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A retrospective review of Cochlear implants at Chris Hani Baragwanath Hospital since 2006

van Aardt, Michael Gustaf

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Title:

A retrospective review of Cochlear implants at Chris Hani Baragwanath Hospital since 2006.

Authors:

Dr. Michael Gustaf van Aardt (MBBCH – Wits; FCORL(SA).

Student No: 0303373J

Degree:

Master of Medicine in Otorhinolaryngology, university code MFOSENTS60.

(MMed-ORL).

Supervisor:

Dr. Yahya Atiya (MBBCH – Wits; FCORL(SA); MMed-ORL)

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Dedication

To my loving wife Ashleigh, for her patience and unwavering support throughout my career.

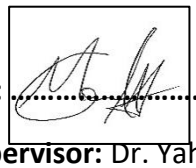
To my beautiful daughter Evelyn, you make everything worthwhile and all I do is for you.

For my parents, Gustaf & Sandra, Straf & Sue your dedication to our family and never-ending encouragement has made this possible.

Co-author Declaration

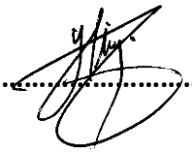
Declaration: Student's contribution to article(s) and agreement of co-author(s)

I, Michael Gustaf van Aardt, student number 0303373J, declare that this Research Report is my own work and that I contributed towards research findings published in the article(s) stated below which are included in my research report.

Signature of Student:  **Date: 19/01/22**

Name of Primary Supervisor: Dr. Yahya Atiya

Signature of Primary Supervisor:

 **Date: 19/01/22**

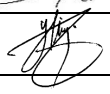
Agreement by co-authors: By signing this declaration, the co-authors listed below agree to the use of the articles(s) by the student as part of his/her Thesis/Dissertation/Research Report. In cases where the student is not the 1st author of a published article, the primary supervisor must explain (under comments) why the student is entitled to use the paper for his/her degree purposes.

Article 1: Title:

A retrospective review of Cochlear implants at Chris Hani Baragwanath Hospital since 2006.

Journal name, year, volume and page numbers: ……..

……….

Authors	**Name**	**Signature**	**Date**
1st author	Dr Michael Gustaf van Aardt		19/01/22
2nd author	Dr Yahya Atiya		19/01/22
3rd author			
4th author			
5th author			
6th author			

Comments by Primary Supervisor:

The bulk of the article content was done by Dr MG van Aardt. This included data collection, statistical analysis and final write up. It is my opinion that the work done suffices for the awarding of the MMed degree by way of publication.……

Article 2: Title ……

Journal name, year, volume and page numbers ……..

Authors	Name	Signature	Date
1st author			
2nd author			
3rd author			
4th author			
5th author			
6th author			

Comments by primary supervisor:

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Article 3: Title ……

Journal name, year, volume and page numbers ……

Authors	Name	Signature	Date
1st author			
2nd author			
3rd author			
4th author			
5th author			
6th author			

Comments by primary supervisor:

……

……

Letter of Contribution

To whom it may concern

The MMed titled ‘A retrospective review of Cochlear implants at Chris Hani Baragwanath Hospital since 2006’, in submissible format for the Journal of Laryngology and Otology, is primarily my work, and has not been submitted elsewhere.

I, Dr MG van Aardt, student number 0303373J, conceived the idea for this study, wrote the protocol, collected all the data personally with no assistance, calculated the statistics with assistance from a statistician and assistance from my supervisor, and I wrote the final paper.

Dr Y Atiya assisted as my supervisor for this study, he reviewed the protocol and manuscript at each stage and provided valuable input and guidance for the work being submitted.

Sincerely



Dr Michael Gustaf van Aardt

Student number: 0303373J

MBBCH-Wits; FCORL (SA).



Primary Supervisor:

Dr Yahya Atiya

MBBCH-Wits; FCORL (SA); MMed-Otol.

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List of Abbreviation / Acronyms

Abbreviation	Meaning
ASHA	American Speech and Hearing Association
CD4	Cluster of differentiation 4
CHBAH	Chris Hani Baragwanath Academic Hospital
CI	Cochlear implantation
CID	Central Institute for the Deaf (sentence list)
CNC	Consonant nucleus consonant (word list)
CNT	Could not test
dB HL	Decibels hearing level
FDA	(U.S.) Food and Drug Administration
GLM	Univariate General Linear Model (statistical tool)
HIV	Human immunodeficiency virus
Hz	Hertz (Frequency)
MDR	Multi-drug resistant
MSTB	Minimum speech testing battery
NU-6	Northwestern university auditory test 6 (CNC word list)
PTA	Pure tone average
TB	Tuberculosis
WHO	World Health Organization
WRS	Word recognition score (or speech discrimination score)

Title: A retrospective review of Cochlear implants at Chris Hani Baragwanath Hospital since 2006.

Authors:

Primary: van Aardt MG MBBCH (Wits), FCORL (SA)

Secondary: Atiya Y MBBCH (Wits), FCORL (SA) MMed (Otol)

Department of Otorhinolaryngology, University of the Witwatersrand and Chris Hani Baragwanath Academic Hospital, Johannesburg, South Africa

Corresponding author: Dr MG van Aardt

5 Rio Road Blairgowrie, Johannesburg 2194

mgvanaardt@gmail.com

Abstract:

Objectives:

To conduct an audit of all cochlear implant recipients in a South African public hospital, describing hearing loss etiology and audiometric profiles between age categories. This was contrasted to local implant candidacy criteria and compared to international criteria.

Methods:

Retrospective review

Results:

Of the 117 implanted recipients included, the majority were female and of African ethnicity. The predominant cause of deafness was ototoxicity related to the treatment of tuberculosis (32% of all recipients). The prevalence of human immunodeficiency virus in the sample was 34%, mostly adults (92.5%).

Pre-operative unaided audiometric thresholds appear to be similar between all subgroups, but aided thresholds are significantly better in patients with tuberculosis related deafness.

Human immunodeficiency virus appears to not affect hearing thresholds on regression analysis.

All patients performed uniformly poorly on aided speech discrimination scoring.

Conclusion:

The etiology for hearing loss for implant recipients at our institution are different to those in international studies with idiopathic hearing loss accounting for far fewer cases.

Based on the current funding model, the indications for implantations at our institution are limited to profound bilateral hearing loss, despite having more lenient criteria for implant candidacy.

Keywords:

Cochlear implantation; Patient selection; Audiometry, Pure-Tone; Audiometry, Speech; Speech Perception; HIV Infections; Tuberculosis; Tuberculosis, Multidrug-Resistant; Ototoxicity.

Introduction

Cochlear implantation (CI) for profound hearing loss has long been the established standard of care, with the U.S Food and Drug Administration (FDA) estimating that approximately 736900 devices have been implanted worldwide as at December 2019.[1]

The latest World Health Organization (WHO) prevalence statistics state that disabling hearing loss (defined as hearing loss of more than 35 dB in the better hearing ear) affects about 5% (450 million people) of the world's current population and is estimated to increase to around 7% (700 million people) or one in every ten people by the year 2050.[2]

Based on these estimates the geographical areas expected to be more significantly impacted by this rising trend proportionate to their respective populations are the African and Eastern Mediterranean regions.[2]

Certainly, the vast majority of these people could be expected to benefit from hearing rehabilitation such as conventional hearing aids, assuming they have access to this. But despite measures and strategies suggested by the WHO to mitigate this alarming trend, it is likely that CI will need to become ever more accessible to rehabilitate those that derive little or no benefit with conventional aids.

Since the first CI in 1961, less than a million devices have been implanted worldwide, despite 17,2 million people living with profound (>90dB hearing level) hearing loss and 30,7 million living with severe (> 70dB hearing level) loss between 1990 and 2019.[3]

There is clearly a lack of access to implantation as well as a clear need to address this discrepancy.

Patient candidacy criteria for cochlear implantation in terms of the audiometric criteria, uni- or bilateral implantations, exclusion criteria (such as age and duration of deafness) as well as practices regarding adults and pediatric populations varies considerably between, as well as within countries.[4-6]

Candidacy criteria are dependent on many factors, including whether national or local guidelines exist that govern candidacy and the source of funding for the implant. Publicly or state funded programs tend to adopt more conservative and selective approaches to candidacy compared to privately funded programs where candidacy is approached with more leniency.[5]

The Chris Hani Baragwanath Academic Hospital (CHBAH) is a tertiary public hospital in South Africa, and the cochlear implant program is jointly managed by the department of Audiology and the department of Otorhinolaryngology, the program is the largest in the country and the only one that is completely state funded. Over and above the lack of funding and inequality with regards to access to health care, South Africa is also faced with the one of the largest human immunodeficiency virus (HIV) burdens worldwide, with an estimated incidence of 4.6 (2.78 – 6.43) per 1000 (across all ages) of the population.[7] Patients who are HIV positive, especially those who are treated for multi-drug resistant tuberculosis (MDR TB), the treatment of which is known to be ototoxic, are at increased risk for hearing loss.[8,9]

Study Aims

Due to the rising trends in disabling hearing loss and the high prevalence of severe to profound hearing loss globally as well as within our continent[2,3], it is important to evaluate the patients that have accessed CI within our current program, to determine what caused

the hearing loss and the severity thereof. It is important to know how long they wait for the implant and the duration of hearing loss prior to implantation. In resource constrained settings, it is important to demonstrate what the current program is able to achieve, in order to identify areas where improvements can be made so we may hopefully improve access to CI for patients that require it.

The primary goal for the study, in light of the above was to conduct a comprehensive audit of all CI recipients, in terms of the following; demographics, hearing loss etiology, age category, patient waiting times within the program and duration of hearing loss. Additionally, pre-operative audiometric profiles and hearing loss severity and speech discrimination for recipients within the context of CI candidacy criteria at our institution, were evaluated and contrasted to candidacy criteria from higher income countries.

Despite patients with HIV and patients treated for TB being at higher risk for hearing loss,[8,9]

There are no studies evaluating the pre-operative audiometric profiles and hearing loss severity of CI recipients with HIV and or TB related hearing loss.

The secondary aims were to evaluate whether any significant differences existed in pre-operative audiometric profiles, hearing loss severity and speech discrimination scores between HIV positive and negative CI recipients as well as between recipients with TB related hearing loss and those with non-TB related hearing loss.

Methods

Participants

A retrospective chart review and statistical analysis was done at the CHBAH, with the approval from the relevant departments.

Ethical approval was obtained from the Human Research Ethics Committee (HREC) at the University of the Witwatersrand (clearance number M200158). As this was a retrospective chart review and not an interventional study no informed consent was required from study participants.

The study period extended from 15 November 2006 to 12 February 2020.

All patients who underwent a CI since the inception of the program were included. Patients were excluded when it was not possible to retrieve patient data.

Data collection

The participants were divided into age categories (as defined by the onset of hearing loss) as follows: pre-lingual pediatric (<3 years[10]); post-lingual pediatric (3 – 18 years); post-lingual adults (>18 years).

Within the age categories, the following variables were recorded: Demographics (gender and ethnicity); age at onset of hearing loss; age at presentation for CI candidacy evaluation; age at implantation; hearing loss etiology; pre-operative hearing loss severity; pre-operative aided hearing thresholds and speech discrimination data; HIV status and CD4 counts; exposure to MDR TB or non-MDR TB and treatment regimens if known.

Participants were further subdivided into HIV and TB-related ototoxicity subgroups based on HIV status and history of exposure to ototoxic medications when previously treated for TB.

Procedures

The waiting time for recipients entering the program, (interval between the age at presentation for implant candidacy evaluation and age at implantation) was recorded to evaluate the average waiting times between age categories. For pre-lingual pediatric patients, the goal at our center is to implant before the age of 3 years.

The duration of hearing loss, (time interval between age at onset of hearing loss and age at implantation)[11], was recorded within each age category to evaluate the trends within age groupings.

Hearing loss severity was recorded as per the minimum reporting standards for adult and pediatric cochlear implantation.[12,13] Unaided (without hearing aids) pure tone average (PTA) thresholds (Four frequency average, 500Hz; 1000Hz; 2000Hz and 4000Hz) was recorded for the left as well as the right ear, binaural testing was too infrequently recorded and was thus omitted. Unaided PTA was then categorized in terms of severity with the American Speech and Hearing Association (ASHA) classification.[14]

Aided PTA (with hearing aids) thresholds were recorded to demonstrate the behavioral response and softest sounds these patients could perceive (or audibility) with validated and fitted conventional hearing aids, one of the implantation criteria at our institution is that patients have aided PTA thresholds above 55dB HL. Above this level, patients are unlikely able to demonstrate audibility for any of the functional speech phonemes based on their intensity level and frequency distribution.[15]

Pre-operative word recognition scoring (WRS) was recorded according to the minimum speech testing battery (MSTB - 2011) for the left as well as the right ear, using consonant-nucleus-consonant word lists (Northwestern university auditory test 6 / NU-6) and Central Institute for the Deaf (CID) sentence lists at 50 dB HL (in quiet).[16] Binaural testing was too infrequently reported and was thus omitted.

