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PREDICTORS OF COCHLEAR IMPLANT OUTCOMES

IN SOUTH AFRICA

by

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PUBLICATIONS AND RESEARCH OUTPUTS

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1. **Le Roux, T**., Swanepoel, D., Louw, A., Vinck, B. & Tshifularo, M. (2015). Profound childhood hearing loss in a South African cohort: Risk profile, diagnosis and age of intervention. *International Journal of Pediatric Otorhinolaryngology,* 79(1), 8-14. doi: 10.1016/j.ijporl.2014.09.033
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ABSTRACT

This research focused on the identification and description of predictors of pediatric and adult cochlear implantation outcomes in a South African cohort and the depiction of profound childhood hearing loss in terms of risk and intervention profiles.

Study I described profound childhood hearing loss in a South African cohort of pediatric cochlear implant (CI) recipients in terms of risk profile and age of diagnosis and intervention. A retrospective review of patient files for 264 pediatric CI recipients from five CI programs was conducted. For all subjects, permanent congenital and early onset hearing loss (PCEHL) was confirmed under the age of five years old.

The most prevalent risks for profound PCEHL were neonatal intesive care unit (NICU) admittance (28.1%), family history of childhood hearing loss (19.6%) and prematurity (15.1%). An associated syndrome was diagnosed in 10% of children and 23.5% had at least one additional developmental condition. Hearing loss for most (77.6%) children was confirmed as congenital or early onset, while 20.3% presented with postnatal onset of hearing loss. Auditory Neuropathy Spectrum Disorder (ANSD) was diagnosed in 5% of children, with admittance to NICU (80%) and hyperbilirubinemia (50%) being the most prevalent risk factors for these cases. Hearing loss was typically diagnosed late (15.3 months), resulting in delayed initial hearing aid fitting (18.8 months), enrollment in early intervention services (19.5 months), and eventual cochlear implantation (43.6 months). Delayed diagnosis and intervention predispose this population to poorer outcomes.

Study II identified and described predictors of pediatric cochlear implantation outcomes in a South African cohort. A retrospective study of 301 pediatric CI recipients from five CI programs, implanted between 1996 and 2013, was conducted. Cross-sectional outcome data were added at the time of data collection. Twenty potential prognostic factors were identified from the retrospective dataset, including biographical, CI, family and risk factors. Regression analyses were performed to identify predictor variables that influence outcomes in terms of auditory performance (CAP scores), speech production (SIR scores), communication mode and educational placement.

Although implanted children within this sample did not have equal opportunity to access a second implant, bilateral implantation was strongly predictive of better auditory performance and speech production scores, an oral mode of communication and mainstream education. NICU admittance and prematurity were associated with poorer auditory performance and speech production scores, together with a higher probability for non-oral communication and non-mainstream education. The presence of one or more additional developmental condition was predictive of poorer speech production and educational placement outcomes, while a delay between diagnosis and implantation of more than one year was also related to non-mainstream education. Ethnicities other than Caucasian were predictive of poorer auditory performance scores and a lower probability for mainstream education. An extensive range of prognostic indicators were identified for pediatric CI outcomes in South Africa. These predictive factors of better and poorer outcomes should guide pediatric CI services to promote optimal outcomes and assist professionals in providing evidence-based informational counselling.

Study III identified and described predictors of health-related quality of life (HRQoL) outcomes for adult CI recipients in a South African cohort. A retrospective study of 100 adult CI recipients from four CI programs, implanted between 1991 and 2013, was conducted. Cross-sectional HRQoL outcome data were added at the time of data-collection, using the Nijmegen Cochlear Implant Questionnaire (NCIQ). Twenty-two potential predictive factors were identified from the retrospective dataset, including demographic, hearing loss, CI and risk related factors. Multiple regression analyses were performed to identify predictor variables that influence HRQoL outcomes.

