2009). This is evidenced in all current patients who underwent CI surgery, including two with viral load counts >40cpy/ml and one with a CD4+ cell count <200cells/mm^3. The decision to proceed with CI surgery could be explained by the fact that all three patients, not adhering to HIV-specific surgical considerations, were clinically healthy, had received pneumococcal vaccinations and had been compliant on HAART. Studies on the value of preoperative CD4+ cell counts and viral load counts have been inconclusive in predicting intraoperative morbidity and mortality and should be avoided as being the sole predictor of intraoperative risk (Madiba et al., 2009; Smit, 2010).

Notably, the recommended duration of 2-4 hours for CI surgery in general, was adhered to for all patients in this study, and is comparable to the time-frame of CI surgery for HIVneg CI recipients (Johns Hopkins Medicine, 2020). The limited medical and surgical complications that occurred did not relate to HIV as such. In general, the findings of the current study point to the fact that a comprehensive preoperative medical test battery, adherence to recent HIV-specific CI guidelines (SACIG, 2020b), and a highly individualized surgical and medical risk assessment approach should be used to select PLWHA for CI surgery, as evidenced in all patients who performed well with their cochlear implants. This included two patients with a history of preoperative meningitis, three patients with less than 100% adherence to the recommended HIV-specific guidelines and one patient with postoperative electrode migration.

Postoperative audiological and medical considerations

A recent “scoping” review of 201 peer-reviewed publications on CI outcomes in adults by Boisvert et al., (2020), documented improved speech perception outcomes in 82% of postlingually deafened adult CI recipients with poor preoperative speech perception abilities.

These authors concluded that CI surgery can be undertaken in adults with poor preoperative speech perception abilities, as patients seldom obtain poorer postoperative speech perception scores in comparison to preoperative performance (5-8%) (Boisvert et al., 2020). Although speech perception abilities should be interpreted with caution, the current study confirmed improved postoperative speech perception abilities and auditory performance for all patients. CI device data logging showed consistent device usage in all patients for whom data were available.

Immunological suppression, as seen in PLWHA (de Jong et al., 2019) and in patients with immune-compromising disorders, require the prevention of surgical site/wound infections as well as postoperative meningitis (Mahalingam et al., 2014). Surgical wound infections and meningitis are typically caused by bacteria, such as Staphylococcus aureus and Streptococcus pneumonia, respectively (Mahalingam et al., 2014). Particularly in immunocompromised patients and PLWHA, pneumococcal vaccinations should be administered, as Streptococcus pneumonia is known to cause significant infection in immunocompromised patients (Mahalingam et al., 2014). The absence of postoperative pneumonia or meningitis in all patients, could have contributed to positive functional outcomes. Postoperative oral antibiotics should also be administered in the first few weeks postoperatively, as the risk of postoperative meningitis is particularly high (Mahalingam et al., 2014). Positive postoperative outcomes in this study could possibly be due to all patients receiving pneumococcal vaccinations, and the majority for whom data were available, had also received intravenous antibiotics and been discharged on oral antibiotics. CI guidelines for immunocompromised patients who have received organ transplants and who are receiving immunosuppressive therapy, should include intensive antibiotic coverage, with stringent vaccination schedules and asepsis, to prevent wound healing complications and surgical site infections (Di Lella et al., 2019).

Postoperative CI complications, regardless of HIV status, could include surgical site infection, wound healing complications, bleeding, tinnitus, dizziness/vertigo, and in severe cases, meningitis, facial injury (paralysis) or implant receiver extrusion due to failure of the CI device (Johns Hopkins Medicine, 2020). Short-term postoperative medical complications in the form postoperative hemotympanum was documented in one patient. However, this did not affect this patient's CI performance, as postoperative hemotympanum is common in CI recipients and will resolve spontaneously (The Ear Center of Greensboro, 2011). One patient had undergone CI re-implantation of the first CI after 1.3 years, due to failure of the original CI device. To date, long-term CI complications remain absent in the four patients for whom data was available. The limited medical and surgical complications that occurred in this study did not relate to HIV as such.

Similarly to previous studies (Jain & Bansal, 2016; Roland et al., 2003; Vincenti et al., 2005), the current results provide additional information that cochlear implantation is a safe and effective treatment strategy for PLWHA with severe to profound SNHL, as all patients had improved postoperative outcomes when compared to preoperative outcomes. This suggests that cochlear implantation can be undertaken in medically cleared PLWHA with severe to profound SNHL, provided that individualised surgical risk assessments and the patient's physiological state allows entrance to CI surgery.

4.2 Clinical implications and recommendations

Results from the current study suggest that PLWHA can be successful candidates for cochlear implantation and can achieve positive functional postoperative outcomes. However, findings from this study also suggest that due to the lack of universal HIV-specific guidelines and considerations for PLWHA to undergo CI surgery, expansion and further description of such considerations for cochlear implantation in PLWHA are required. These considerations are discussed below.

Proposed HIV-specific guidelines for PLWHA with severe to profound SNHL

Despite the fact that PLWHA nowadays have access to CI surgery, there is a small number of observational studies with limited observational data about positive outcomes in HIVpos CI recipients (Jain & Bansal, 2016; Roland et al., 2003; Vincenti et al., 2005). Previously, ambiguity as to whether surgery may hasten HIV disease progression, increased risk of post-surgical infections, delay in wound healing, skin flap necrosis or implant receiver extrusion and the lack of universal HIV-specific CI guidelines possibly have prevented PLWHA from undergoing CI surgery (Fatoki, 2016; Jain & Bansal, 2016; Vincenti et al., 2005). Particularly in South Africa and in other LMICs, barriers to CI surgery for PLWHA may include unequal levels of access to healthcare services and stigmatization regarding HIV status (Buchman et al., 2020; Fatoki, 2016). Therefore, the need to develop universal HIV-specific CI guidelines is evident. In addition, awareness of the benefits associated with CI surgery in PLWHA should be increased and barriers contributing to PLHWA being excluded from CI surgery should be addressed. HIV-specific considerations and guidelines to determine CI candidacy for PLWHA are proposed in Figure 2 (Chapter 3). The proposed figure was developed based on the principles of SAGIC's "*Protocols for management of HIV in cochlear implant candidates and users*" (SACIG, 2020b). Conclusions and recommendations regarding HIV-specific guidelines in this study are based on the availability of data in clinical patient files. These guidelines propose individualised

preoperative medical examinations, physiological state, viral load, CD4+ cell count, pneumococcal vaccinations and preoperative imaging. Adherence to these guidelines will possibly contribute to optimal functional postoperative outcome for HIVpos CI recipients.