HIV Elisa results were recorded and if positive CD4 counts were recorded and categorized according to the WHO revised clinical staging and immunological classification.[17]

Voluntary counselling and consent for HIV testing usually forms part of the work-up for cochlear implant candidacy in all cases.

Statistical analysis

Statistical analysis was performed using SPSS® (version 25) software. Responses of categorical variables are described using frequencies and percentages; while continuous variables are described using means and standard deviations or medians and IQR (inter quartile range), where there is significant deviation from normality.

Spearman's rho was used to determine the correlation between two interval variables, at least one of which is ordinal.

When analyzing the relationship between two categorical variables, Pearson's chi-square was applied. When conditions for this were not met, Fisher's exact test was used.

To determine differences in a continuous variable across two independent groups, the independent sample t-test was applied and where there was deviation of normality Mann-Whitney U test was used instead.

Univariate General Linear Model (GLM) was applied to determine the effect of categorical independent variables on a continuous dependent variable.

Findings were reported as statistically significant when $p < 0.05$.

Results

All Participants

A total of 134 implantations occurred at CHBAH during the study period, on a total of 129 patients. Five patients had received bilateral implantations; even though only unilateral implants are offered based on the funding for the program at our hospital, bilateral implants were done if the patients could privately raise funds for the second implant. Only data for unilateral implants (and the first implant of those who had bilateral implants) was captured and analyzed.

The indication for implantation for all recipients was bilateral hearing loss, no implant was done for single sided deafness or for tinnitus suppression.

Of the 129 patients, 12 were excluded as their patient records were not accessible due to transfer to other departments for follow-up.

One hundred and seventeen patients (unilateral implants) were thus included into the study. Of these, patients were predominately female (55.6%) and the majority of recipients (76.9%) were of African ethnicity (Table I).

Forty-nine patients (41.8%) were pre-lingually deafened pediatric patients (< 3 years of age), 15 (12.8%) were post-lingual deafened pediatric patients (3 – 18 years of age), 53 (45.3%) patients were post-lingual deafened adults (>18 years of age) (Table II).

The most common hearing loss etiology for all recipients was exposure to ototoxic medications and therapy (n=39; 33.3%), followed by non-syndromic congenital hearing loss (n=30; 25.6%) then idiopathic hearing loss (n=21; 17.9%) and hearing loss due to meningitis (n=19; 16.2%), other causes accounting for the remainder are summarized in figure I.

Figure II, shows the collective audiometric profile of the entire cohort and mean audiometric tracing (highlighted in red) of the unaided preoperative audiometric thresholds for the left and right ears (n=117).

The pre-operative unaided hearing severity data for all recipients showed that the majority of left ears (83.8%) and right ears (89.7%) were classified as having profound hearing loss (>90 dB HL) and most recipients (n=79; 67.5%) had the right ear implanted (Table II).

Figure III shows the collective and mean (highlighted) aided pre-operative audiometric profiles for the left and right ears.

Overall, 73.5% of aided, pre-operative left-sided PTA thresholds were worse than 55dB HL, for the right 70.1% were worse than 55dB HL (Table II).

The mean waiting time for patients across all groups was 1.11 years (SD=0.76 years), a marginally significant relationship existed between waiting time of less than a year and congenital hearing loss (syndromic and non-syndromic), (Fischer's exact = 7.355, p =0.056).

Analysis of prelingual pediatric group (n=49)

The mean duration of hearing loss was lowest in this age category (3.5years) and the median age at implantation was 3.08 years which meets the current pediatric implantation goals for the program (Table II).

The most commonly recorded aetiology for hearing loss in this group was non-syndromic congenital hearing loss, accounting for 69.3% (n=34) followed in descending order by meningitis – associated hearing loss (10,2%); hearing loss as result of peri-natal insult (8.16%); syndromic congenital hearing loss (6.1%); auditory neuropathy spectrum disorder (6.1%) and ototoxicity & idiopathic causes accounting for 2.04% each (Figure I).

The data for pre-operative unaided hearing severity in this subgroup shows that 85.7% of left ears and 93.9% of right ears are classified as having profound hearing loss (>90 dB HL) (Table II).

In this subgroup, 79.6% (n=39) of left sided aided, pre-operative PTA thresholds are ≥56dB HL, for the right 81.6% (n=40) are ≥56db HL (Table II).

The majority of this subgroup n=46 (94%) did not have word recognition testing as they were too young and had not developed speech. For the three patients that had speech data, all had WRS scores of less than 50%.

Analysis of post-lingual pediatric group (n=15)

There appears to be a longer delay between hearing loss and implantation in this subgroup, with a mean duration of hearing loss of 8.5 years , on average about 2 years longer than post-lingual adults and 5 years longer than pre-lingual pediatric recipients. (Table II)

Idiopathic hearing loss accounted for the majority (46.6%), followed in descending order by meningitis – associated hearing loss (33.3%); ototoxicity (26.6%) and temporal bone trauma associated hearing loss (6.6%) (Figure I).

Pre-operative unaided hearing severity data shows that 73.3% of left ears and 86.7% of right ears are classified as having profound hearing loss (>90dB HL) (Table II).

Sixty percent (n=9) of left and right sided aided, preoperative PTA thresholds were ≥56 dB HL.

With conventional hearing amplification (tested at 50dB HL), the mean baseline CNC word score (using NU6 word lists) was 9.18% (SD=15.63) for the left ear and 9.40% (SD=16.04) for the right ear. Mean CID sentence score was 9.54% (SD=3.57) for the left and 3.1% (SD=6.57) for the right ear. All patients in this group had WRS scores of <50%.

Analysis of post-lingual adult group (n=53)

From the data it appears that the delay between hearing loss onset and presentation for candidacy evaluation is similar to post lingual pediatric recipients (about 5 years on average),although the duration of hearing loss appears to be shorter. (Table II)

Hearing loss was caused by ototoxicity in the majority (64.15%) of adult recipients followed, in descending order, by idiopathic hearing loss (24.52%), meningitis-associated hearing loss (16.98%) and noise-induced hearing loss (1.88%) (Figure I).

The pre-operative unaided hearing severity data shows that 86.79% of left ears and 86.8% of right ears are classified as having profound hearing loss (>90dB HL) (Table II).

In this subgroup, the majority of left ears (71.7%; n=38) and right ears (62.3%; n=32) had aided, pre-operative thresholds of ≥56 dB HL (Table II).

The speech discrimination results for this subgroup are summarized in table III and in figure IX, the majority of recipients scored 0% for CNC word lists and CID sentences in either ear when presented at 50 dB HL. Additionally, for a number of recipients, results were recorded as “CNT” (could not test).

Analysis of patients with HIV (n=40)

The overall prevalence of HIV across all patients was 34.2% (n=40) and 87.5% of HIV positive patients had absolute CD4 counts of more than 200 cell/mm^3.

Almost all HIV positive patients were adults (92.5%); only one pre-lingual and two post-lingually deafened pediatric patients were HIV positive.

The prevalence of HIV among the various etiological categories was highest among the ototoxicity group, with 30 of the 39 patients (76.9%) in this group being HIV positive. The group with the second highest HIV rate was the meningitis subgroup, where 8/19 (42.1%) were HIV positive.

As the majority of HIV patients fell into the adult age category, comparative analysis of pre-operative unaided and aided PTA thresholds for the left and right ears was only done in that age category to prevent skewing of the data. Analysis revealed no significant differences in pre-operative unaided PTA thresholds between HIV positive (n=37) and negative (n=16) adults (Table II; Figures IV & VIII).

Comparing mean aided PTA results for the left ear between HIV negative and HIV positive adults, an independent samples t-test show that aided PTA is significantly worse in HIV negative adults, $t(51) = 2.980$, $p=0.004$ (Figures V & VIII).

Aided PTA results for the right ear between HIV negative and HIV positive adults, these results were not, however, significantly different using independent samples t-test, $t(51) =1.310$, $p=0.196$ (Figure V & VIII).

Comparing CNC word scores and CID sentence scores between HIV positive and negative patients revealed marginally better CNC scores in HIV negative patients $p=0.079$, this was

only found in the left ear and no significant differences existed between CNC scores for the right ear and for CID sentence scores for either ear (Table III & Figure IX).

Analysis of TB related ototoxicity (n=36)

The vast majority of these patients (23/36 – 63.88%) who had their hearing loss as a result of ototoxic exposure, were exposed to aminoglycosides used in the second line treatment of multi-drug resistant (MDR) tuberculosis.

For the patients with a history of MDR TB, the most commonly reported aminoglycoside was Kanamycin (43%; n=10), however the exact regimen was not reported in another 43%, and Streptomycin for 8% (n=2) and 1 patient was exposed to combinations of Kanamycin, Streptomycin and Capreomycin.

Non-MDR TB related ototoxicity accounted for 13/36 – 36.11%. Non-MDR TB patients reported hearing loss after exposure to the standard anti-tuberculous regimen (rifampicin; isoniazid; ethambutol; pyrazinamide) in 61% of cases (n=8), whilst the exact regimen was not reported in the remainder (38.5%; n=5).

Again, as most of the patients with TB related ototoxicity fell in the adult age category, comparative analysis between pre-operative unaided and aided PTAs was only done within this category to prevent skewing of the data.

Analysis of the pre-operative, unaided hearing severity for the left and right ears revealed no significant differences between adults with TB related (MDR + non MDR) ototoxicity (n=31) and adults with any other cause of hearing loss (n=22) or non-TB group (Table II; Figures VI & VIII).

However, results from independent samples t-test show that, for the left and right ears, the mean aided PTA of the adult non-TB group is significantly worse than adults with TB related ototoxicity. For the left, t(35.72) =3.036, p=0.004 and for the right, t(51) =2.180, p=0.034 (Table II & Figures VII & VIII).

Mean unaided and aided PTA thresholds for the left and right ears between all patients in the MDR TB group and non-MDR TB group were not significantly different.

With CNC word scores and CID sentences, the non-TB group had significantly better CNC word scores than in the TB group (MDR and non-MDR), p=0.016 in the left ear, however there were no significant differences in CNC word scores for the right ear and no significant differences with CID sentence scores for either ear (Table III & Figure IX).

A similar trend between the HIV positive group and the TB group were noted in terms of better pre-operative aided PTA thresholds. Given the high prevalence of HIV within the TB group, regression analysis (univariate GLM) was done to ascertain whether the presence or absence of ototoxicity was an independent risk factor for better aided PTAs in HIV patients. This showed that ototoxicity accounts for 16.3% (R^2 = 0.163) of the variance in aided PTA for the left ear, F(1,38) = 7.392, p=0.01. The absence of ototoxicity is a significant predictor of worse aided PTAs in HIV patients, β=22.400, p=0.01.

For the right ear, ototoxicity accounts for 19.1% (R^2 =0.191) of the variance in aided PTA for the right ear, F(1,38) = 8.977, p=0.005. The absence of ototoxicity is a significant predictor of worse aided PTAs in HIV patients, β=26.167, p=0.005.

Discussion:

The primary purpose of this study was to determine what had caused the hearing loss in our CI recipients, and to evaluate the pre-operative severity of hearing loss in light of the current local implantation criteria, and international criteria.

Etiology of hearing loss within cochlear implant studies are seldom reported and idiopathic hearing loss frequently accounts for the majority of participants in studies that do, with a focus predominately on paediatric recipients[18].