A range of significant prognostic indicators were identified for HRQoL outcomes in adult CI recipients. History of no tinnitus prior to CI, bilateral implantation and mainstream schooling were strongly predictive of better overall HRQoL outcomes. Other factors such as age, age at implant, gender, duration of CI use, onset of hearing loss and presence of risk factors did not predict HRQoL scores. This study contributed to a better understanding of factors influencing HRQoL outcomes enabling clinicians to provide evidence-based information counselling to adult CI patients and their families.

Findings from this research provide valuable guidance and understanding into the causes of variation of pediatric and adult CI outcomes in South Africa and provide further insight into the risk and intervention profiles of pediatric CI recipients specifically. With the vast majority of CI recipients in this study representing the private healthcare sector, research results cannot be generalized to the larger South African population. Irrespective, results of this research enable CI teams to plan appropriately for post-implantation intervention and provide evidence-based CI services that promote optimal outcomes.

KEYWORDS

Adult cochlear implantation

Auditory neuropathy

Profound hearing loss

Risk factors

Childhood hearing loss

Cochlear implant

Health-related quality of life

Hyperbilirubinemia

Intervention

Neonatal Intensive Care Unit

Nijmegen Cochlear Implant Questionnaire

Pediatric cochlear implantation

Prognostic factors

Outcomes

Quality of life

ABBREVIATIONS

ANSD	Auditory Neuropathy Spectrum Disorder
CAP	Categories of Auditory Performance
CI	Cochlear Implant
EHDI	Early Hearing Detection and Intervention
HL	Hearing Loss
HRQoL	Health-related Quality of Life
NCIQ	Nijmegen Cochlear Implant Questionnaire
NHS	Newborn Hearing Screening
NICU	Neonatal Intensive Care Unit
PCEHL	Permanent Congenital and Early Onset Hearing Loss
SNHL	Sensorineural Hearing Loss
SASL	South African Sign Language
SIR	Speech Intelligibility Rating
QoL	Quality of Life

CHAPTER 1
INTRODUCTION

1.1 Background

Profound hearing loss impairs the quality of life of individuals from all ages by relentlessly dismantling the machinery of human communication (O'Donoghue, 2013). Profound childhood hearing loss has far-reaching, lifelong consequences for children, including the lack of development of spoken language which results in restricted learning, literacy and educational achievements, as well as later employment opportunities (Kral & O'Donoghue, 2010; Mohr et al., 2000). Deafness in adulthood is associated with an increased risk of depression, poor health, dementia and unemployment (Gurgel et al., 2014; Kochkin & Rogin, 2000; O'Donoghue, 2013; Saito et al., 2010). Not only does profound hearing loss impose a social burden on individuals and families, but it also results in a considerable cost for both the individual and society (Mohr et al., 2000).

Cochlear implantation is considered as a well-established intervention for individuals with severe-profound sensorineural hearing loss (SNHL) who obtain insufficient benefit from acoustic amplification. More than 300 000 deaf individuals around the world, of whom 80 000 are children, have been given access to sound through cochlear implantation (Kral & O'Donoghue, 2011; O'Donoghue, 2013). Recent reports indicate that speech and language skills comparable to normal hearing children can be achieved in some pre-lingually deaf children implanted within the first year of life (T Ching et al., 2009; Niparko et al., 2010; Wie, 2010). For adults, improvement in audiological performance post implantation is well

documented and it is expected that most cochlear implant (CI) recipients will achieve some degree of open-set speech recognition with or without lip-reading (Hinderink, Krabbe, & Van Den Broek, 2000; Loeffler et al., 2010). Understandably, expectations for cochlear implantation are high. However, outcomes vary as multiple internal and external factors have the potential to affect clinical outcomes (Black, Hickson, Black, & Khan, 2014; Hawker et al., 2008). As a result many CI cases present with sub-optimal outcomes, which necessitates the need for accurate prognostic information. Pre-operative predictions of outcomes would enable clinicians to counsel caregivers or adult patients to such an extent that they will be able to make informed judgements of the benefits their children or themselves might receive from implantation (A. Summerfield & Marshall, 1995).