Implementation of uniform surgical and audiological CI protocols for PLWHA

When PLWHA are considered for cochlear implantation, CI centres should prioritize the use of uniform pre-, intra- and postoperative audiological and surgical protocols. Currently, international guidelines for CI candidacy in adults are limited and differ among countries (Herbers, 2020; Raine & Vickers, 2017), complicating the implementation of uniform CI protocols worldwide. Increased awareness of CI audiological and surgical requirements among medical professionals and the establishment of clearer referral pathways would also improve the identification of eligible CI candidates, resulting in improved access to CI surgery (Buchman et al., 2020). This could possibly contribute to the development of universal CI guidelines. The development of uniform CI protocols would also ensure standardization of CI candidacy for all PLWHA and should be applicable to all CI centres in South Africa and worldwide.

Measurement and documentation of CI outcomes at fixed periods

CI centres should measure and document outcomes of all PLWHA preoperatively and at fixed postoperative periods in order to document CI progress and track CI outcomes over time. This would simplify data collection procedures and result in documentation of longitudinal CI outcomes in HIVpos CI recipients. This would also allow accurate and reliable comparison between pre- and postoperative CI performance, providing evidence of CI benefit in HIVpos CI recipients. Specifically, for PLWHA that undergo CI surgery, detailed case history, consistent and accurate documentation of HIV-specific considerations, as well as documentation of outcomes using standardized outcome measures, are essential.

Flexibility in CI surgical decision making for PLWHA

In spite of a small sample size, this study provides some support for PLWHA with a history of preoperative meningitis and less than 100% adherence to the recommended HIV-specific guidelines (SACIG, 2020b) to still be considered as candidates for CI surgery. The positive functional outcomes observed for PLWHA with preoperative meningitis and for PLWHA with less than 100% adherence to HIV-specific guidelines, suggests some flexibility in surgical decision making, in which risks must be weighed against potential benefits in these patients being found medically fit for CI surgery (Schecter & Stock, 2003; Smit, 2010). Standard, individualized surgical risk assessments for PLWHA are therefore crucial to appropriately determine CI candidacy and to determine postoperative functional outcomes.

Access to cochlear implantation for PLWHA in South Africa

An estimated 430 million people worldwide experience some degree of moderate or severe disabling hearing loss, requiring some form of rehabilitation, with 80% of people living in LMICs (WHO, 2021). Yet, less than 5% of the world's population with disabling hearing loss have access to rehabilitation by means of cochlear implantation, with the majority of the CI services being only readily available in developed countries (Fagan & Tarabichi, 2018). With an estimated population of 59.62 million (Stats SA, 2020), approximately 84% of the South African population depend on the public health sector for health care services, with 16% belonging to the private sector (Naidoo, 2012). With only four government funded CI centres in South Africa currently, CI has been regarded as a privileged intervention method, being made only available to a limited number of individuals within the public health care sector (Bhamjee et al., 2019; SACIG, 2017). Of 228 CI devices that were implanted in South Africa in 2017, only 47 of them were government funded (SACIG, 2017). Particularly within South Africa, the upfront expenses of obtaining a CI, accompanied by the long-term maintenance and repair costs are evident. In addition, challenges such as a lack of healthcare infrastructure, shortage of trained CI personnel and transport problems to and from CI

centres, may prevent many PLWHA from obtaining access to cochlear implantation (Fagan & Tarabichi, 2018; Kerr et al., 2012).

4.3 Critical evaluation

A critical evaluation of this study was conducted to evaluate its strengths and weaknesses.

Study strengths

To the researcher's knowledge, there are only a small number of published studies, with small sample sizes, describing cochlear implantation in adults with HIV (Jain & Bansal, 2016; Roland et al., 2003; Vincenti et al., 2005). The current study reports on candidacy, audiological and surgical considerations for cochlear implantation in a larger cohort of 14 HIVpos CI recipients in SA (double the number of observations as compared with previously published cases). Therefore, with the largest cohort of HIVpos CI recipients to date, this study adds to the literature documenting the benefits of cochlear implantation in PLWHA with bilateral severe to profound SNHL.

This study reports on HIVpos CI recipients within an HIV-prevalent and TB-burdened South African context. Study results may therefore also be applicable to other LMICs who share similarities in terms of burden of disease, high rates of poverty, lack of medical infrastructure and medical resources, as well as unequal levels of access to rehabilitation services after cochlear implantation.

Furthermore, this study is the first of its kind to document outcomes of HIVpos CI recipients in South Africa, using HIV-specific CI considerations that were developed for South Africa and published on a local platform (SACIG, 2020b). To the researcher's knowledge, no other studies have provided data in terms of HIV-specific CI considerations and guidelines. The

"*Protocols for management of HIV in cochlear implant candidates and users*" (SACIG, 2020b) that was adhered to and documented for all patients in this study, contributes to and suggests HIV-specific considerations for determining CI candidacy for PLWHA. This is to ensure optimal functional postoperative outcomes for all HIVpos CI recipients.

Study limitations

As with all retrospective studies, the results of this study were limited by data availability and the inconsistent and heterogeneous documentation of data in patient files. Due to the study's retrospective nature, variables in clinical patient files were not always complete. Study results are therefore based on the available data for each variable at the preoperative, first postoperative and most recent postoperative time period.

Two CI centres in South Africa participated in the study, resulting in a relatively small dataset of only 14 participants. With an estimated 7,8 million PLWHA in South Africa in 2020 (Stats SA, 2020), the study sample can therefore not be seen as a representation of the larger population of HIVpos individuals with severe to profound SNHL in South Africa. Not all HIVpos CI recipients from all CI centres were included, limiting the generalizability of the findings. The inclusion of participants from more CI centres could have resulted in a broader and larger study sample with greater variability and diversity among participants.

During the retrospective study period of 2011 to 2021, preoperative and postoperative CI audiological and surgical assessment protocols were altered. Therefore, different pre- and postoperative protocols were followed at the two CI centres involved, making it difficult to draw conclusions about outcomes, as not all patients had postoperative data captured at the recommended time periods of 3 months, 6 months and 12 months post CI device activation (SACIG, 2020c). The challenges associated with heterogenous and inconsistent retrospective data collection in this study, emphasizes the critical need for the implementation of a standard data recording methodology at all CI centres in South Africa.

Pre- and postoperative speech recognition abilities should be determined using linguistically appropriate speech audiometry material, incorporating both word and sentence recognition testing measures (Buchman et al., 2020; Pascoe & Norman, 2011; SACIG, 2020c). Speech audiometry material should also be standardized to allow comparison of CI outcomes across different countries and studies (Buchman et al., 2020). Particularly in South Africa, the delivery of audiological assessment services to a culturally and linguistically diverse patient workload, accompanied by an absence of standardized speech audiometry material for each of the 11 official languages (Pascoe & Norman, 2011; Theunissen et al., 2011) resulted in some patients not being tested in their home language, but rather in an alternative language in which they were proficient. Speech perception outcomes in the study should therefore be interpreted with caution.