Etiology was consistently recorded in this study and although it still accounted for 18% of hearing loss for all patients, idiopathic hearing loss accounted for far fewer cases in pre-lingual paediatric, and in the post-lingual adult groups by comparison. The possible reasons for this are that paediatric patients are prioritized in our programme, as are adults with hearing loss related to TB therapy and meningitis. In our study, TB related ototoxicity was the leading cause of hearing loss, especially among adult recipients. This reflects the incidence of MDR TB in South Africa which ranked 6th highest (approximately 23 per 100 000 population) in 2019 among the 30 countries with the highest burden of MDR-TB globally[19]. The incidence of severe to profound hearing loss (>70 dB HL) among treated MDR TB patients was 15% in a retrospective study of 353 patients, and HIV co-infection has been shown to increase the risk of hearing loss due to ototoxicity compared to HIV negative MDR TB patients.[9,20,21]

The prevalence of any degree of hearing loss as well as other auditory symptoms among HIV patients can be as high as 25-33%, the causes of which, are multifactorial.[22]

The audiological criteria for implant candidacy at CHBAH require bilateral hearing loss with unaided thresholds >70 dB HL and/or aided thresholds > 55dB HL (above 2000Hz) and / or aided word recognition and sentence scores < 50% correct (for adults and paediatric patients). Despite being a state (or public) funded program in a low/middle income country, compared to some publicly funded programs in the high-income countries, the audiometric criteria are more lenient. In the United Kingdom, the requirement is hearing loss >90dB HL and currently research has recommended this be lowered to >80dB HL (above 2000Hz). The local criteria resemble that from Australia – unaided thresholds >70dB above 1500Hz. The international trend among most clinics according to a recent survey use a an average 75-80dB HL cutoff above 1000Hz.[5]

Despite having a lower hearing threshold as a criterion for candidacy, only 9.4% of left and 6.8% of right ears had a PTA between 70 – 85 dB HL, more than 80% of both sides had >90dB HL loss, so patients with less severe hearing loss appear to have less access to implantation at our institution. We suspect multiple possible reasons for the disproportionate amount of profoundly deaf patients; the most likely reason is that these are the patients currently being prioritized, our numbers are low compared to other centers and our funding model does play a rate-limiting role in the number of implantations we can do. However, it is also likely that patients with hearing loss between 70-90dB HL are just not being referred for candidacy evaluation, or may still be deriving some benefit from conventional aids.

No significant differences were found between age categories for either ear in terms of pre-operative unaided thresholds, very few patients had any residual low frequency hearing;

almost all of these could be considered to have left corner audiograms, as few have recorded thresholds less than 70dB HL above 1000Hz.

Over a third of the recipients in this study (n=40) were HIV positive, and almost all had hearing loss caused by TB related ototoxicity or from meningitis. The question as to whether HIV resulted in any differences in terms of hearing severity and/or in other audiological criteria among patients who are otherwise candidates for cochlear implantation, is poorly documented and the secondary aim of the study was intended to provide more clarification.

Compared to HIV negative adult recipients, HIV positive adult recipients had no significant differences in pre-operative unaided hearing thresholds for either ear. This was not unexpected, as this analysis was conducted on a sample where a selective criterion had already been applied, as more than 80% of the study population had profound hearing loss (>90 dB HL). This did however, provide a baseline for additional comparative analysis between other audiological criteria, as unaided thresholds are typically the first criterion by which a patient would be selected for implant candidacy evaluation.

For the same reasons, pre-operative unaided hearing loss thresholds of adult recipients with TB related ototoxicity compared to non-TB related adult hearing loss were not significantly different, and for pre-operative unaided thresholds within the TB group, MDR and non-MDR subgroups had no differences for either ear in terms of preoperative hearing severity.

Aided thresholds were noted to be significantly better in the left ear for HIV positive adults compared to HIV negative adults, but not significantly different in right ears. A confounding variable was suspected, seeing as the majority of HIV patients were also part of the TB group. Mean aided PTAs were found to be significantly better in the TB group compared to the non-TB group and regression analysis showed that TB related ototoxicity was considered

an independent risk factor for better aided thresholds in HIV patients. So, it would appear that the presence of HIV is indeed a confounding variable in this analysis, and does not appear to play a significant causal role in better aided thresholds in the left ears of the HIV group.

The better aided thresholds in patients with TB related ototoxicity could be explained considering the pathophysiology of aminoglycoside ototoxicity causing proportionately more high frequency hearing loss by damaging the basal cochlea outer hear cells (OHC) and supporting cells and initially sparing the lower frequency apical cells of the cochlea.[23]

Speech candidacy criteria at CHBH require that a patient demonstrates aided (at 50dB HL) scores of less than 50% for CNC (NU6 – phonemic score) as well as with CID sentences (tested in quiet). The 50% cutoff seems constant in many other countries and remains the recommended cutoff by the FDA, however emerging evidence is supportive of including patients with scores of 60% or less[24,25].

International practice varies considerably in the utilization of word test measures or sentence test measures, either only doing a single test measure or a combination and then either in quiet or in noise. This makes comparison of pre-operative performance between different centers difficult[5].

In this study, our adult patients appear to have worse WRS and sentence scores as compared to other series that similarly evaluated pre-operative audiological profiles for implant recipients[15,26]. However, it is admittedly difficult to draw direct comparisons to these series as the material used to test word and speech recognition differ from that used at CHBAH, as do the testing conditions (e.g., testing in noise).

More than half of all adults in this study had 0% scores for CNC word lists and CID sentences, 17% of tests were recorded as CNT (could not test) as there was no response at the 50 dB HL presenting level. It could be assumed that these tests could have essentially been scored 0% as well, but it is not clear if a response would have been measured at higher presentation levels or if English word and sentence lists affected results given that many patients have English as a second, or even third or fourth, language.

Another interesting observation was that, for most CNC word and CID sentence tests, all patient subgroups performed equally as poorly, despite TB groups having better mean aided PTAs in general. Referring to the aided individual and mean audiograms for the TB (and HIV) groups (Figures V & VII) many would appear to be able to access some speech phonemes (usually vowels and mixed vowels and some consonants located between 30 to 55dB HL between 250-2000Hz) but the majority would not access high frequency consonants (usually above 40 dB HL over 2000Hz).

Although it is important to bear in mind that audibility of speech sounds with aided thresholds does not reliably predict or reflect speech discrimination or intelligibility[27], we don't think this fully explains why the patients in our series do as badly as they did.

South Africa has 11 official languages, and the average South African is multilingual and speaks 2 to 3 languages, and English is predominately a second language[28]. We theorize that this may possibly explain the high rate of 0% scores and "CNT" recordings in our cohort, especially among patients with better aided thresholds. We were not able to correlate patients first spoken language to word or sentence scores tested in English due the lack of available data, and our sample would have been too small to draw meaningful conclusions from such an analysis.

Furthermore, although some word and sentence lists exist in certain African languages, these are often developed for local use in audiology clinics as a cross-check for speech reception thresholds done with English word lists, none of these are validated for use in candidacy determination.[29]

The only validated word and sentence material used in speech discrimination testing to determine implant candidacy is in English, and monosyllabic word lists are currently being favored over sentence scores as a candidacy measure, as they more reliably evaluate peripheral hearing and for monitoring improvement post implantation. [30,31]

To develop and validate word and sentence lists for an African language is likely going to be faced with challenges, monosyllables occur very infrequently in African languages and are not sufficiently representative of the relevant language to meet the criteria for the word structure used in monosyllabic word lists.[32]

Another possible theory for poor performance with speech discrimination tests for patients with better audibility measured by aided pure tones, is the possible effect of HIV co-infection causing central demyelination.[33] HIV has been associated with a form of auditory neuropathy, which may cause some degree of dys-synchrony enough to significantly affect the understanding of speech in noise.[33-36] It is possible that this effect may be exacerbated in patients who have profound hearing loss for other reasons.

We would not be able to test this theory with the data captured for the purposes of this study, but further research to evaluate this is to be encouraged.

Conclusion:

Our study has demonstrated that the etiological causes for hearing loss among our recipients differs considerably from other studies that report them. Idiopathic hearing loss accounts for far fewer referrals to our program.

Since the inception and writing up of this study, the candidacy criteria for cochlear implantation has undergone some revision in South Africa, the latest audiometric criteria for adults are PTA > 80dB HL and monosyllabic word recognition <40% in the ear to be implanted, further changes were implemented regarding criteria for single sided deafness, asymmetrical hearing loss, bilateral implantation and implant timing for pediatric patients.[37]

It is likely that individual cochlear implantation clinics in South Africa will adopt some or all of these recommendations based on funding models in place and will prioritize patients on a case – by case basis. The expectation, at least in publicly funded hospitals where the highest burden of patients with disabling hearing exists, is that patients with more severe hearing loss will be prioritized over patients with less severe hearing loss or those with single sided hearing loss. This is evident in this study as the vast majority of patients had profound hearing loss (>90 dB HL), despite having lenient audiometric candidacy criteria since the inception of the program.

This study has evaluated the pre-operative audiological profile for post-lingually deafened cochlear implant recipients with HIV and with hearing loss due to ototoxic treatment for TB (both MDR and non-MDR). We have found that although no significant differences exist between age groups, and hearing loss etiologies in terms of unaided hearing thresholds, significant differences are apparent with aided threshold testing, patients with TB related

hearing loss achieving better aided thresholds and despite this, word and sentence scoring was uniformly poor.

An HIV positive status appears to play a confounding role in the differences in pre-operative aided audiometric thresholds of between recipients, although it is possible that the presence of HIV could explain the poor speech discrimination scoring. As a theory, this could not be tested with the data available in this study.

Further research into developing speech testing material for African languages should be encouraged and validated against currently available English word lists for cochlear implant candidacy determination.

Additionally, the post-operative hearing outcomes (thresholds and word and sentence recognition) among HIV and TB related hearing loss patients should be researched and compared to appropriate controls to evaluate for any significant differences and whether these outcomes can be predicted on pre-operative evaluation.

Study Limitations:

This study is retrospective on a select group of patients and caution is advised against generalizing the findings therein to broader groups of patients.

Data comparison between institutions is likely to be imperfect as the methods used to evaluate hearing and speech discrimination may vary considerably.

The poor speech discrimination results are theorized to be not only as a direct result of the hearing loss but possibly influenced by differences in spoken language and English speech testing. This is based on an assumption as no data regarding patients first language was captured and furthermore, fluency in English could not be assessed and can vary widely in any given population, this theory should be thoroughly researched before any conclusion can be drawn.

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Summary

- Cochlear implant candidacy criteria vary considerably worldwide with regards to audiometric thresholds and speech discrimination scoring.
- Not only does speech discrimination score cutoffs vary for implant candidacy, it also varies regarding the testing material used (monosyllables vs. sentences) and testing environment.
- Comparison between different centers is thus difficult.
- In our study, the commonest aetiology for hearing loss among adult cochlear implant recipients is aminoglycoside ototoxicity related to tuberculosis treatment (mostly second line regimens in multi-drug resistant cases).
- HIV prevalence is high in our patient population, almost exclusively among adult CI recipients, the majority of whom have aminoglycoside related hearing loss related to TB treatment.
- There are no significant differences in preoperative hearing thresholds (unaided) between HIV positive and negative recipients or between recipients with TB related and non-TB related hearing loss.
- There are significant differences in pre-operative aided threshold testing between recipients with TB related and non-TB related hearing loss, recipients with TB related loss have better aided PTAs, although this does not translate into better speech discrimination scores in this group of recipients.
- In fact, the study showed, that all patients performed poorly, the majority of WRS and sentence scores were 0% or were recorded as “CNT” (no response at 50db HL presentation in quiet).

- There does not appear to be a difference in aided PTAs between HIV positive and negative recipients on regression analysis.
- Theories for why patients in our study performed as poorly as they did with speech discrimination scoring include:
    - Effect of using English word or sentence lists in second, third or fourth English language speaking recipients affecting speech understanding.
    - HIV co-infection possibly causing demyelination and dys-synchrony and affecting speech understanding.
- None of these theories could be tested in the current study.
- Despite our center having lenient audiometric candidacy criteria, the majority of our recipients have profound (>90dB HL) loss, indicating that these recipients are prioritized over those with less severe hearing loss (70 – 90dB HL) due to our funding model.

Tables and Figures

Variable	Categories	n (%)
Gender	Male	52 (44.4)
	Female	65 (55.6)
Ethnicity	African	90 (76.9)
	Caucasian	20 (17.1)
	Indian	5 (4.3)
	Coloured	2 (1.7)

Table I. Study participants gender and ethnicity demographics (n=117).

Variables	All Patients	Prelingual Paediatric (<3yrs)	Post-lingual Paediatric (3-18yrs)	Post-lingual Adults (>18yrs)	HIV+ adults	HIV – adults	TB-related hearing loss	Non-TB related hearing loss
Patients, n(%)	117 (100)	49 (41,8)	15 (12,8)	53 (45,3)	37 (64,9)	16 (30,1)	31 (58,4)	22 (41,5)
Left ear Unaided PTA (dB HL): mean±SD	103.33 ± 12.61	102.63 ± 12.33	102.73 ± 14.26	104.15 ± 12.6	103.83 ± 12.35	104.87 ± 13.53	103.93 ± 10.48	104.45 ± 15.36
Right ear Unaided PTA (dB HL): mean±SD	104.71 ± 11.21	104.85 ± 9.61	105.66 ± 13.1	104.32 ± 12.19	104.29 ± 10.85	104.37 ± 15.24	103.09 ± 9.74	106.04 ± 15.07
Left ear Aided PTA (dB HL): mean±SD	80.7 ± 29.06	90.32 ± 29.09	70.80 ± 29.83	74.6 ± 26.65	67.91 ± 23.97	90.06 ± 26.79	65.48 ± 20.79	87.45 ± 29.06
Right ear Aided PTA (dB HL): mean±SD	80.1 ± 29.17	88.85 ± 27.06	76.33 ± 33.29	73.07 ± 28.24	69.75 ± 26.08	80.75 ± 32.30	66.19 ± 23.92	82. 77 ± 31.45
Age at onset of hearing loss (mean±SD)		0.19 ± 0.5	10.12 ± 3.52)	33.78 ± 8.04				
Age at presentation (mean/median)		2.33 (1.66 - 2.79) IQR	15.83 (12.83 - 24.58) IQR	38.49 ± 9.41				
Age at implantation (mean/median)		3.08 (2.54 - 3.49) IQR	16.58 (13.25 - 26.66) IQR	39.92 ± 9.45				
Duration of hearing loss (mean±SD)		3.5 ± 4.26	8.5 ± 9.93	6.93 ± 6.06				

Table II. Summary statistics for cochlear implant recipients (pre-operative unaided and aided pure tone average thresholds, age data and time intervals) for the overall group and subgroups.