This chapter provides an overview of profound childhood hearing loss in South Africa and summarizes the current body of evidence on predictors of pediatric and adult CI outcomes. Also, the context for this research is described in the section on cochlear implantation in South Africa. Lastly, the rationale for this study is given, leading to three research questions.

1.2 Profound childhood hearing loss in South Africa

Worldwide, an estimated 798 000 children are annually born with permanent hearing loss or will develop early onset hearing loss, with at least 90% of these residing in developing countries (Olusanya, Wirz, & Luxon, 2008; Swanepoel, Storbeck, & Friedland, 2009). As a result almost 2000 infants with hearing loss are born daily in developing world regions (Swanepoel et al., 2009). Based on an estimated incidence of six per 1000 live births,

180 000 infants with permanent hearing loss are born annually in sub-Saharan Africa alone (Olusanya, 2008; Swanepoel & Storbeck, 2008).

The prevalence of profound hearing loss in developing regions is largely unknown with only a few previously reported estimates (Arslan & Genovese, 1996; Berruecos, 2000; A. Smith, 2008; Zeng, 1995). In the developed world it is estimated that between 20 and 30% of children with permanent childhood hearing loss have a profound degree of hearing loss (Kral & O'Donoghue, 2010). Even though comprehensive population studies for Africa do not exist, available reports suggest that the prevalence of profound hearing loss among African children with permanent childhood hearing loss is higher (Kral & O'Donoghue, 2010; Olusanya, 2008; Saunders & Barrs, 2011; Westerberg et al., 2008).

With newborn hearing screening (NHS) services being offered in only a few hospitals in both the public and private health care sectors, less than 10% of the more than one million babies born annually in South Africa will have the prospect of having their hearing screened (Meyer, Swanepoel, le Roux, & van der Linde, 2012; Theunissen & Swanepoel, 2008). As a result, the average age of hearing loss diagnosis in South Africa has been reported to be between 23 to 44.5 months (Butler et al., 2013; Swanepoel, Johl, & Pienaar, 2013; Van der Spuy & Pottas, 2008), in contrast to the recommended age of three months (Joint Committee on Infant Hearing, 2007). It is known that children with profound hearing losses are to be identified at earlier ages and enter early intervention services earlier than children with less severe degrees of hearing loss (Durieux-Smith, Fitzpatrick, & Whittingham, 2008). However, the initiation of early intervention services are often delayed in resource limited settings such as sub-Saharan Africa, where poor healthcare infrastructure, the lack of audiological services and widespread poverty impede the attainment of developed world

benchmarks for intervention (Joint Committee on Infant Hearing, 2007; Olusanya, 2012; Swanepoel & Storbeck, 2008; Van der Spuy & Pottas, 2008).

The prevalence and nature of permanent congenital and early onset hearing loss (PCEHL) in South Africa is largely unknown, with contextual data on profound childhood hearing loss, in particular, being non-existing. This dearth in contextual data could be the result of limited early hearing detection and intervention (EHDI) programs, as well as poor data capturing and management amongst existing programs (Meyer et al., 2012; Swanepoel et al., 2013). Except for a series of etiological surveys of children in schools for the deaf dating back to the 1970s and early 1980s (Sellars & Breighton, 1983), no data have been available to describe the risk profile of PCEHL in South Africa. Only recently, Swanepoel et al. (2013) provided preliminary data on the nature of hearing loss and associated risk profiles for a small sample of infants with varying types and degrees of hearing loss in South Africa. Results indicated that hearing loss across the sample was typically permanent with a high prevalence (21.4% of permanent non-conductive hearing loss cases) of Auditory Neuropathy Spectrum Disorder (ANSD). The most prevalent risk for SNHL was family history of hearing loss and for ANSD it was admittance to the neonatal intensive care unit (NICU) for more than 5 days, with the majority of children being diagnosed at ages which preclude optimal benefits from early detection and subsequent intervention (Swanepoel et al., 2013).