Postoperative CI outcomes for all patients in this study could only be described using data logging and subjective auditory performance scores due to an absence of standardized postoperative outcome measures.

4.4 Future perspectives

Future studies should consider documenting fixed postoperative CI outcomes using standardized outcome measures in a larger sample of HIVpos CI recipients. The use of standardized speech audiometry material to assess speech recognition abilities in the South African context has been challenging (Pascoe & Norman, 2011; Theunissen et al., 2011). Therefore, standardized outcome measures for HIVpos CI recipients should not only be limited to the description of speech recognition abilities, but should also include the description of other CI-related outcome measures such as psychosocial well-being and HRQoL. It is well known that cochlear implantation can improve numerous aspects of psychosocial well-being, such as depression, social isolation and anxiety (Buchman et al., 2020). HRQoL has also become an established outcome measure to assess and monitor CI outcomes and has resulted in significant improvements in HRQoL for individuals with severe to profound SNHL (Buchman et al., 2020; le Roux et al., 2017). Information on the perceived challenges and benefits associated with cochlear implantation in HIVpos CI recipients could also provide valuable insights into CI outcomes from a patient-centred approach and could result in improved patient-centred care. Therefore, longitudinal CI outcome studies should include a variety of outcome measures, including measures of self-reported patient benefit.

Previous studies have suggested that CI outcomes in adults with severe to profound SNHL vary and may be influenced by different interacting factors, such as age at implantation, duration of deafness prior to CI surgery and bilateral as opposed to unilateral cochlear implantation (Boisvert et al., 2020; Buchman et al., 2020; le Roux et al., 2017). HIV-specific variables in PLWHA, such as adherence to the recommended preoperative blood counts, adherence to ARV medications, pneumococcal vaccinations, the presence of preoperative OIs and the use of its medications could have an influence on CI outcomes in HIVpos CI recipients. Thus, longitudinal research studies are needed to identify pre- and postoperative variables that could influence and predict CI outcomes in HIVpos CI recipients. The potential

effects of these variables on CI outcomes should also be further investigated and understood.

4.5 Conclusion

CI outcomes in PLWHA with severe to profound SNHL have been inconsistently described and remain limited with only a small number of published observational studies. The current study, with positive outcomes reported for all patients, provides valuable insights into the potential CI benefit that could be obtained in HIVpos CI recipients. The results of this study confirm and provide additional information that cochlear implantation is a safe and effective treatment strategy for PLWHA with severe to profound SNHL, as all patients had improved postoperative outcomes when compared to preoperative outcomes. It is recommended that all PLWHA should be medically cleared, surgical risk assessments should be performed prior to CI surgery to prevent postoperative complications and that the patient's physiological state allows entrance to CI surgery. The limited medical and surgical complications that occurred for the patients in this study did not relate to HIV as such. Findings from this study contributes to and also suggests HIV-specific considerations for determining CI candidacy for PLWHA and to ensure optimal functional postoperative outcome for HIVpos CI recipients.

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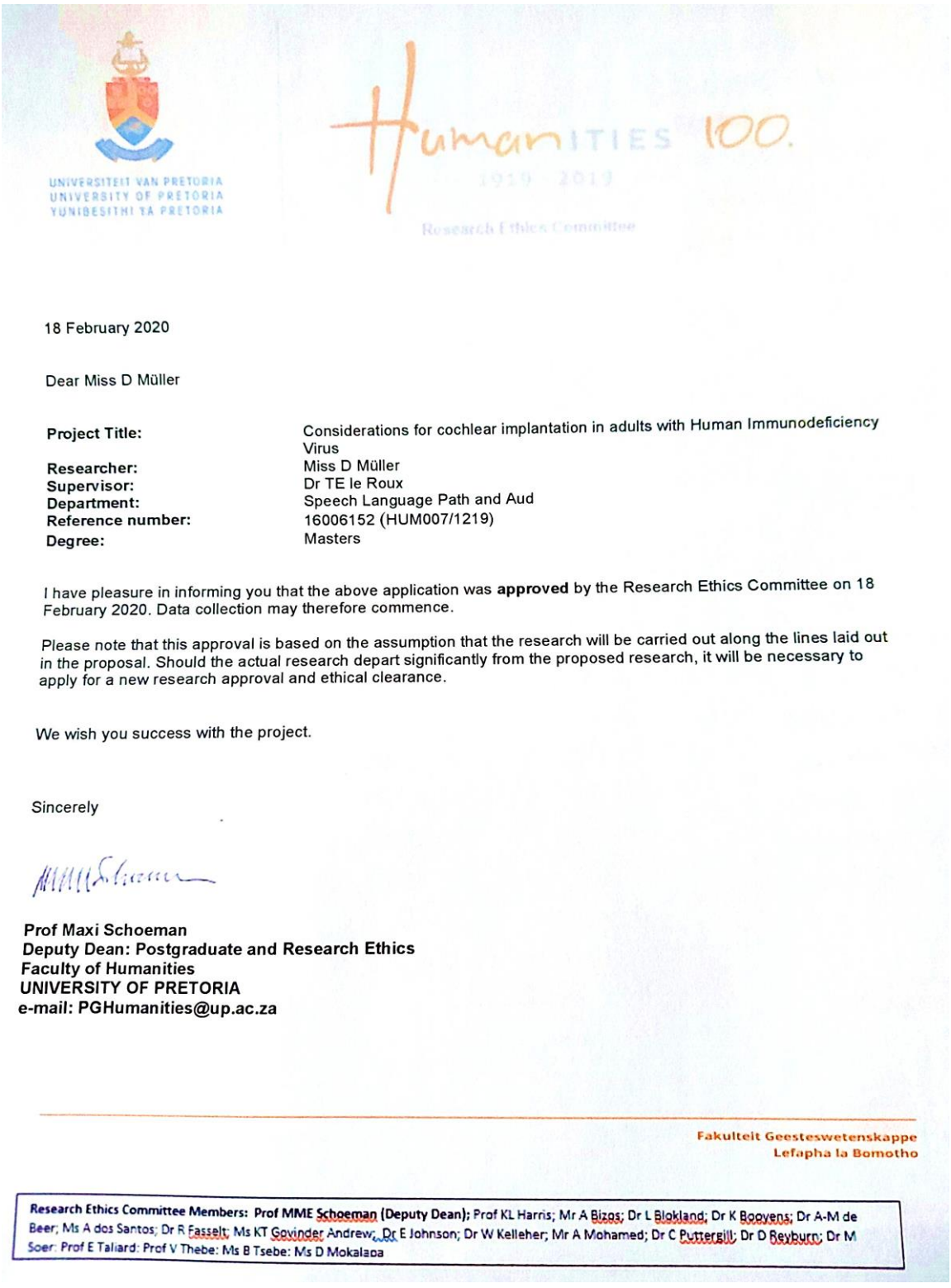
LIST OF APPENDICES