Variables	Post-lingual Adults (>18yrs)	HIV+ adults	HIV – adults	TB-related hearing loss	Non-TB related hearing loss
Left ear CNC score (%): Adults (Median & IQR)	19 (25)*	8 (6)†	30 (12)‡	5 (6)§	30 (19)‖
Right ear CNC score (%): Adults (Median & IQR)	10 (13)*	7 (18)†	10 (12)‡	7 (12)§	14 (13)‖
Left ear CID sentence score (%): Adults (Median & IQR)	14 (11)*	12 (13)†	23 (21)‡	12 (7)§	17 (11)‖
Right ear CID sentence score (%): Adults (Median & IQR)	17 (13)*	23 (20)†	14 (6)‡	17 (12)§	16 (14)‖

(*) Frequency of scoring 0% for all tests (n = 212) in post-lingual adult group was 69,3% (n=147 tests); Frequency of "CNT" entries in this category was 18,4% (n=39 tests); Frequency of tests scoring >0% was 12.3% (n=26 tests).

(†) Frequency of scoring 0% for all tests (n= 148) in HIV + adults was 74,3% (n=110 tests); Frequency of "CNT" entries in this category was 13,5% (n=20 tests); Frequency of tests scoring >0% was 12,1% (n=18 tests).

(‡) Frequency of scoring 0% for all tests (n=64) in HIV negative adults was 57,8% (n=37 tests); Frequency of "CNT" entries was 29,7% (n=19 tests); Frequency of tests scoring >0% was 12,5% (n=8 tests).

(§) Frequency of scoring 0% for all tests (n=124) in adults with TB related hearing loss was 80,6% (n=100 tests); Frequency of "CNT" entries was 9,7% (n=12 tests); Frequency of scoring >0% was 9,7% (n=12 tests).

(‖) Frequency of scoring 0% for all tests (n=88) in adults with non-TB related hearing loss was 53,4% (n=47 tests); Frequency of "CNT" entries was 30,7% (n=27 tests); Frequency of scoring >0% was 15,9% (n=14 tests).

Table III. Pre-operative speech discrimination data for all adult implant recipients and per adult HIV and TB subgroups.

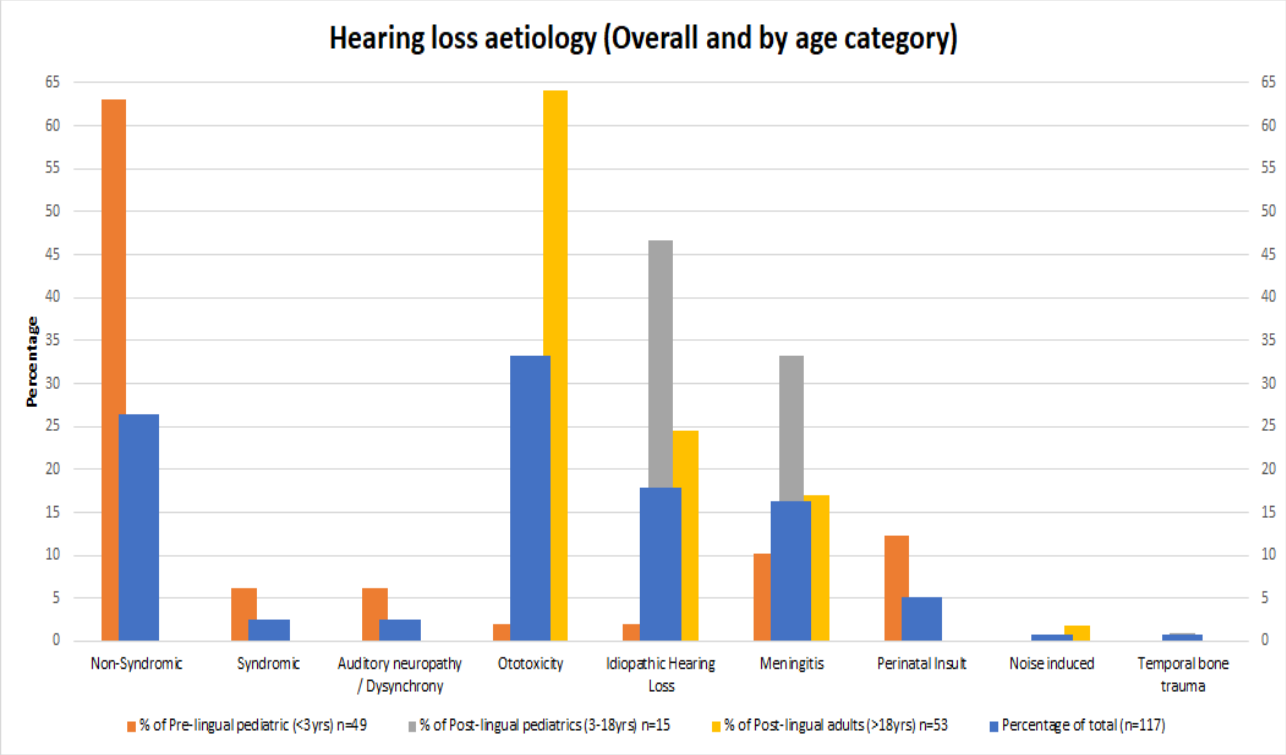


Figure I. Hearing loss aetiology (overall and by age category).

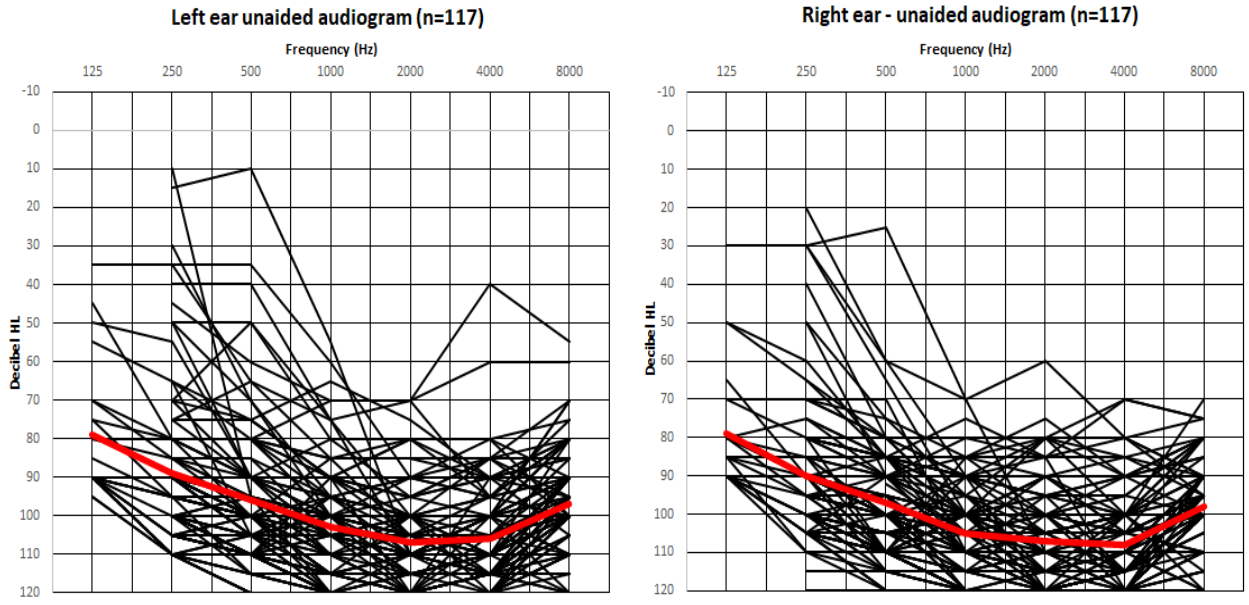


Figure II. Pre-operative unaided audiometric thresholds for the left and right ears of all (n=117) cochlear implant recipients, mean thresholds highlighted (in red).

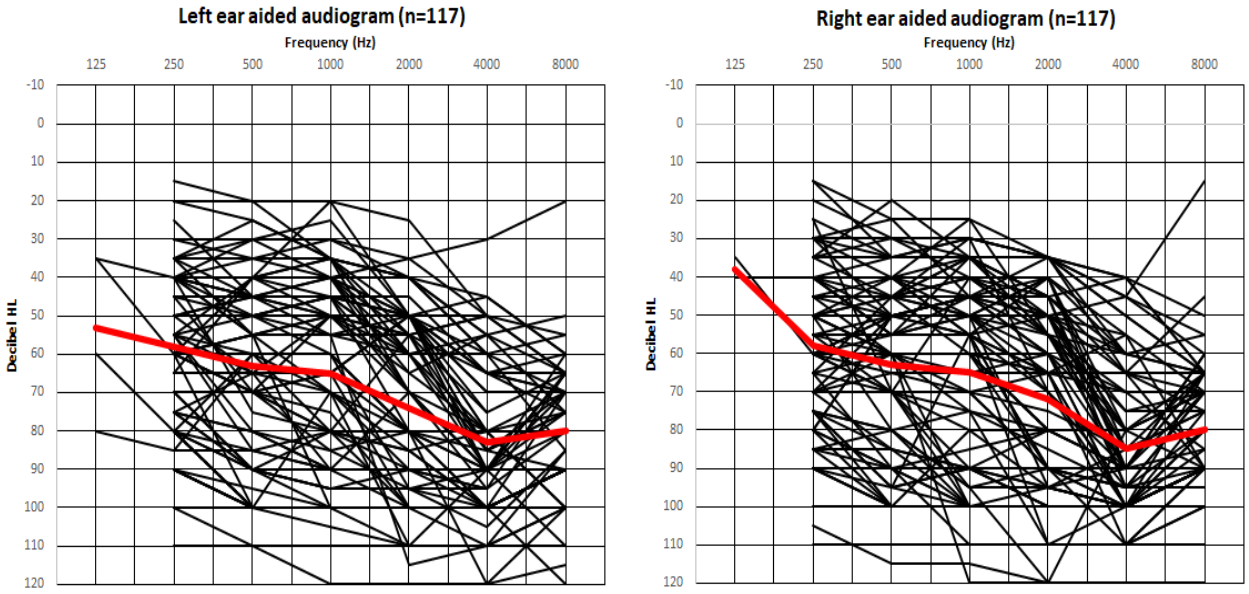


Figure III. Pre-operative aided audiometric thresholds for the left and right ears of all (n=117) cochlear implant recipients, mean aided thresholds highlighted (in red).