It can be expected that the risk profile for children with profound hearing loss may show marked distinctions from children with less severe degrees of hearing loss. Since central nervous system consequences of congenital deafness are aggravated with an increase in degree of hearing loss, profound childhood hearing loss is more than just a sensory loss, (Kral & O'Donoghue, 2010). Moreover, approximately 30% of children with a profound

hearing loss are reported to have an additional disability, with cognitive impairment and neurodevelopmental disabilities being the most common (Chilosi et al., 2010; Naarden, Decoufle, & Caldwell, 1999). Thus, profiling the risk factors for profound hearing loss in young children in developing countries should be considered as a critical epidemiological endeavor (Olusanya, 2011).

1.3 Predictors of pediatric cochlear implant outcomes

Case evaluation remains to be a critical aspect of pediatric cochlear implantation and the estimation of an individual child's prospects requires recognition of the factors that are likely to impact the implantation and intervention process (Black, Hickson, Black, & Perry, 2011). With an increase in bilateral implantation and a growing number of children with multiple medical conditions and less severe hearing losses being implanted, the indications for pediatric cochlear implantation are becoming more multifaceted (Black et al., 2011; Dettman et al., 2004; Fitzpatrick et al., 2009; Sparreboom, Leeuw, Snik, & Mylanus, 2012; Tait et al., 2010; Teagle, 2012). Consequently the number of pediatric cochlear implantation surgeries has increased significantly since 1990, which necessitates a clear understanding of potential threats to overall outcomes in this population (Black et al., 2014; Özdemir et al., 2013).

In a recent systematic literature review on prognostic indicators in pediatric CI surgery, only four factors influencing pediatric CI outcomes consistently were identified, namely age at implantation, presence of inner ear malformations, occurrence of meningitis and Connexin 26 GJB2 gene-related deafness (Black et al., 2011). Early implantation is undeniably

considered as a strong positive predictor of expressive and receptive language skills (Black et al., 2014; Boons, Brokx, Dhooge, et al., 2012; Govaerts et al., 2002; Habib, Waltzman, Tajudeen, & Svirsky, 2010; Manrique, Cervera-Paz, Huarte, & Molina, 2004; May-Mederake, 2012; Nicholas & Geers, 2007; Svirsky, Teoh, & Neuburger, 2004; Zwolan et al., 2004). Inner ear malformations are strongly associated with speech perception and expressive language skills outcomes, with children who have more severe cochlear malformations (e.g. cochlear dysplasia and common cavity) performing worse than children with less severe malformations (e.g. incomplete partition or enlarged vestibular aqueduct) (Black et al., 2014; Broomfield, Bruce, Henderson, Ramsden, & Green, 2010; Eisenman, Ashbaugh, Zwolan, Arts, & Telian, 2001; Kim, Jeong, Huh, & Park, 2006; Rachovitsas et al., 2012). Children with post-meningitic hearing loss do appear to benefit from CIs in terms of auditory receptive abilities, provided they receive an implant early (Nikolopoulos, Archbold, & O'Donoghue, 2006). However, for children with ossified cochleae as a result of meningitis, speech perception is frequently poorer than children with non-ossified cochleae (El-Kashlan, Ashbaugh, Zwolan, & Telian, 2003). Connexin 26 GJB2-related deafness in children with CIs predicts better speech intelligibility, speech discrimination and communication abilities when compared to implanted children with other etiologies of hearing loss (Gérard et al., 2010; Sinnathuray, Toner, Clarke-Lyttle, et al., 2004; Sinnathuray, Toner, Geddis, et al., 2004).

Emerging trends in pediatric cochlear implantation such as multiple disabilities, family influences and the impact of prematurity are described in literature, but still require further evaluation as prognostic indicators (Black et al., 2014). Even though the presence of additional disabilities negatively effects the language development of implanted children (Birman, Elliott, & Gibson, 2012; Boons, Brokx, Dhooge, et al., 2012; Gérard et al., 2010;