Appendix A: Approved ethical clearance from the Research Ethics Committee of the Faculty of Humanities, University of Pretoria



UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Humanities 100
1919 - 2019
Research Ethics Committee

18 February 2020

Dear Miss D Müller

Project Title:	Considerations for cochlear implantation in adults with Human Immunodeficiency Virus
Researcher:	Miss D Müller
Supervisor:	Dr TE le Roux
Department:	Speech Language Path and Aud
Reference number:	16006152 (HUM007/1219)
Degree:	Masters

I have pleasure in informing you that the above application was **approved** by the Research Ethics Committee on 18 February 2020. Data collection may therefore commence.

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

We wish you success with the project.

Sincerely

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

Fakulteit Geesteswetenskappe
Lefapha la Bomotho

Research Ethics Committee Members: **Prof MME Schoeman (Deputy Dean);** Prof KL Harris; Mr A Bizos; Dr L Blokland; Dr K Booyens; Dr A-M de Beer; Ms A dos Santos; Dr R Fasselt; Ms KT Govinder Andrew; Dr E Johnson; Dr W Kelleher; Mr A Mohamed; Dr C Puttergill; Dr D Reyburn; Dr M Soer; Prof E Taliard; Prof V Thebe; Ms B Tsebe; Ms D Mokalapa

Appendix B: Information letter to the PCIU and JCIC

PCIU information letter

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Humanities 100.
1919 - 2019
Department of Speech-Language Pathology & Audiology

June 2019

Attention: Mrs Nicolize Cass
Cochlear implant team coordinator: Pretoria Cochlear Implant Unit (PCIU)

Dear Mrs Cass,

RE: Permission to conduct a research study at the Pretoria Cochlear Implant Unit (PCIU) that requires access to patient files/clinical data of adult (>18 years) CI recipients diagnosed with HIV prior to cochlear implantation.

I am a Master's degree student conducting research in the field of cochlear implantation in adults with Human Immunodeficiency Virus (HIV). The study is following a retrospective, cohort design and will collect retrospective quantitative data from patient files/clinical data. The aim of this study is to describe candidacy, audiological and surgical considerations for cochlear implantation in adults with HIV.

Title: *Considerations for cochlear implantation in adults with Human Immunodeficiency Virus (HIV)*

Researcher: Daniélle Müller
Study leaders: Dr Talita le Roux and Prof Claude Laurent

Design and procedure:
A retrospective cohort design will be followed and adult CI recipients with HIV will be included as participants. The research will be descriptive in nature and quantitative retrospective data will be collected. Inclusion criteria will include adult (>18 years) CI recipients who were diagnosed with HIV prior to cochlear

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Email: talita.leroux@up.ac.za

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Faculty of Humanities
Fakulteit Geesteswetenskappe
Lefapha la Bomotho

implantation. Retrospective data will be captured from patient records/clinical files and organized in a Microsoft Excel spread sheet to prepare for data analysis. Retrospective data will include demographical data, hearing loss related data, medical data, cochlear implant data and surgical data.

Confidentiality:

Since patient privacy should be maintained at all times, no identifying information will be utilized for the purpose of this study. Thus, each CI recipient will be allocated a unique alphanumeric code in order to ensure confidentiality. The identities of all participants will remain only known to the researcher and will remain confidential.

Written consent:

Permission to access the database and patient records/clinical files of adult CI recipients of the PCIU will be obtained from the coordinator of the PCIU. Adult (>18 years) CI recipients at the PCIU sign a letter of consent on release of information prior to cochlear implantation, that indicates that they give permission to the PCIU to have access and copying rights to any of their medical, audiological and psychological records. Consent is given that this information may be used for the purpose of research, publication in scientific literature, and to share with the appropriate bodies concerned with the performance of the cochlear implant. Only adult CI recipients diagnosed with HIV who have signed this consent letter will be included in the study as participants.

Risks:

Due to the retrospective nature of this study, there are no risks involved.

Release of findings:

Data obtained from this research study will be published in accredited academic journals.

Data storage:

Upon completion of the study, all relevant data will be stored in both hard and electronic copy in a scientific format and will be archived at the Department of Speech-Language Pathology and Audiology at the University of Pretoria for a period of 15 years.

Pretoria Cochlear Implant Unit (PCIU) and Johannesburg Cochlear Implant Centre (JCIC) will be required to provide access to patient files and clinical data of adult (>18 years) CI recipients diagnosed with HIV prior to cochlear implantation. Only adult CI recipients who adhere to the inclusion criteria and who have signed the PCIU consent letter on release of information will be included as participants in the study. Retrospective data will be captured from patient records/clinical files and organized in a Microsoft Excel spread sheet to prepare for data analysis. Retrospective data will include demographical data, hearing loss related data, medical data, cochlear implant data and surgical data.

If permission is granted by you as team coordinator of the PCIU to participate in the study, you are requested to copy and paste the consent slip (found on the next page) onto the PCIU's official letterhead, sign it and return it to the researcher as an indication of your consent.

Should you require any further information, please feel free to contact us. Thank you in advance for your time and co-operation.

Yours sincerely,

Daniélle Müller
Researcher

Dr Talita le Roux
Supervisor

Prof Claude Laurent
Supervisor

JCIC information letter

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Humanities 100.
1919 - 2019
Department of Speech-Language Pathology & Audiology

June 2019

Attention: Mrs Leone Nauta, Dr Maurice Hockman

Cochlear implant team coordinator: Johannesburg Cochlear Implant Centre (JCIC)

Dear Mrs Nauta and Dr Hockman,

RE: Permission to conduct a research study at the Johannesburg Cochlear Implant Centre (JCIC) that requires access to patient files/clinical data of adult (>18 years) CI recipients diagnosed with HIV prior to cochlear implantation.

I am a Master's degree student conducting research in the field of cochlear implantation in adults with Human Immunodeficiency Virus (HIV). The study is following a retrospective, cohort design and will collect retrospective quantitative data from patient files/clinical data. The aim of this study is to describe candidacy, audiological and surgical considerations for cochlear implantation in adults with HIV.