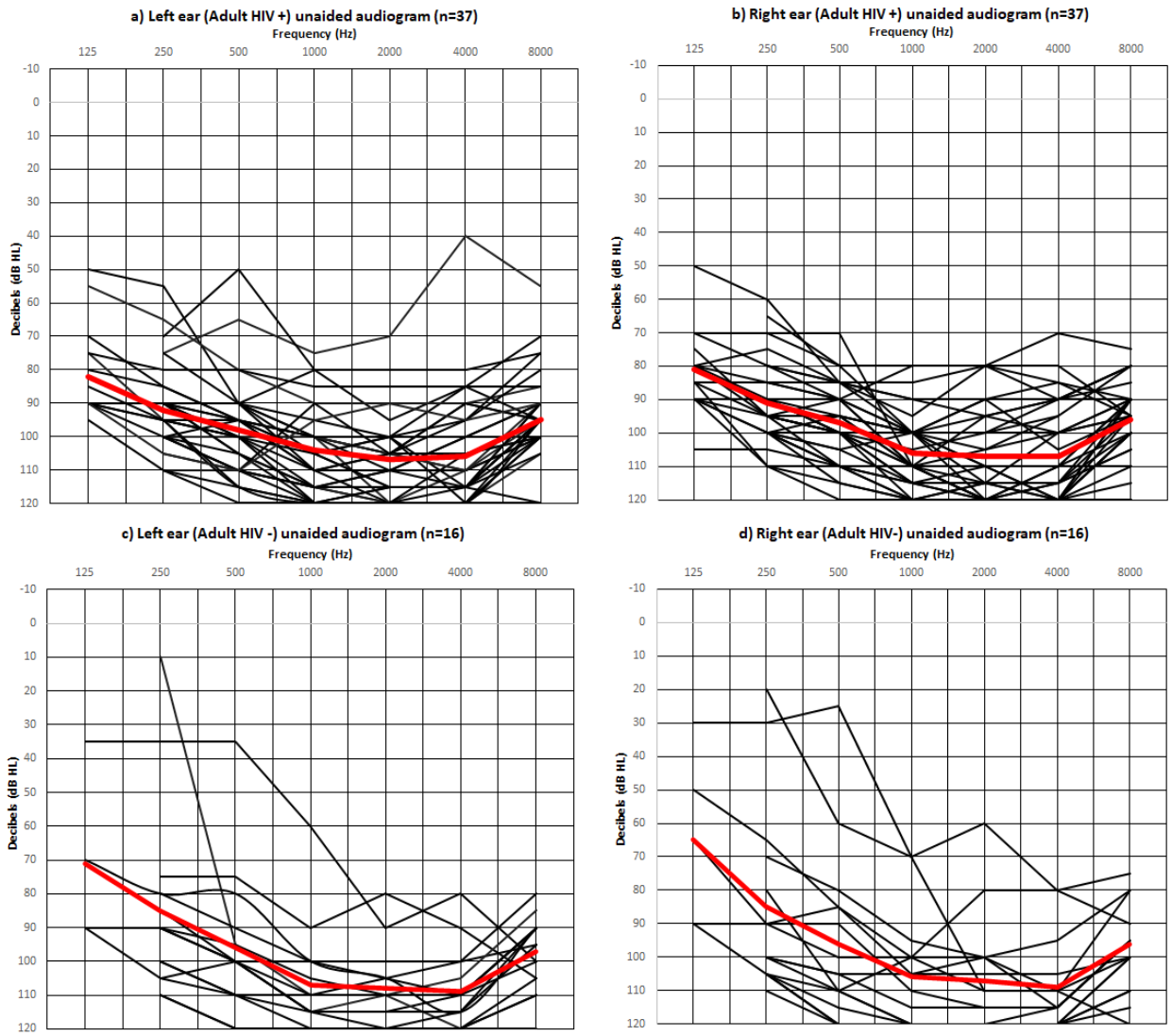


Figure IV. Pre-operative unaided audiometric thresholds for the left and right ears of recipients with human immunodeficiency virus (HIV+)[a & b] and recipients without (HIV-) [c & d] adult implant recipients, with mean threshold highlighted (in red).

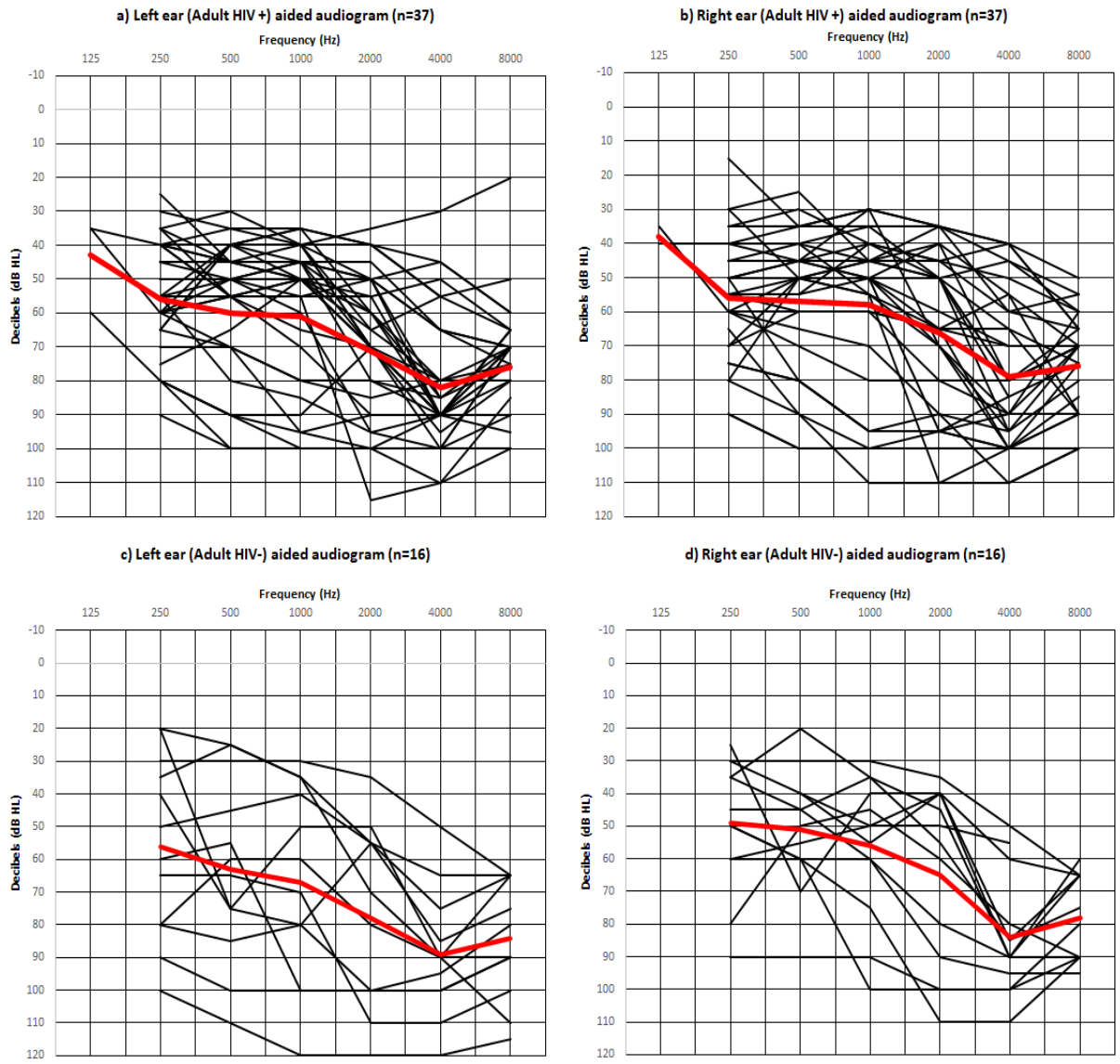


Figure V. Pre-operative aided audiometric thresholds for the left and right ears of recipients with human immunodeficiency virus (HIV+)[a & b] and recipients without (HIV-) [c & d] adult implant recipients, with mean threshold highlighted (in red).

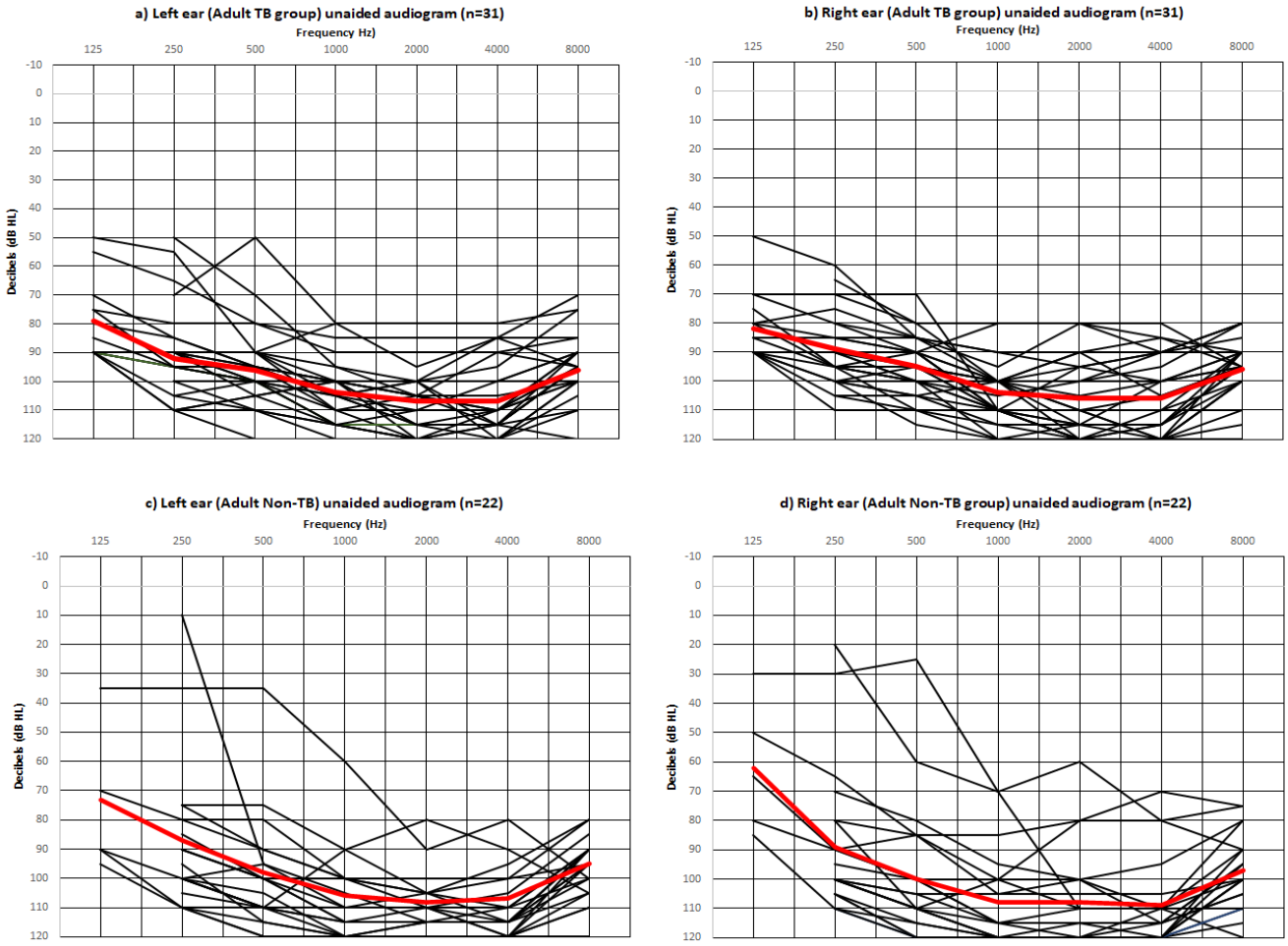


Figure VI. Pre-operative unaided thresholds for the left and right ear of adult implant recipients with tuberculosis (TB) related ototoxicity (a & b), and adult recipients with non-tuberculosis (non-TB) related hearing loss (c &d). The mean thresholds are highlighted red.