Rajput, Brown, & Bamiou, 2003), outcomes after implantation, even if variable, show a positive evolution in speech perception, communication abilities, social engagement and quality of life (Berrettini et al., 2008; Kral & O'Donoghue, 2011). Family factors such as a high socioeconomic level (Geers, Nicholas, & Sedey, 2003; Gérard et al., 2010; Niparko et al., 2010), sufficient parental involvement in the rehabilitation process (Boons, Brokx, Dhooge, et al., 2012; Sarant, Holt, Dowell, Rickards, & Blamey, 2008; Spencer, 2004) and higher levels of maternal education (Cupples et al., 2014) are all related to improved language outcomes. However, problematic and challenging family environments are significantly associated with poorer speech and language outcomes (Black et al., 2014; Holt, Beer, Kronenberger, Pisoni, & Lalonde, 2012). Even though prematurity is often described in pediatric CI literature and considered as an anecdotal prognostic factor, it has not been consistently proven (Black, Hickson, & Black, 2012). The same holds for other probable etiological factors or risk indicators associated with permanent childhood hearing loss, such as NICU admittance, low birth weight and assisted ventilation (Joint Committee on Infant Hearing, 2007).

Bilateral implantation has become the standard of care for children with severe to profound hearing loss in developed countries (Sarant, Harris, Bennet, & Bant, 2014; Tait et al., 2010). As a result, there has been increasing interest in the outcomes of children implanted with a second CI. The benefits of bilateral implantation in children are well documented in terms of improved localization (Lovett, Kitterick, Hewitt, & Summerfield, 2010; Sparreboom et al., 2010; Van Deun et al., 2009) and enhanced speech recognition in quiet (Scherf et al., 2007; Zeitler et al., 2008) and in noise (Litovsky, Johnstone, & Godar, 2006; Lovett et al., 2010; Van Deun, van Wieringen, & Wouters, 2010) when compared to listening with a unilateral CI. As recently confirmed, children with bilateral CIs also have significantly better language outcomes compared to children with unilateral CIs (Boons, Brokx, Frijns, et al., 2012; Sarant

et al., 2014). Whether bilateral implantation is done simultaneously or sequentially should also be taken into consideration, since providing two CIs simultaneously or with minimal delay is more advantageous for optimizing cortical brain activity than providing them sequentially after a long time (Gordon, Wong, & Papsin, 2010).

However, evidence regarding the effect of bilateral cochlear implantation on broader outcomes such as literacy, academic skills and overall quality of life is still lacking (Johnston, Durieux-Smith, Angus, O'Connor, & Fitzpatrick, 2009; Sarant et al., 2014; Sparreboom et al., 2010).

Even though prognostication is considered as a key component in pediatric cochlear implantation, a paucity of proven prognostic factors for this population exists (Black et al., 2012). Although many prognostic indicators are described in literature, it is done mostly anecdotally due to small sample sizes (Black et al., 2011). A better understanding of the causes of variation in pediatric CI outcomes will not only enable parents to set achievable expectations for their children, but will also contribute to evidence-based pediatric CI services that promote optimal outcomes.

1.4 Predictors of adult cochlear implant outcomes

With the broadening of implantation criteria, increased numbers of adult patients are being implanted at advanced ages and with less severe hearing losses (Olze et al, 2011). As with children, various factors can potentially limit adult CI outcomes. These factors can act singularly or collectively to restrict an individual's performance to varying degrees (Holden et al., 2013). In adults, success with a CI is typically measured using open-set speech

recognition tests (Caposecco, Hickson, & Pedley, 2012) and it is expected that most adult CI recipients will achieve some degree of open-set speech recognition with or without lip-reading post-implantation (Hinderink et al., 2000; Loeffler et al., 2010). In terms of speech recognition performance, numerous factors have been identified as predictors of improved outcomes in adult CI recipients, including better pre-operative speech recognition, shorter duration of deafness, higher educational level, oral mode of communication during childhood, progressive hearing loss, earlier age at implantation and positioning of electrode arrays closer to the modiolar wall (Caposecco et al., 2012; Friedland, Runge-Samuelson, Baig, & Jensen, 2010; Hirschfelder, Gräbel, & Olze, 2008; Holden et al., 2013; Klop et al., 2008; Leung et al., 2005). In spite of these proven prognostic indicators for speech recognition outcomes, a great deal of variability still exists (Holden et al., 2013).