Title: *Considerations for cochlear implantation in adults with Human Immunodeficiency Virus (HIV)*

Researcher: Daniélle Müller
Study leaders: Dr Talita le Roux and Prof Claude Laurent

Design and procedure:
A retrospective cohort design will be followed and adult CI recipients with HIV will be included as participants. The research will be descriptive in nature and quantitative retrospective data will be collected. Inclusion criteria will include adult (>18 years) CI recipients who were diagnosed with HIV prior to cochlear

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Faculty of Humanities
Fakulteit Geesteswetenskappe
Lefapha la Bomotho

implantation. Retrospective data will be captured from patient records/clinical files and organized in a Microsoft Excel spread sheet to prepare for data analysis. Retrospective data will include demographical data, hearing loss related data, medical data, cochlear implant data and surgical data.

Confidentiality:

Since patient privacy should be maintained at all times, no identifying information will be utilized for the purpose of this study. Thus, each CI recipient will be allocated a unique alphanumeric code in order to ensure confidentiality. The identities of all participants will remain only known to the researcher and will remain confidential.

Written consent:

Permission to access the database and patient records/clinical files of adult CI recipients of the JCIC will be obtained from the coordinator of the JCIC. Adult (>18 years) CI recipients at the JCIC sign a letter of consent on release of information prior to cochlear implantation, that indicates that they give permission to the JCIC to have access and copying rights to any of their medical, audiological and psychological records. Consent is given that this information may be used for the purpose of research, publication in scientific literature, and to share with the appropriate bodies concerned with the performance of the cochlear implant. Only adult CI recipients diagnosed with HIV who have signed this consent letter will be included in the study as participants.

Risks:

Due to the retrospective nature of this study, there are no risks involved.

Release of findings:

Data obtained from this research study will be published in accredited academic journals.

Data storage:

Upon completion of the study, all relevant data will be stored in both hard and electronic copy in a scientific format and will be archived at the Department of Speech-Language Pathology and Audiology at the University of Pretoria for a period of 15 years.

Pretoria Cochlear Implant Unit (PCIU) and Johannesburg Cochlear Implant Centre (JCIC) will be required to provide access to patient files and clinical data of adult (>18 years) CI recipients diagnosed with HIV prior to cochlear implantation. Only adult CI recipients who adhere to the inclusion criteria and who have signed the JCIC consent letter on release of information will be included as participants in the study. Retrospective data will be captured from patient records/clinical files and organized in a Microsoft Excel spread sheet to prepare for data analysis. Retrospective data will include demographical data, hearing loss related data, medical data, cochlear implant data and surgical data.

If permission is granted by you as team coordinator of the JCIC to participate in the study, you are requested to copy and paste the consent slip (found on the next page) onto the JCIC's official letterhead, sign it and return it to the researcher as an indication of your consent.

Should you require any further information, please feel free to contact us. Thank you in advance for your time and co-operation.

Yours sincerely,

Daniélle Müller
Researcher

Dr Talita le Roux
Supervisor

Prof Claude Laurent
Supervisor

Appendix C: Approved consent slip from the coordinator of the PCIU

PCIU
PRETORIA COCHLEAR IMPLANT UNIT

PERMISSION TO ACCESS RETROSPECTIVE DATA OF ADULT CI RECIPIENTS WITH HIV

Herewith I, Nicolize Cass, give permission that the involved researcher(s) may access patient files/clinical data of adult (>18 years) CI recipients of the PCIU, diagnosed with HIV prior to implantation. Retrospective data may be used in the research project titled: *Considerations for cochlear implantation in adults with Human Immunodeficiency Virus (HIV).* I do understand that data will be utilized with strict confidentiality.

I have received the required information about this study. I do understand what is expected from me as team coordinator of the PCIU and had the opportunity to ask questions regarding his project.

NICOLIZE CASS AUDIOLOGIST
PRACTICE NR: 0248924
PRETORIA COCHLEAR
IMPLANT UNIT
NPC 2015/24147/08

Mrs Nicolize Cass Team coordinator: Pretoria Cochlear Implant Unit (PCIU)

Date: 24/7/2019

NPO Reg nr: 2015/241478/08 PBO Reg nr: 930052611
Communication Pathology Building, Room 3-32, Lynnwood Road, Pretoria, 0002
Phone: 012 420 3684 | Fax: 012 420 3517 | Email: admin@pretoriacochlear.com

Appendix D: Approved consent slip from the coordinator of the JCIC

JCIC

JCIC
Lower Level
18 Eton Rd
Parktown

011 482 6141
011 356 6198

admin@jcic.co.za

PERMISSION TO ACCESS RETROSPECTIVE DATA OF ADULT CI RECIPIENTS WITH HIV

Herewith I, Leone' Nauta., give permission that the involved researcher(s)
may access patient files/clinical data of adult (>18 years) CI recipients of the JCIC, diagnosed with HIV prior to
implantation. Retrospective data may be used in the research project titled: Considerations for cochlear
implantation in adults with Human Immunodeficiency Virus (HIV). I do understand that data will be utilized
with strict confidentiality.
I have received the required information about this study. I do understand what is expected from me as team
coordinator of the JCIC and had the opportunity to ask questions regarding his project.

L Nauta

Mrs Leone Nauta
Team coordinator: Johannesburg Cochlear Implant Centre

Date: 18/09/2019

Appendix E: Informed consent form of PCIU and JCIC participants

PCIU informed consent form

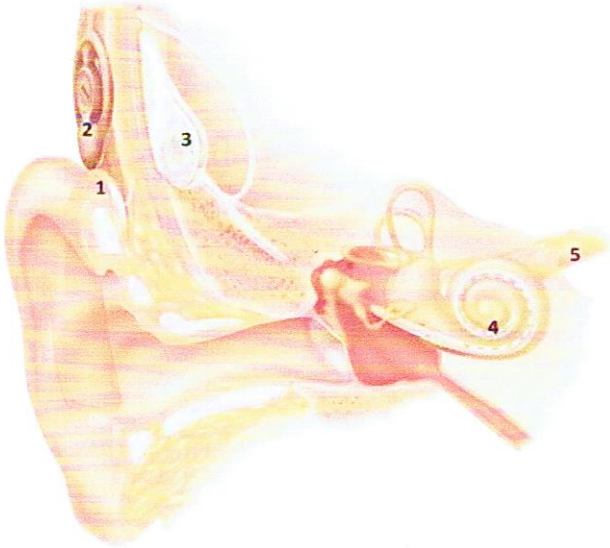
PCIU
PRETORIA COCHLEAR IMPLANT UNIT

INFORMED CONSENT

Name:_____

Case manager:_____ **Date:**_____

Please read the following information carefully before signing the consent form. By signing the consent form you are indicating that you understand and are willing to accept the risks associated with this procedure. The hearing process using a Cochlear Implant (CI) can be summarized as follows:



1) The sound processor captures sounds. It then analyses the information and converts it into a digital (electrical) code.
2) The digitally coded signal travels via the coil cable to the transmitting coil. The coil is kept in position by a magnet. Radio waves from the coil transmit the coded signal through the skin to the implant underneath.