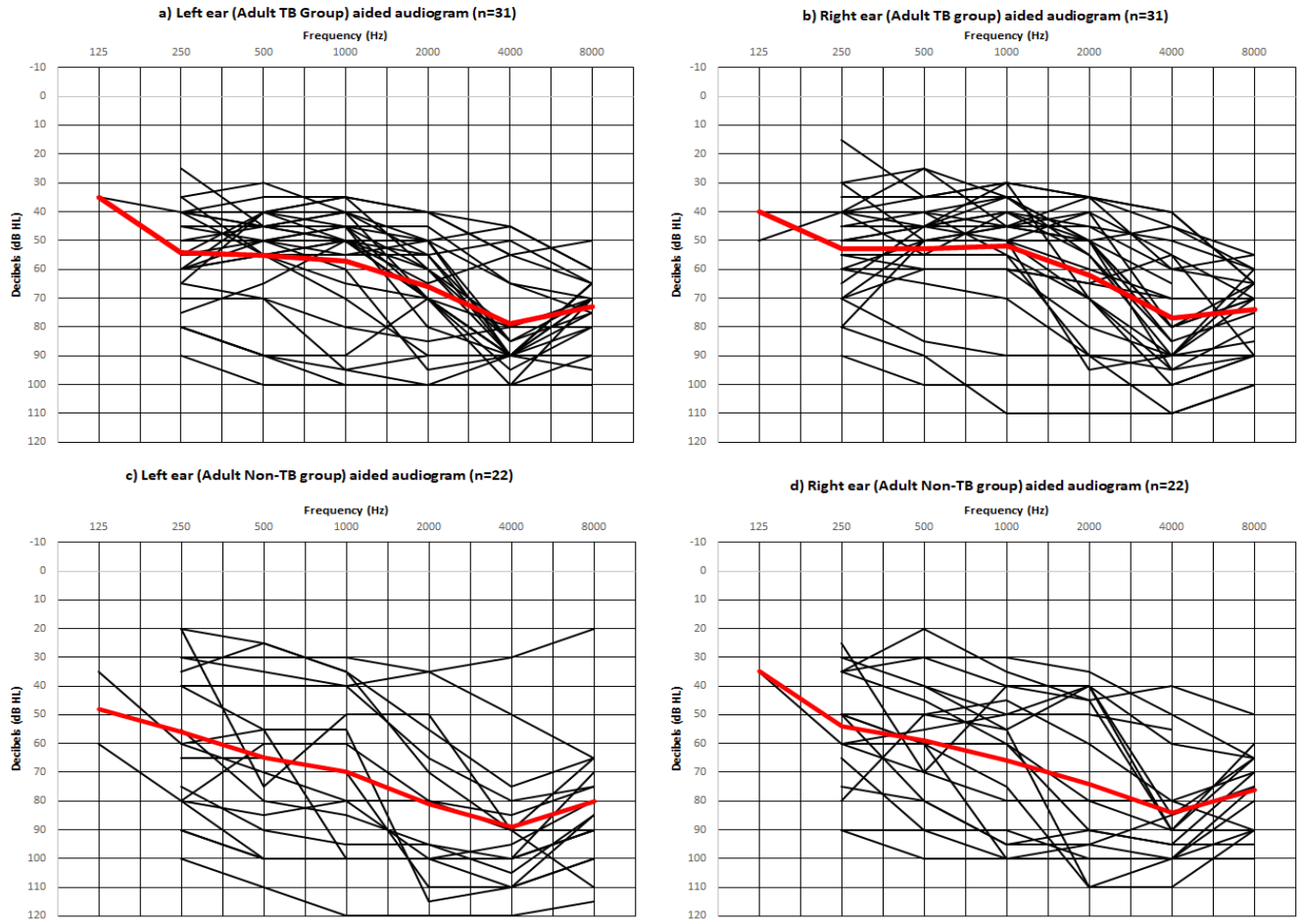


Figure VII. Pre-operative aided thresholds for the left and right ear of adult implant recipients with tuberculosis (TB) related ototoxicity (a & b), and adult recipients with non-tuberculosis (non-TB) related hearing loss (c &d). The mean thresholds are highlighted red.

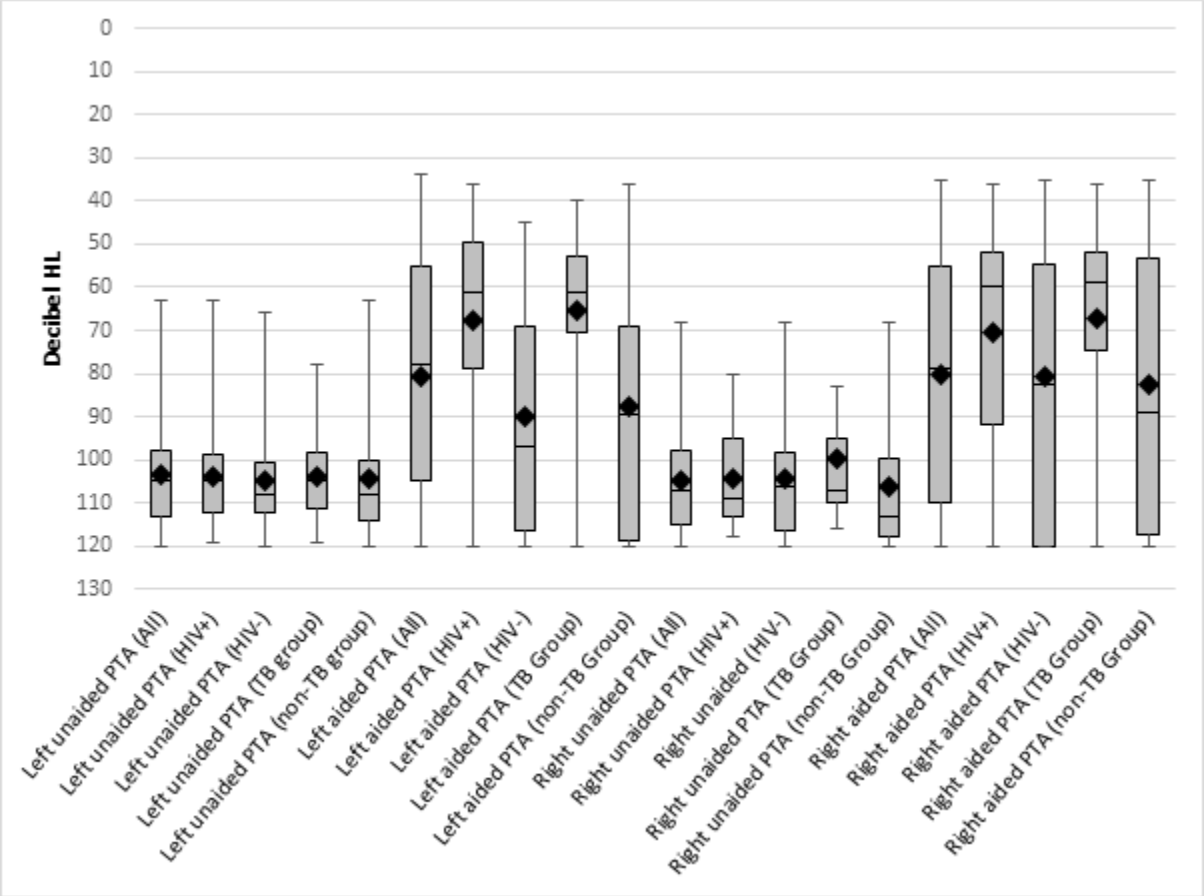


Figure VIII. Pre-operative pure tone average (PTA) boxplots for cochlear implant recipients (both left ear unaided & aided PTA's and right ear unaided & aided PTA's) of overall group, human immunodeficiency virus (HIV) and tuberculosis (TB) subgroups (the mean PTA is depicted by a diamond marker).

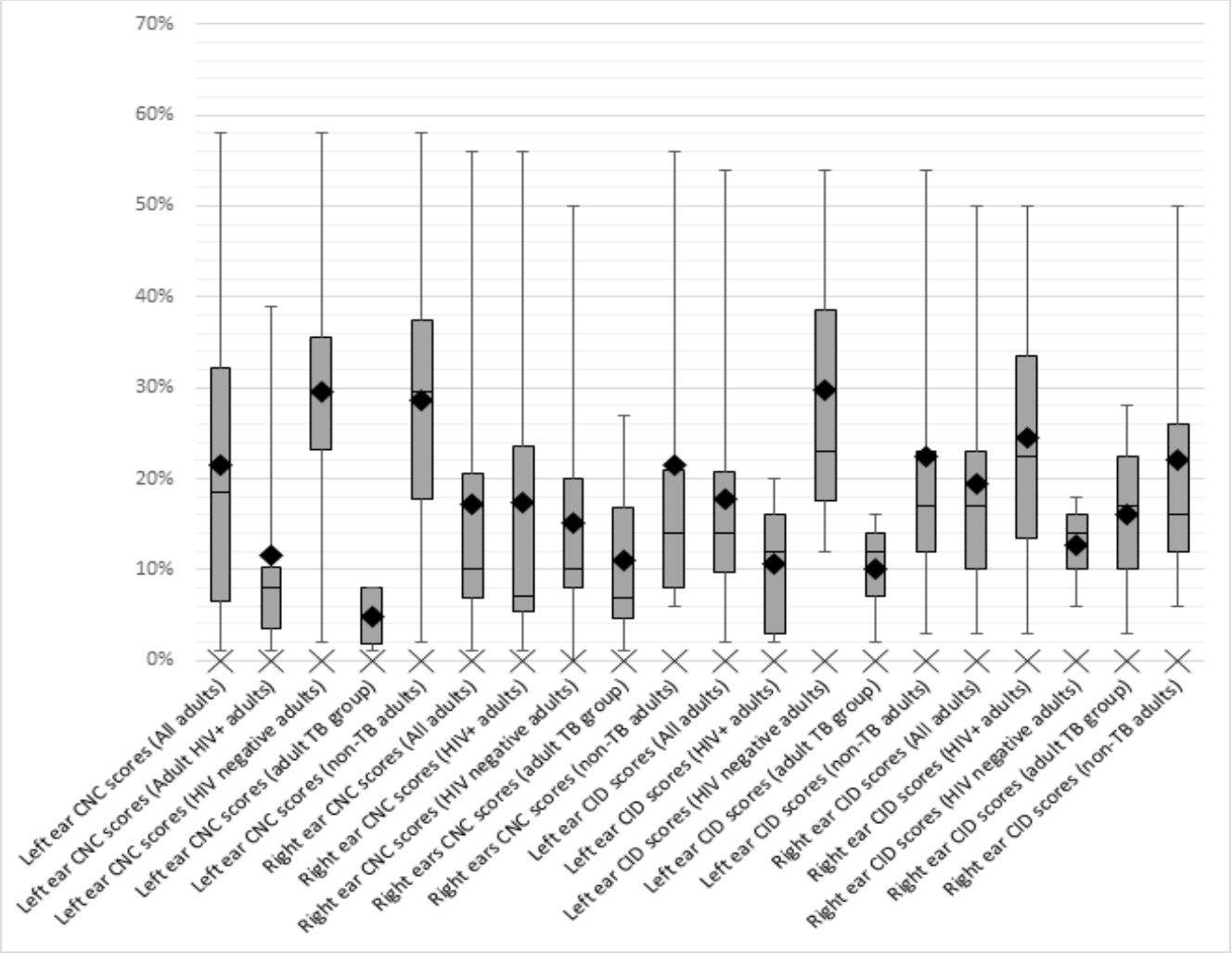


Figure XI. Boxplots for pre-operative consonant-nucleus-consonant (CNC) word scores and Central Institute of the Deaf (CID) sentence scores (in quiet) for post-lingually deafened adult implant recipients and respective sub-groups. The annotation X on the 0% line is to demonstrate that the lowest score possible was 0% (which accounted for a significant majority of tests). Mean % depicted by the diamond marker.

Appendix A

APPROVED PROTOCOL

A protocol in planning for a Research Report (NEUS7009) in part fulfilment towards the degree of Master of Medicine in Otorhinolaryngology, university code MFOSENTS60.

Candidate:

Dr Michael Gustaf van Aardt

Student number:

0303373J

Supervisor:

Dr Yahya Atiya

Division:
OTORHINOLARYNGOLOGY-HEAD NECK SURGERY

Department: Neurosciences
School of Clinical Medicine
Faculty of Health Sciences
University of the Witwatersrand. Johannesburg

TITLE:

A retrospective review of Cochlear implants at Chris Hani Baragwanath Hospital since 2006.

1. Literature review

Cochlear implantation has progressed from an experimental procedure over the past 30 years to become accepted as the standard of care for profound hearing loss.[1] The wide-ranging spectrum of effects of cochlear implantation not only impacts on hearing outcomes and speech perception but spans communication, psychosocial & cognitive outcomes as well as having significant impact on the quality of life and economic outcomes.

Cochlear implants are the most successful neural prosthesis to date, and by 2011 more than 220 000 patients had been implanted worldwide.[2] As the benefits of cochlear implantation have grown, the candidacy for implantation has expanded and become more inclusive.[3]

Therefore, as the Cochlear implant team at Chris Hani Baragwanath Hospital reaches an important milestone since the inception of its program, the process of reviewing these 100 patients will be important. South Africa is faced with unique challenges, the availability of funds and inequality with regards to access to health care. Within these restrictions, cochlear implant candidates in South Africa's public health sector would need to understandably undergo a far more rigorous selection process to gain access to funding (if available) for this limited resource, compared with first world cochlear implant candidates.

1.1. Prevalence

The scope of hearing loss worldwide is remarkably under-appreciated. The WHO in 2012 (updated Feb 2017) estimated that 5% (360 million) of the world's population have disabling hearing loss, defined as >40 dB in the better-hearing ear in adults (>15 years) and >30 dB in children (0 - 14 years). Adults make up the majority, accounting for 91% (M:F ~ 1.26:1) and children the remaining 9%. The prevalence is the highest in South Asia, Asia Pacific and Sub-Saharan Africa.[4]

The majority of these patients suffer from mild to moderate (25-55dB) hearing loss and patients with severe to profound (>70dB) hearing loss account for less than 10%.[5]

Unfortunately, due to poor screening and under-resourced, understaffed, and outdated ENT, audiology, and speech therapy services as well as limited patient access to health care in these subcontinents, the figures might well be underestimating the true scope of the problem. A survey conducted in 2009 into the status of ENT related services in sub-Saharan Africa, revealed that even though hearing disability ranks 3rd on the list of non-fatal disabling conditions in low and middle-income countries, these problems receive scant attention when discussing global health challenges which tend to focus more on communicable diseases.[6]

This was also despite evidence that apart from individual biopsychosocial effects, hearing loss substantially affects social and economic development in communities and countries.[7]

It is estimated that 718 000 infants are either born annually with, or acquire early-onset, permanent bilateral hearing impairment.[8] To date no large-scale systematic new-born or infant hearing screening programs have been conducted to determine the true prevalence of infant hearing loss in South Africa. The extent of infant hearing loss can however be estimated using reported prevalence rates for developing countries (6/1000 live births)[9].