Not only does cochlear implantation affect the hearing, speech perception and speech production abilities of an adult patient, but it also has a broader impact on self-esteem and social functioning (Hinderink et al., 2000; Hirschfelder et al., 2008). This general health status of patients, often referred to as health-related quality of life (HRQoL), has been recognized as a more comprehensive measure of medical intervention outcomes, including cochlear implantation (Mo et al, 2005). Therefore, in addition to standard speech perception testing, HRQoL has become a widespread outcome measure to quantify and monitor CI outcomes.

Significant improvement between pre- and post-implantation HRQoL scores was documented for unilaterally implanted post-lingually (Chung et al., 2012; Damen, Beynon, Krabbe, Mulder, & Mylanus, 2007; Hinderink et al., 2000; Hirschfelder et al., 2008; Klop et al., 2008; Mo, Lindbaek, & Harris, 2005; Olze et al., 2011) as well as pre-lingually (Klop,

Briaire, Stiggelbout, & Frijns, 2007; Straatman, Huinck, Langereis, Snik, & Mulder, 2014) deafened adult CI recipients. Similarly, HRQoL measures revealed a positive effect of implantation for unilaterally implanted post-lingually deafened elderly patients (Orabi, Mawman, Al-Zoubi, Saeed, & Ramsden, 2006; Sanchez-Cuadrado et al., 2013; Vermeire et al., 2005) and also adult patients implanted for single-sided deafness (Arndt et al., 2011; Vermeire & Van De Heyning, 2009). Improved HRQoL for bilateral sequential cochlear implantation compared to unilateral implantation has also been demonstrated in recent studies (Härkönen et al., 2015; King, Nahm, Liberatos, Shi, & Kim, 2014; Olze, Gräbel, Haupt, Förster, & Mazurek, 2012).

Predictive factors for improved speech recognition performance in adult CI recipients do not necessarily contribute to broader HRQoL outcomes (Capretta & Moberly, 2015). Hence the identification of patient factors that predict outcomes in terms of HRQoL is of specific interest. As indicated in several studies, a significant association exists between speech perception testing outcomes and HRQoL scores (Francis et al, 2002; Cohen et al, 2004; Vermeire et al, 2005; Damen et al, 2007; Hirschfelder et al, 2008). Conversely, this association could not be replicated by a number of studies (Capretta & Moberly, 2015; Hinderink et al, 2000; Mo et al, 2005; Maillet et al, 1995; Straatman et al, 2014), arguably due to the fact that subjective perceptions of benefit from a CI could not be linked directly to the objective performance level on speech perception testing (Hinderink et al, 2000).

Additionally to speech perception scores, various other factors having an influence on HRQoL outcomes in adult CI recipients have been investigated, including duration of deafness, age, socio-economic status, duration of CI use and tinnitus. However, some of these predictive factors have been inconclusive among studies. While no association was

found between duration of deafness and HRQoL scores by a number of studies (Hawthorne et al, 2004; Capretta & Moberly, 2015; Cohen et al, 2004; Mo et al, 2005; Hirschfelder et al, 2008; Olze et al, 2011), Maillet et al. (1995) indicated that the longer the duration of deafness, the less improvement in HRQoL is perceived. An association between younger age and better HRQoL scores was found by Chung et al. (2012) and Klop et al. (2008), whereas numerous other studies could not confirm this association (Hirschfelder et al, 2008; Capretta & Moberly, 2015; Vermeire et al, 2005). Study results from Hirschfelder et al. (2008) showed a significant association between duration of CI use and HRQoL scores, while Capretta and Moberly (2015) found that duration of CI use, socio-economic status, reading ability, vocabulary size and cognitive status did not consistently predict HRQoL scores. Hawthorne et al. (2004) indicated that HRQoL outcomes depend on socio-economic status, with CI recipients in the top socio-economic tertile obtaining greater gains in HRQoL scores. It was revealed in the study of Olze et al. (2011) that a high level of tinnitus impairment is associated with lower HRQoL scores before and after CI. Furthermore, negative correlations between HRQoL and stress, depression and anxiety were also confirmed (Olze et al., 2011).