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3) The implant converts the digitally coded signal into electrical signals. The electrical signals contain information that determines how much electrical current will be sent to the different electrodes on the electrode array, which is positioned in the cochlea.
4) The position of the stimulating electrodes within the cochlea will determine the frequency and pitch of the sounds. The amount of electrical current will determine the loudness of the sounds.
5) The implant's electrodes stimulate the cochlea's hearing nerve fibres, which relay the sound signals to the brain to produce hearing sensations.

The evaluations to determine whether you are a candidate for a CI have been completed, and the results indicate that, as far as it is possible to predict, you will benefit from a Cochlear Implant. The following information is brought to your attention:

- ☐ You will probably not be able to use a hearing aid on the CI ear.
- ☐ You should wear a hearing aid in your other ear if possible. You may find that the sound from the CI combines well with the sound from the other ear. It may be easier to locate where sound is coming from and to understand speech in noisy situations when listening with both ears. It is also important to keep the hearing nerve stimulated should the possibility of a bilateral CI arise.

At the moment it is not possible to predict the long-term outcomes with a CI, but we know that certain factors may play a role in the success of a CI, namely:

- ☐ Age at implantation
- ☐ Pre-implant duration of deafness
- ☐ Age appropriate sign or spoken language competence
- ☐ Previous use of hearing aids and listening experience
- ☐ Status of cochlea
- ☐ Family willingness to follow recommendations
- ☐ Enrol in speech, language and listening therapy
- ☐ Return for follow-up appointments
- ☐ Educational and home environments that are supportive of Cochlear Implants
- ☐ Additional special needs

A Cochlear Implant CAN

- ☐ Provide access to sound by bypassing the damaged hair cells in the cochlea
- ☐ Convert sound into electrical signals and send these signals to the hearing nerve and then the brain

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- ☐ Provide more access to speech information that hearing aids
- ☐ Provide improved speech perception for many adults with intensive training
- ☐ Allow a significant portion of profoundly deaf (post-lingual) people useful hearing and speech

A Cochlear Implant CANNOT

- ☐ Interpret sound
- ☐ Provide full access to spoken language for all
- ☐ Provide enough benefit to allow an adult who is profoundly deaf (pre-lingual) to learn spoken language (as the CI might only provide access to environmental sounds and only contribute to quality of life)

- ☐ Outcomes will vary for each person.
- ☐ Developing effective listening skills is a process.

Operation and hospital stay

- ☐ Date of the operation: _____
- ☐ Hospital:_____
- ☐ Surgeon: _____
- ☐ Time to be at the hospital:_____
- ☐ Preparations for surgery: _____
  - Extent of operation scar: 5-6cm
  - Length of operation: usually 3 hours, but can vary
  - Numbness around scar for some weeks
  - Head bandage for 3 days to prevent swelling
  - Slight raised area over internal receiver site
  - Length of stay in hospital is usually one or two nights
  - The surgeon will explain about caring of the wound
  - There are usually no stitches to be removed.

- ☐ Take along:
  - **For yourself:** toiletries and clothes / pyjamas with wide necks or that can open in front so that it can easily slip over the head bandage
  - **For the hospital:** Medical aid details (if you have one), authorization number, CT scans & MRI (if they are in your possession)

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Possible Operation Risks

- ☐ General and anaesthetic risks – discuss with surgeon
- ☐ As the surgery is performed in the vicinity of the nerve that moves the muscles of the face, there is a rare possibility that temporary or permanent facial paralysis may occur
- ☐ There may be pain at the wound following surgery – this is typically temporary
- ☐ There is a slight risk of taste disturbance, such as having a metallic taste
- ☐ Residual hearing in the ear to be implanted will most likely be lost (although with improvements in technology and surgical procedures, this is not always the case)
- ☐ Following the surgery, dizziness is sometimes noted.
- ☐ Increased tinnitus. Tinnitus or head noises may be troublesome after the operation.
- ☐ There is a possible association between cochlear implants and meningitis. There is not a proven casual relationship yet established between the two. Nevertheless, as a precaution, vaccination against meningitis is prescribed.

Restrictions on medical treatments and activities after implantation

- ☐ Magnetic Resonance Imaging (MRI)
- ☐ Scuba diving, physical contact sports, such as rugby

Initial programming of electrodes

- ☐ Initial programming takes place approximately 3-4 weeks post-operatively, once the implant system has been fully paid and delivered to the PCIU office
- ☐ The basic components of setting a program (also called a MAP), include determining threshold levels (T-levels) and comfort levels (C-levels), and "flagging" of (turning off) electrodes that may cause problems. A MAP is determined by setting each of the electrodes to be loud enough for a person to be aware of sound, but not too loud as to cause discomfort.
- ☐ During the initial programming session, an audiologist will seek to determine:
  the type of speech strategy to use; the sensitivity setting; program choices & locks and controls.

Programming and assessments

- ☐ Initial programming will be over a period of 6 weeks.
- ☐ Follow-up programming sessions will be at 3 months, 6 months, 12 months and 2 years.
- ☐ Rehabilitation sessions will be scheduled over a period of 2-3 months dependent on need.
- ☐ Assessments at the following intervals: 6 months and 12 months. Annual reviews will follow thereafter.

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- ☐ Assessments include hearing and speech perception testing, and speech and language assessment (if indicated).
- ☐ These visits may require you to be available for a period of up to 1 week if you do not stay locally.
- ☐ If you receive other therapies, reports are required from these professionals

Costs

- ☐ Travel and accommodation expenses (where applicable)
- ☐ Cables for sound processor
- ☐ Repairs / availability of loaners / deposit & rental fees
- ☐ Insurance
- ☐ Battery costs per month (where applicable)
- ☐ Therapy and assessment
- ☐ Income tax

Research Projects

The Pretoria Cochlear Implant Unit is actively involved in a number of research projects and training. We see this as an integral and essential part of our Unit. Our aims are to improve the greater understanding of the function of the hearing system and to improve our services to our Cochlear Implant users.

You will be invited to participate in research and training projects, but you are under no obligation to do so. These may involve additional visits.

Release of information

The PCIU may require audiological and other relevant information from other health care professionals.

Realistic expectations

It is important for families to be realistic regarding their expected outcomes from Cochlear Implants. While the media often portrays Cochlear Implants as a "cure" for deafness, those directly involved in the process with implanted adults are keenly aware of how individualized the outcomes may be for each individual.