Likewise, the true prevalence of adult hearing loss in South Africa is not known, due to lack of adequate screening and under-reporting.

1.2. Aetiology and indications

The aetiology of paediatric and adult hearing loss is extensive, and the exact prevalence of each specific cause is difficult to determine. This in part due to a large proportion of cases being idiopathic, or unknown. A recent meta-analysis review looking at the prevalence of various aetiologies among cochlear implant recipients found that 69% of the studies fail to mention a detailed description of the evaluation of the aetiology of hearing loss and had higher proportions of patients with idiopathic or unknown causes.[3]

Apart from a few specific aetiological causes of hearing loss (e.g., cochlea agenesis, absent vestibulocochlear nerve etc.) that would be contra-indications for cochlear implants, the other causes are not likely to influence the decision to implant. More important determinants are the degree of hearing loss and whether there is benefit from conventional hearing aids, general medical conditions that would preclude surgery and patient / parent expectations and motivation as well as social support structures.

Figure 1 lists the various aetiologies of sensorineural hearing loss that could be an indication for cochlear implantation.

These aetiologies can result in profound sensorineural hearing loss that manifests in either prelingual or post-lingual deafness.

The main indication for cochlear implantation is bilateral profound sensorineural hearing loss, but the list of indications has since expanded to include:

- Unilateral hearing loss.
- Tinnitus suppression[10].
- High frequency hearing loss with residual low frequency hearing[11].

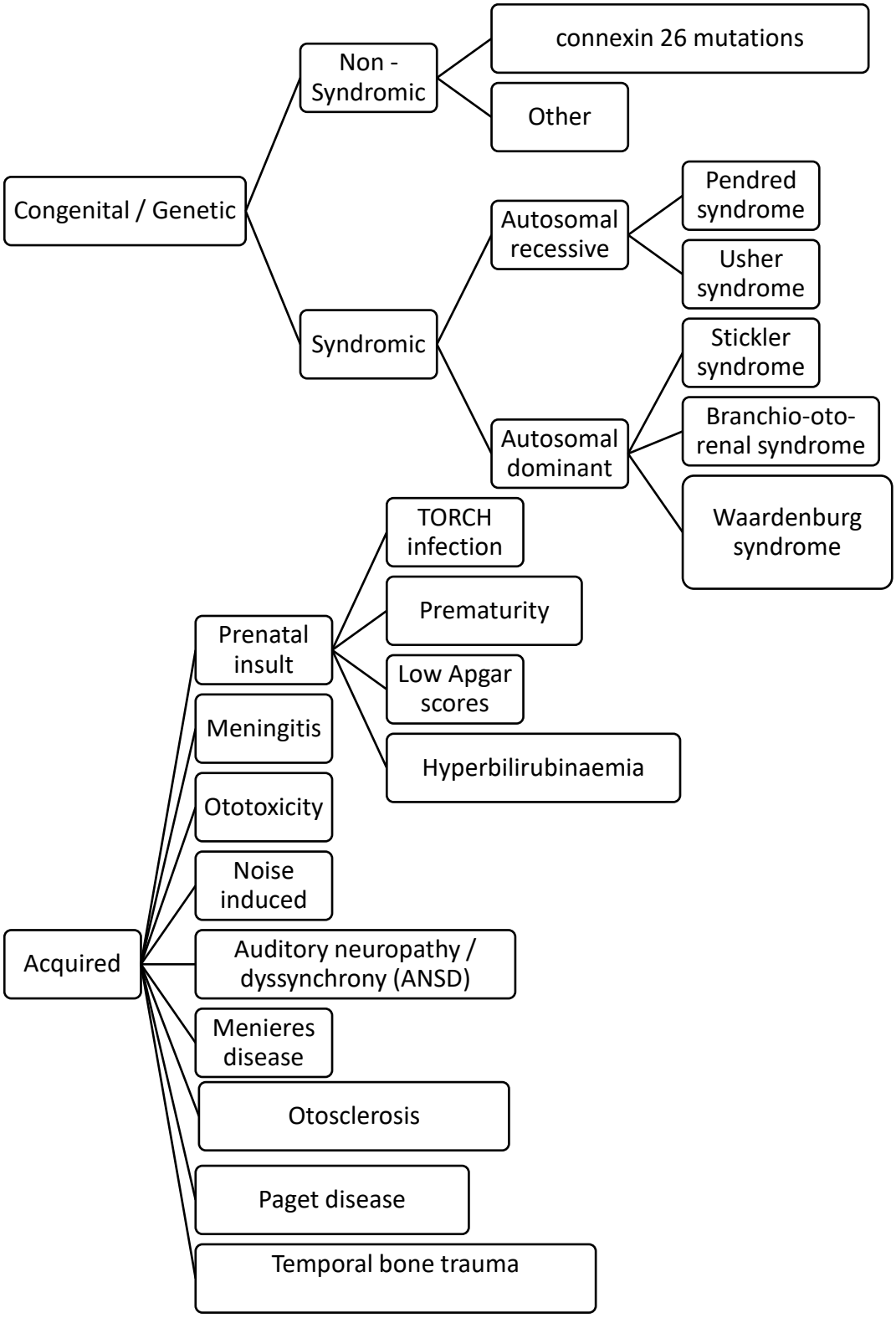


Figure 1

1.3. The Role of HIV

South Africa faces the largest HIV epidemic in the world, accounting for 19% of the global number of people living with HIV, 15% of new infections and 11% of AIDS related deaths.[12]

In 2016, South Africa had 270 000 (240 000 - 290 000) new HIV infections and 110 000 (88 000 - 140 000) AIDS-related deaths. There were 7 100 000 (6 400 000 - 7 800 000) people living with HIV in 2016, among whom 56% (50% - 61%) were accessing antiretroviral therapy. Among pregnant women living with HIV, >95% (76% - >95%) were accessing treatment or prophylaxis to prevent transmission of HIV to their children. An estimated 12 000 (9600 - 22 000) children were newly infected with HIV due to mother-to-child transmission. Among people living with HIV, approximately 45% (41% - 50%) had suppressed viral loads.[12]

South Africa has the largest treatment programme for HIV in the world, accounting for 20% of people on antiretroviral therapy globally. The country also has one of the largest domestically funded programmes, with about 80% of the AIDS response funded by the government.[12]

Although evidence suggests that hearing loss is more prevalent in HIV infected individuals compared to patients that are HIV negative, more research is needed to assess the aetiology of hearing loss in relation to HIV. There also seems to be a considerable paucity of evidence whether antiretroviral drugs are associated with hearing loss.[13]

Linked to the HIV epidemic, the incidence of MDR Tuberculosis infections is high in South Africa, with the current WHO guidelines on 2nd line treatment being injectable aminoglycosides known to be nephro- and ototoxic; 57% of these patients develop high-frequency hearing loss. HIV-positive patients (70%) are more likely to develop hearing loss than HIV-negative patients (42%).[14]

1.4. Economics

There is considerable evidence in the literature that cochlear implant outcomes are good in terms of hearing outcomes and improved sound localization as well as improved quality of life in adult cochlear implant patients.[15] Outcome literature for paediatric patients is even more compelling, especially if implanted at an earlier age with greater gains in speech perception with no plateau over time.[16]

Cost analysis studies have also shown that cochlear implants in adults and paediatric patients, are cost effective, and result in a nett savings in society.[17 & 18]

It must be remembered however that most of these cost analyses were done in first world /developed countries and may not be applicable to developing countries. The costs are sometimes considered from a 3rd party perspective (e.g., medical insurance), or society without considering the costs incurred by individuals who were implanted. In developing countries like South Africa, where the majority of the population access public health care, the prioritization of basic health services and communicable diseases take precedence over highly specialized rehabilitation procedures and implants. A cost analysis study conducted in South Africa took this into consideration, and found that significant costs are involved. Aside from the cost of the implant, maintenance and replacement of consumables as well as transport costs and extended rehabilitation by speech therapy and audiology can place a considerable burden on families and individuals who will have to bear the costs unless otherwise financially assisted by private or government funding.[19]

1.5. **Background of Cochlear implants at Chris Hani Baragwanath Hospital and Patient criteria for implantation**:

The cochlear implant programme was initiated in 2006, one of a few programs in South Africa and the only program that is completely state-funded.

Apart from audiological criteria, all patients need to fulfil certain requirements in order to be a cochlear implant candidate.

As alluded to earlier, this is necessary to best allocate scarce resources to patients that are likely to benefit the most from the implant, as well as those who have the financial and social support structures in place for ongoing maintenance and care for the device.

Appendix B - provides all patient selection criteria for adult and paediatric population groups.

2. Research question:

What are the causes of hearing loss in patients receiving cochlear implants in South Africa, how does the cause of hearing loss influence the decision to implant, and how does it differ from cochlear implant programmes in developed countries?

3. Aims and Objectives

- To determine the aetiology of hearing loss in cochlear implant patients at CHBAH
- To determine associated co-morbidities in these patients
- To compare indications to those elsewhere in the world.
- To describe the patient demographics of cochlear implant recipients.

4. Materials & Methods

4.1 Study design

Retrospective chart review.

4.2 Study location

The site will be the Chris Hani Baragwanath Academic Hospital ENT department. This is the third largest hospital in the world, and the largest in Africa, servicing an impoverished community, as well as accepting referrals from sub-Saharan Africa. The cochlear implant program is the largest of its kind in South Africa, and the only one that is completely State-funded.

4.3 Study population

All patients who received cochlear implantation at Chris Hani Baragwanath Hospital, since its inception in 2006.

4.3.1 Inclusion criteria:

All patients in the study population will be included in this study.

4.3.2 Exclusion criteria:

Patients with incomplete recorded data.

4.4 Data collection

Records will be reviewed with permission from the following departments.

- Outpatient records for Otorhinolaryngology Department of Chris Hani Baragwanath Hospital.
- Audiology department at Chris Hani Baragwanath Hospital.

The list of patients who have already undergone implantation will be selected and their relevant files will be retrieved and reviewed.

These patients will be subdivided into:

- Adult (>18yrs).
- Paediatric (<18yrs).

The following data will be recorded for each patient:

- Age (at implantation).
- Sex.
- Ethnic background.
- Age at onset of hearing loss.
- Inciting events and aetiology of hearing loss.
- HIV status.
- Exposure to Ototoxic Tuberculosis treatment.

All data will be recorded electronically using Microsoft Access & Excel.

4.5 **Data analysis and presentation:**

- Data will be stored and analysed using Microsoft Access 2010 and Microsoft Excel 2010 will be used for descriptive analysis summary statistics and comparison of sample means.
- Microsoft Word 2010 will be used for the write up of the final report.
- Categorical data will be assessed using a Chi-squared test, and Fischer's exact test will be utilized if the assumptions of frequencies are not met.
- Continuous data will be analysed using a one-way ANOVA and if the assumptions are not satisfied a Kruskal-Wallis test will be used.
- A p (probability) value less than or equal to 0.05 will be considered significant.

4.6 **Ethics Approval**

Ethics approval will be obtained from the Human Research and Ethics Council of the University of the Witwatersrand. As this is a retrospective chart review, no informed consent is required.

4.7 **Timing**

	July	**Aug**	**Sept**	**Oct**	**Nov**	**Dec**	**Jan**	**Feb**	**Mar**	**Apr**	**May**	**June**
Literature review												

Preparing protocol											
Protocol assessment											
Ethics application											
Collecting data											
Data analysis											
Writing up											

4.8 **Funding**

No significant costs are expected to be incurred in this study. The minimal costs (approx. R500.00) associated with printing and binding, will be borne by the principle investigator.

5 Limitations

- As this is a retrospective study, there are possible limitations inherent with this type of study design (e.g., selection bias, confounding variables).
- Inadequate or missing patient records.
- Small sample size.

6 Dissemination of findings

The aim is to submit the results to an international peer-reviewed journal for publication.

The findings will also be made available to the University of the Witwatersrand.

7 References:

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7 Jamison, D. (2006). Disease control priorities in developing countries. New York: Oxford University Press. Chapter 50.