Accurate pre-operative predictions of adult CI outcomes would enable clinicians to counsel patients to such an extent that they will be able to make informed judgements of the personal benefits they might receive from implantation (Summerfield & Marshall, 1995). Knowledge of when and how these predictive factors affect not only performance, but also HRQoL, can positively influence counselling and rehabilitation (Holden et al., 2013). In spite of the recent focus to assess the broader personal impact of permanent hearing loss and cochlear implantation in patients, the multifaceted nature of HRQoL as an outcome measure requires further study to explore relative significance of different interacting factors (Klop et al, 2008).

1.5 Cochlear implantation in South Africa

On the African continent, CI programs have only been established in South Africa and in Egypt. Since the first multichannel cochlear implantation took place in South Africa in 1986, more than 1500 individuals has been implanted at nine respective CI programs (Kerr, Tuomi, & Müller, 2012; South African Cochlear Implant Group, 2015). The first CI program in South Africa was established in 1986 at the Department of Otorhinolaryngology of the University of Stellenbosch at Tygerberg hospital (Western Cape Province). In 1991 CI programs were also established in Pretoria and in Johannesburg (Gauteng Province). A fourth CI program was established in Bloemfontein in 2002 (Free State Province). There are currently nine independent CI programs throughout South Africa.

The South African health care system is divided into public and private sectors. Only 15% of the population are covered by private health care financing, while the majority (85%) of the population rely on public health care for health services (Blecher & Harrison, 2006). Private sector hospitals in South Africa often benefit from the expertise of trained and experienced world-class medical staff and use state-of-the-art technology, such as CIs. As a result, public sector hospitals often still render a “developing world” type of service to the hearing impaired population (Theunissen & Swanepoel, 2008), reflecting the current health care inequalities for advanced interventions such as CIs in South Africa. Currently in South Africa, CIs are not provided by the National Department of Health (Kerr et al., 2012). Irrespective, a singled-out effort led to the official opening of the first public sector driven CI program in South Africa in 2006 at the Chris Hani Baragwanath Hospital in Soweto, Johannesburg (Gauteng Province), performing fully government funded CI surgery. Since then, three more government funded CI programs have been established. However, due to funding

constraints, these programs can offer CIs to only a very limited number of individuals with severe to profound deafness from the public health care sector in South Africa. As a result, the majority of adults and caregivers of children requiring cochlear implantation in South Africa need to have adequate finances or access to funding from a private medical aid to be able to obtain and maintain a CI device and related pre- and post-operative services.

A persistent challenge to the field of cochlear implantation in South Africa has been the severe dearth of contextual data regarding the clinical profile and outcomes of pediatric and adult cochlear implantation. The South African Cochlear Implant Group (SACIG) has produced a set of quality standards to secure standards of service delivery and the effectiveness of adult and pediatric cochlear implantation in South Africa (South African Cochlear Implant Group, 2011). CI service monitoring is addressed within these guidelines in that annual reports should be submitted to SACIG by each CI program in South Africa, in which clinical activity and broad patient performance outcomes should be reported on (South African Cochlear Implant Group, 2011). To date, these annual reports have been the only available source of information about the general status of CIs in South Africa. Except for a small number of local unpublished research reports on outcomes of CI recipients of specific CI programs (Celliers, 2009; Jessop, 2005; Swart, 2009; Yallitsis, 2006), no published data is yet available on cochlear implantation in South Africa, other than a study by Kerr et al. (2012) that reported on the costs involved in using a CI in South Africa, and a recent study by Moroe and Kathrada (2016) describing the long-term concerns post cochlear implantation as experienced by five parents/caregivers of pre-lingually deaf children.