It is important to acknowledge that although a Cochlear Implant provides an opportunity for a deaf person to access spoken language skills, it is not a guarantee. Deaf persons present with varied and wide-ranging characteristics related to their age, history, progress, and development that will impact on their degree of success with a Cochlear Implant.

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Cochlear Implant Systems used in South Africa

There are currently three different implant systems used by Cochlear Implant programs in South Africa. They are:

- Cochlear Limited (Cochlear™) manufacturing the Nucleus® implant system
- MedEL Elektromedizinische Geräte GmbH manufacturing the MedEL implant system
- Advanced Bionics, LLC, manufacturing the Advanced Bionics implant system

As a requirement for you to have a Cochlear Implant you must undertake to be available to attend all necessary electrode programming and evaluation sessions as well as required speech & language therapy sessions.

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CONSENT FORM

PATIENT DETAILS

Name of patient: _____ Age:_____

Name of person/s completing form:_____

PERMISSION TO OPERATE

I, _____ give permission for the surgeons authorized by the Pretoria Cochlear Implant Unit (PCIU) to carry out the procedures that are appropriate for performing a cochlear implant operation on my _____ ear/s. I have been informed by the surgeon/audiologist, nominated by the PCIU, of the procedures involved and the nature of the device that will be implanted. I am aware of the possible risks of the operation and of the post-operative management, testing and training that will be required to obtain optimal results.

I have been informed about the three different cochlear implant system options that are available in South Africa. The implant system I will be receiving is the _____ implant and the _____ sound processor.

I have been informed of the long-term costs involved in the maintenance of the device. I am also aware that I may be asked to participate in extra test sessions for the purpose of research, but that involvement in these sessions is at my discretion.

In giving my permission I accept the risks which may be involved in undergoing the operation and using a cochlear implant.

Signed:_____ **Date:** _____

Name: _____

Witness: _____

Name:_____

Role: _____

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PERMISSION TO RELEASE INFORMATION

I, _____ give permission to the Pretoria Cochlear Implant Unit (PCIU), to have access and copying rights to any of my medical, audiological and psychological records. This information may be used for the purpose of research, publication in scientific literature, and to share with the appropriate bodies concerned with the performance of the cochlear implant. I understand that patient confidentiality will be maintained at all times unless specific permission to release identifying data is granted by me.

Signed:_____ **Date:**_____
Name: _____
Witness: _____
Name:_____
Role: _____

PERMISSION TO PUBLISH PHOTOGRAPHS

I, _____ agree to the publication of photographs of myself by the Pretoria Cochlear Implant Unit (PCIU). I understand that these may be used in scientific literature, books, and other reports.

Signed:_____ **Date:**_____
Name: _____
Witness: _____
Name:_____
Role: _____

University of Pretoria, Department of Speech-Language Pathology & Audiology, Communication Pathology Building, Room 3-32, Lynnwood Road, Pretoria, 0002
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JCIC informed consent form

JOHANNESBURG COCHLEAR IMPLANT CENTRE

INFORMED CONSENT

Name _____

Case manager_____ _____Date_____

The evaluations to determine whether you are a candidate for a Cochlear Implant (CI) have been completed, and the results indicate that, as far as it is possible to predict, you will benefit from a Cochlear Implant. The following information is brought to your attention:

- ☐ You won't be able to use a hearing aid on the CI ear
- ☐ You should wear a hearing aid in your other ear if possible

Factors which play a role in the success of a Cochlear Implant:

- ☐ Age at implantation
- ☐ Pre-implant duration of deafness
- ☐ Age appropriate sign or spoken language competence
- ☐ Previous use of hearing aids and listening experience
- ☐ Status of cochlea
- ☐ Family willingness to follow recommendations
- ☐ Enrol in speech, language, and listening therapy
- ☐ Return for follow-up appointments
- ☐ Educational and home environments that are supportive of Cochlear Implants
- ☐ Additional special needs

A Cochlear Implant CAN:

- ☐ Provide access to sound by bypassing the damaged hair cells in the cochlea
- ☐ Convert sound into electrical signals and send these signals to the hearing nerve and then the brain
- ☐ Provide more access to speech information than hearing aids
- ☐ Provide improved speech perception for many children with intensive training
- ☐ Allow a significant portion of profoundly deaf (post-lingual) people useful hearing and speech.

A Cochlear Implant CANNOT:

- ☐ Interpret sound
- ☐ Provide full access to spoken language for all
- ☐ Provide enough benefit to allow an adult who is profoundly deaf (pre-lingual) to learn spoken language (as the CI might only provide access to environmental sounds and only contribute to quality of life)

- ☐ Outcomes will vary for each person
- ☐ Developing effective listening skills is a process

Operation and hospital stay

- ☐ Date of the operation: _____
- ☐ Hospital: _____
- ☐ Surgeon: _____
- ☐ Time to be at the hospital: _____
- ☐ Preparations for surgery: _____
  - Preparation of implant site
  - Extent of operation scar
  - Length of operation
  - Numbness around scar for some weeks
  - Head bandage
  - Slight raised area over internal receiver site
  - Length of stay in hospital usually one or two nights
  - The surgeon will explain about caring of the wound
- ☐ Take along:
  - **For yourself:** toiletries and clothes / pyjamas with wide necks or that can open in front so that it can easily slip over the head bandage
  - **For the hospital:** Medical aid details (if you have one), authorisation number, CT scans & MRI

Operation Risks

- ☐ General surgical and anaesthetic risks – discuss with surgeon
- ☐ As the surgery is performed in the vicinity of the nerve that moves the muscles of the face, there is the rare possibility that temporary or permanent facial paralysis may occur
- ☐ There may be pain at the wound following surgery – this is typically temporary
- ☐ There is slight risk of taste disturbance, such as having metallic taste

- Residual hearing in the ear to be implanted will most likely be lost (although with improvements in the technology and surgical procedures, this is not always the case)
- Following the surgery, dizziness is sometimes noted
- There is a possible association between cochlear implants and meningitis. There is not a proven casual relationship yet established between the two. Nevertheless, as a precaution, vaccination against meningitis is prescribed.