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8 Appendix A – Data Collection Sheet

Study No:	
Age (at implantation):	
Gender:	Male
	Female
Ethnic Background	Black
	White
	Indian
	Coloured
Age at onset of hearing loss:	<2yrs
	2 – 10yrs
	11-20yrs
	21-40yrs
	41-60yrs
	>60yrs
Aetiology of hearing loss	Congenital (with further subdivisions)
	Acquired (with further subdivisions)
HIV status:	Positive
	Negative
Exposure to Ototoxic TB treatment	Yes
	No

9 Appendix B – Chris Hani Baragwanath Academic Hospital Cochlear Implant Criteria:

Criteria for adult patients:

1. Audiological criteria:
    a. Bilateral severe-profound hearing sensori-neural hearing loss at 2-4 kHz.
    b. And/or Aided thresholds of 55dB or worse at 2-4 kHz.
    c. And/or aided speech perception scores (with optimally fitted hearing aid) of less than 50%.
2. Duration of hearing loss and hearing aid use:
    a. Post-lingual deafened adult with less than 10 years of hearing loss.
    b. Or post-lingual deafened adult with over 10 years of hearing loss if there has been consistent use of hearing aids and testing shows evidence of some speech discrimination with hearing aids.
    c. Or adults with congenital hearing loss who have had consistent use of hearing aids and evidence of some speech discrimination with hearing aids, who communicate verbally as the primary mode of communication.
3. Other criteria:
    a. Communication mode is verbal.
    b. Eager to be part of hearing world.
    c. Eager to take part in work place/school.
    d. Skills for employment.
    e. Any psychiatric conditions to be well controlled.
    f. Realistic expectations.
    g. Financial means to attend appointments and support maintenance of cochlear implant (family member to assist / use of social grant with the aim of accessing work to support self over time).

4. Other considerations:
    a. Radiological imaging should suggest that auditory nerve and cochlear anatomy are likely to support full insertion of the cochlear implant and transmission of auditory signal to the brain.

b. For HIV positive patients – viral load must be undetectable.
c. For patients with TB-related hearing loss – must have completed TB treatment and test negative to TB.
d. No additional medical or surgical concerns that contraindicate surgery.
e. Psychological assessment should suggest patient and family are appropriate candidates for a CI.
f. Where required, an OT vocational assessment may be required to determine ability to return to work.

Criteria for paediatric patients:

1. Audiological criteria:
    a. Bilateral severe-profound sensori-neural hearing loss.
    b. Or aided thresholds of 55dB or worse at 2-4 kHz.
    c. Or for children with ANSD criteria will not depend on thresholds but will be dependent on poor development of auditory skills despite consistent use of hearing aids and attendance at speech therapy regardless of auditory thresholds in the booth.
2. Age and hearing aid use:
    a. Children with congenital deafness and limited spoken language must be referred into the programme by 2 ½ years with the aim to implant the child by 3 years (sometimes stretches to closer to 3 ½ years in reality).
    b. Children with progressive or acquired hearing loss may be considered at any age on the condition that they have developed spoken language and present with speech discrimination skills and have worn hearing aids consistently since the onset of the hearing loss.
3. Other criteria:
    a. At least one family working or access to financial support to cope with transport and device maintenance.
    b. Access to appropriate educational setting.
    c. Parental (or caregiver's) commitment to bring child for therapy weekly.
    d. Realistic expectations of family members.
4. Other considerations:

a. Radiological imaging should suggest that auditory nerve and cochlear anatomy are likely to support full insertion of the cochlear implant and transmission of auditory signal to the brain.
b. For HIV positive patients – viral load must be undetectable.
c. For patients with TB-related hearing loss – must have completed TB treatment and test negative to TB.
d. No additional medical or surgical concerns that contraindicate surgery Psychological assessment should suggest patient and family are appropriate candidates for a CI.
e. Occupational therapy assessment must be completed and should indicate any red flags to consider that may impact on outcomes.

Appendix B – Ethics Clearance

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG	HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

Office of the Deputy Vice-Chancellor (Research & Post Graduate Affairs)

TO: Dr MG van Aardt
School of Clinical Medicine
Department of Medicine
Division of Otorhinolaryngology
Medical School
University

E-mail: mgvanaardt@gmail.com

CC: Supervisor: Dr Y Atiya <yatiya@gmailcom>
and <HREC-Medical.ResearchOffice@wits.ac.za>

FROM: Iain Burns
Human Research Ethics Committee (Medical)
Tel: 011 717 1252

E-mail: Iain.Burns@wits.ac.za

DATE: 2020/07/06

REF: *R14/49*

PROTOCOL NO: **M200158** *(This is your ethics application study reference number. Please quote this reference number in all correspondence relating to this study)*

PROJECT TITLE: *A retrospective review of Cochlear implants at Chris Hani Baragwanath Academic Hospital since 2006*

Please find attached the Clearance Certificate for the above project. I hope it goes well and that an article in a recognized publication comes out of it. This will reflect well on your professional standing and contribute to the Government funding of the University.



MSWorks2000/Iain0007/Clearscan.wps

UNIVERSITY OF THE
WITWATERSRAND,
JOHANNESBURG

R14/49 Dr MG van Aardt

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M200158

NAME: (Principal Investigator)	Dr MG van Aardt
DEPARTMENT:	School of Clinical Medicine Department of Medicine Division of Otorhinolaryngology Medical School University
PROJECT TITLE:	A retrospective review of Cochlear implants at Chris Hani Baragwanath Academic Hospital since 2006
DATE CONSIDERED:	2020/01/31
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Y Atiya
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	2020/07/06

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

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the 3rd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to submit details to the Committee. **I agree to submit a yearly progress report**. When a funder requires annual re-certification, the application date will be one year after the date when the study was initially reviewed. In this case, the study was initially reviewed in **January** and will therefore reports and re-certification will be due early in the month of **January** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

Date

Appendix C – Author guidelines for the Journal of Laryngology and Otology

All manuscripts are considered for publication on the understanding that they have been submitted solely to this Journal and that they have not previously been published. Both paper and electronic submissions are allowed.

Electronic submissions should be sent to the Editors via **ScholarOne Manuscripts**. Manuscripts submitted through our online system should not also be submitted by mail.

Please note that the journal uses software to screen papers where there is reason to believe that material may not be original. By submitting your paper, you are agreeing to any necessary originality checks your paper may have to undergo during the peer review and production processes.

Authors should note that the editors may choose to publish accepted material in both paper and electronic formats or in electronic format only. Paper submissions may also be shortened, at the Editor's discretion, with the full text version available in electronic format only.

Non-native English speakers are asked to check their manuscript with a native English speaker prior to submission.

The following will be considered:

Main Articles: These should report clinical research or audit and should not normally exceed 7500 words. Review Articles and Historical Articles will also be considered but should not exceed 3000 words unless specifically commissioned. Longer articles or theses will be considered for publication as Supplements but the authors will normally be expected to meet the costs of publication.

Clinical Records (Case Reports): These should be no more than 1500 words, with four authors as a maximum. To be accepted for publication case reports must convey a clinical message of exceptional value. Articles merely reporting cases of rare pathology are very unlikely to be deemed acceptable for publication. The search strategy used must be detailed.

Short Communications: These should be articles illustrating surgical technique or the use of technical innovation. As with Clinical Records the manuscript should not exceed 1500 words and should have a maximum of four authors. Articles should be clearly illustrated with line art from a laser printer. Cross-hatching is allowed: do not use grey-tints.

Authorship: Authorship credit should be based on criteria established by the International Committee of Medical Journal Editors (ICMJE): (1) substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; (2) acknowledgement of drafting the article or revising it critically for important intellectual content; (3) final approval of the version to be published; and (4) agreement to be accountable for all aspects of the work in

ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Each author must meet all four conditions, and all authors should agree on author order and contributions before submitting the manuscript.

- The corresponding author will confirm authorship contributions, funding, and conflict(s) of interest as part of the submission process.
- All authors must sign a cover letter to indicate that they have read and approved the paper. The cover letter should also indicate the contribution of each author to the data collection and analysis, and drafting or revision of the paper.
- The journal will allow joint first authorship (no more than 2 joint first authors) only in cases where this is clearly justified. Shared co-first authorship is defined as two or more authors who have worked together on a publication and contributed equally. Joint first authors must be identified with an asterisk in the affiliations and denoted 'Equal first authors' at the end of the author listing on the title page of the manuscript.
- In the case of joint first authors, authors should outline in their cover letter the contributions of the two individuals referring to the CREDiT (Contributor Roles Taxonomy) nomenclature: please refer to**https://casrai.org/credit/**. CRediT contributor roles are defined as follows: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Roles/Writing – original draft; Writing – review and editing.
- Any changes to the author list after submission, such as a change in the order of the authors or the deletion or addition of authors, must be approved by every author. To request such a change, the corresponding author should write to the journal editors giving the reason for the change in the author listing, and provide written confirmation (e-mail, or letter) from all authors that they agree with the proposed addition, removal or rearrangement. In the case of the addition or removal of authors, the editors require written confirmation from the author being added or removed. Only in exceptional circumstances will the editors consider the addition, deletion or rearrangement of authors after a manuscript has been accepted.

The following instructions should be observed or the manuscript may be returned:

Each manuscript should be divided into sections on separate pages. These should be: title page, structured abstract and key words, text, acknowledgements, references, summary and tables. All text must be double spaced and should be typed in a 12 point font.

Illustrations should be separately appended. Written permission from the publisher to reproduce any material with copyright elsewhere must be obtained prior to submission.

Title page: This should contain (a) a title; (b) the names of all authors together with their principal higher qualification(s) and details of their departments or affiliated institution(s); (c) the name and address of the author responsible for correspondence. If the paper was presented at a meeting, the details must be given. **The numbers of authors must be commensurate with the complexity of the submitted material. A fax number and e-mail address must be provided and will be used for correspondence.**

Abstract and key words: The abstract should be no longer than 150 words and should be structured. Key Words are used to index the article. Only the words appearing as Medical Subject Headings (MeSH) in the supplement to *Index Medicus* may ordinarily be used. These are also available at **http://www.nlm.nih.gov/mesh/meshhome.html**

Text: Main articles should contain the following headings: Introduction, Materials and methods, Results and analysis (including statistical analysis) and Discussion.

Clinical Records and other submissions should normally comprise Introduction, Case report and a brief Discussion.In all cases the Discussion should clearly indicate how the reported work fits with the current body of world literature. The text should be grammar and spell checked prior to submission. All measurements must normally be reported in metric units. Only approved drug names should be used.

Acknowledgements: You may acknowledge individuals or organisations that provided advice, support (non-financial). Formal financial support and funding should be listed in the following section.

Financial Support: Please provide details of the sources of financial support, including grant numbers, for all authors. For example, "This work was supported by the Medical Research Council (grant number XXXXXXX)". Multiple grant numbers should be separated by a comma and space, and where research was funded by more than one agency the different agencies should be separated by a semi-colon, with "and" before the final funder. Grants held by different authors should be identified as belonging to individual authors by the authors' initials. For example, "This work was supported by the Wellcome Trust (A.B., grant numbers XXXX, YYYY), (C.D., grant number ZZZZ); the Natural Environment Research Council (E.F., grant number FFFF); and the National Institutes of Health (A.B., grant number GGGG), (E.F., grant number HHHH)". Where no specific funding has been provided for research, please provide the following statement: "This research received no specific grant from any funding agency, commercial or not-for-profit sectors."

Ethical Standards: Where research involves human and/or animal experimentation, the following statements should be included (as applicable): "The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional guidelines on human experimentation (please name) and with the Helsinki Declaration of 1975, as revised in 2008." and "The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional guides on the care and use of laboratory animals (please name)."

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- Ghosh S, Panarese A, Parker AJ. Modified technique for introduction of Gröningen speech valves. *J Laryngol Otol* 2000;**144**(suppl 4):701–3

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- Xu J, Gao C, He D, Zhang H, Ma C, Thou Y. Effect of septoplasty on the modality of inferior turbinate: a CT study [in Chinese]. *Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi* 2013;**27**:413–15
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- Watson JD, Crick FH. Molecular structure of nucleic acids; a structure for deoxyribose nucleic acid. *Nature*1953;**171**:737–8

Book:

- Oliver P, Martin DA. *Nutrition in Laboratory Mice*. New York: Macmillan, 1998
- Oliver P, Martin DA, eds. *Nutrition in Laboratory Mice*, 3rd edn. New York: Macmillan, 1998

Book Chapter:

- Smith DC, Jones AF. Vitamin A effects in laboratory mice. In: Oliver P, Martin DAF, eds. *Nutrition in Laboratory Mice*, 3rd edn. New York: Macmillan, 1983;130–42
- Smith DC, Jones AF. Vitamin A effects in laboratory mice. In: Oliver P, Martin DAF, eds. *Nutrition in Laboratory Mice*, 3rd edn. New York: Macmillan, 1983;**3**:130–201

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- Wilson DR, Torres LI, Durham SR. Sublingual immunotherapy for allergic rhinitis. Cochrane Database Syst Rev 2003;(2):CD002893

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Appendix D – Turnitin report.