Restrictions on medical treatments and activities

- Magnetic resonance imaging (MRI)
- Scuba diving, physical contact sports, such as rugby

Initial programming of electrodes

- Initial programming takes place approximately 3-4 weeks postoperatively
- The basic components of setting a program (also called a MAP), include determining threshold levels (T levels), comfort levels (C levels), and "flagging" (turning off) electrodes that may cause problems. A MAP is determined by setting each of the electrodes to be loud enough for a person to be aware of a sound, but not too loud as to cause discomfort.
- During the initial programming session, an audiologist will seek to determine:
    - The type of speech strategy to use
    - The sensitivity setting
    - Program choices
    - Locks and controls

Programming and assessments

- Initial programming will be over a period of 2-4 weeks
- Follow-up programming sessions will be at 3 months, 6 months, 12 months and 2 years
- Rehabilitation sessions will be scheduled over a period of 2-3 months dependant on need
- Assessments at the following intervals: 6 months and 12 months. Annual reviews will follow thereafter
- Assessments include hearing and speech perception testing, and speech and language assessment (if indicated)
- These visits may require you to be available for a period of up to 1 week if you do not stay locally.
- If you receive other therapies, reports are required from these professionals

Costs

- ☐ Travel and accommodation expenses (where applicable)
- ☐ Cables
- ☐ Repairs/availability of loaners
- ☐ Insurance
- ☐ Battery costs per month
- ☐ Therapy and assessment
- ☐ Income tax

Research projects

The Cochlear Implant Centre is actively involved in a number of research projects and training. We see this as an integral and essential part of our programme. Our aims are to improve the greater understanding of the function of the hearing system and to improve our services to our Cochlear Implant users.

You will be invited to participate in research and training projects, but you are under no obligation to do so. These may involve additional visits.

Realistic Expectations

It is important for families to be realistic regarding their expected outcomes from Cochlear Implants. While the media often portrays Cochlear Implants as a "cure" for deafness, those directly involved in the process with implanted adults are keenly aware of how individualised the outcomes may be for each individual.

It is important to acknowledge that although a Cochlear Implant provides an opportunity for a deaf person to access spoken language skills, it is not a guarantee. Deaf persons present varied and wide-ranging characteristics related to their age, history, progress, and development that will impact on their degree of success with a Cochlear Implant.

Any Questions?

_____

_____

_____

As a requirement for you to have a Cochlear Implant you must undertake to be available to attend all necessary electrode programming and evaluation sessions as well as required speech & language therapy sessions.

I/We have been informed about the financial implication for the long term management and maintenance of the Cochlear Implant and all its parts.

I/We have been informed of the Implant devices available in this country and the ones implanted and supported by this Cochlear Implant Team.

I/We have selected the following device.

Nucleus Med-El Advanced Bionics

Implant ..... Processor ..... Colour .....

Additional Information.....

.....

Signed by CI recipient .....

Witnessed by: .....

Case Manager ..... Date .....

PERMISSION TO RELEASE INFORMATION – ADULTS

I, _____ give permission to the Johannesburg Cochlear Implant Centre (JCIC), to have access and copying rights to any of my medical, audiological and psychological records. This information may be used for the purpose of research, publication in scientific literature, and to share with the appropriate bodies concerned with the performance of the cochlear implant. I understand that patient confidentiality will be maintained at all times unless specific permission to release identifying data is granted by me.

Signed:_____ **Date:**_____

Name:_____

Witness signature:_____

Witness name:_____

Role/Relationship:_____

****

PERMISSION TO RELEASE INFORMATION – CHILDREN

I, parent/guardian of_____ give permission to the Johannesburg Cochlear Implant Centre (JCIC), to have access and copying rights to any of my child's medical, audiological and psychological records. This information may be used for the purpose of research, publication in scientific literature, and to share with the appropriate bodies concerned with the performance of the cochlear implant. I understand that patient confidentiality will be maintained at all times unless specific permission to release identifying data is granted by me.

Signed:_____ **Date:**_____

Name:_____

Witness signature:_____

Witness name:_____

Role/Relationship:_____

Appendix F: Declaration of storage at the University of Pretoria

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

FACULTY OF HUMANITIES
RESEARCH ETHICS COMMITTEE

Declaration for the storage of research data and/or documents

I, the principal researcher: Daniélle Müller

and supervisors: Dr Talita le Roux and Prof Claude Laurent

of the following study, titled: *Considerations for cochlear implantation in adults with Human Immunodeficiency Virus*

will be storing all the research data and/or documents referring to the above-mentioned study in the following

department: Department of Speech-Language Pathology and Audiology

We understand that the storage of the mentioned data and/or documents must be maintained for a minimum of 15 years from the commencement of this study.

Start date of study:	February 2020
Anticipated end date of study:	April 2021
Year until which data will be stored:	2036

Name of Principal Researcher(s)	Signature	Date
Daniélle Müller		11/04/2021

Name of Supervisor(s)	Signature	Date
Dr Talita le Roux		12/04/2021
Prof Claude Laurent		12/04/2021

Name of Head of Department	Signature	Date
Prof Jeannie van der Linde		13/04/2021

Appendix G: Revised version of Categories of Auditory Performance (CAPR)

Categories of Auditory Performance (Archbold et al, 1995) – revised version (CAPR)

Category	CAPR description
8	Can use the telephone with an unfamiliar person
7	Can use the telephone with a familiar person
6	Can understand a spoken conversation with an unfamiliar person
5	Can understand a spoken conversation with a familiar person
4	Can understand some common phrases
3	Can understand a few simple spoken words
2	Can identify some environmental sounds
1	Aware of environmental sounds
0	Unaware of environmental sounds

Appendix H: PlosOne article submission

Daniélle Muller

From: em.pone.0.7722de.a271ef19@editorialmanager.com on behalf of PLOS ONE <em@editorialmanager.com>
Sent: 05 November 2021 16:00
To: Daniélle Müller
Subject: Submission Confirmation for PONE-D-21-35332 - [EMID:d13c1de05ef7d961]

PONE-D-21-35332
Title: Considerations for cochlear implantation in adults with Human Immunodeficiency Virus (HIV) - A chart review from two South African cochlear implant centres.
PLOS ONE

Dear Dr. Müller,

Thank you for submitting your manuscript entitled 'Title: Considerations for cochlear implantation in adults with Human Immunodeficiency Virus (HIV) - A chart review from two South African cochlear implant centres.' to PLOS ONE. Your assigned manuscript number is PONE-D-21-35332.

We will now begin processing your manuscript and may contact you if we require any further information. You will receive an update once your manuscript passes our in-house technical check; you can also check the status of your manuscript by logging into your account at https://www.editorialmanager.com/pone/.

If during submission you selected the option for your manuscript to be posted on the bioRxiv preprint server (http://biorxiv.org), we will be assessing the manuscript for suitability shortly. If suitable, your preprint will be made publicly available on bioRxiv and you will receive an email confirmation from them when it has posted. Please check your response to this question and email us as soon as possible at plosone@plos.org if it has been answered incorrectly. Further information about our partnership with bioRxiv to facilitate the rapid availability of life sciences research is available at http://journals.plos.org/plosone/s/preprints.

If you have any inquiries or other comments regarding this manuscript please contact plosone@plos.org.

Thank you for your support of PLOS ONE.

Kind regards,
PLOS ONE