For the developing world at large, available published reports on CIs are also limited. Existing reports address mainly issues related to the viability and sustainability of CIs within specific

developing countries such as China (Zeng, 1995), Pakistan (Khan, Mukhtar, Saeed, & Ramsden, 2007) and Latin America (Berruecos, 2000). Furthermore, Tarabichi and colleagues (2008) disputed the place of cochlear implantation within the developing world, while Saunders and Barrs (2011) reported on cochlear implantation as humanitarian service in developing countries. None of the above publications gave a description of the clinical profile of CI recipients or reported on outcomes. Therefore, within the unique South African context, outcome data are specifically required to critically assess the effectiveness, relevancy and accountability of current CI service delivery. Furthermore, accurate outcome data are required for contextual prognostication in cochlear implantation, in order to plan for sustainable post-implantation intervention and to ensure evidence-based practice.

1.6 Rationale

The lifelong consequences of PCEHL are exacerbated for children and their families when a profound degree of hearing loss is diagnosed. The risk profile, diagnosis and age of intervention for children with profound hearing loss are therefore expected to show marked differences from children with less severe degrees of hearing loss. Since the epidemiological profile of PCEHL also differs across various regions of the world and since risk factors have been reported mostly for school-aged children (Olusanya, 2011), profiling the risk factors for profound hearing loss in younger children is an important epidemiological endeavor, especially in a developing country such as South Africa (Olusanya, 2011).

When children and adults with severe to profound hearing loss receive a CI, the expectations for optimal outcomes are high (Birman et al., 2012). However, CI performance

and outcomes vary among patients and are influenced by a wide variety of multifactorial factors. These predictive factors might be universal, or might relate to specific contexts or world regions. Prognostication is therefore considered as a key element in pediatric and adult cochlear implantation, since many clinical decisions in CI surgery are potentially invalid unless the patient's prognosis is accurately assessed (Black et al., 2012, 2011). The identification of prognostic factors through an evidence-based process enable CI teams to counsel families pre-operatively about the range of possible outcomes and to plan appropriately for post-implantation intervention (Black et al., 2011). Furthermore, the current body of knowledge on predictive factors for CI outcomes originated mainly from samples from the developed world, with no published data yet available on factors affecting CI outcomes within developing world regions.

Given the paucity of proven prognostic factors in pediatric and adult cochlear implantation (Black et al., 2012), this current work was initiated to identify possible predictors of outcomes and to investigate the prognostic significance of these factors, in a large caseload of pediatric and adult CI recipients in South Africa.

The following research questions were therefore posed:

i. *What are the risk and intervention profiles for profound childhood hearing loss in a South African cohort?*
ii. *What are the predictors of pediatric CI outcomes in a South African cohort?*
iii. *What are the predictors of health-related quality of life outcomes in adult CI recipients in a South African cohort?*

CHAPTER 2

METHODOLOGY

2.1 Research objectives

This research described profound childhood hearing loss in terms of risk and intervention profiles, and also identified and described predictors of pediatric and adult cochlear implantation in a South African cohort. Three research objectives were proposed, each constituting a research study for submission in article format to an accredited[1] peer-reviewed journal upon completion. The three studies are summarized in Table 2.1 according to proposed titles, objectives, and journals in which they have been accepted for publication.

[1] Institute for Scientific Information (ISI) or Department of Higher Education and Training (DHET) accreditation list

Table 2.1 Summary of Studies I to III displaying article title, objectives, journal and thesis chapter

Study	I	II	III
Title	Profound childhood hearing loss in a South African cohort: Risk profile, diagnosis and age of intervention	Predictors of pediatric cochlear implantation outcomes in South Africa	Predictors of health-related quality of life in adult cochlear implant recipients in South Africa
Objective	To describe profound childhood hearing loss in a South African cohort of pediatric CI recipients in terms of risk profile, and age of diagnosis and intervention	To identify and describe predictors of pediatric cochlear implantation outcomes in a South African cohort of pediatric CI recipients	To identify and describe predictors of health-related quality of life outcomes in a South African cohort of adult cochlear implant recipients
Journal	International Journal of Pediatric Otorhinolaryngology	International Journal of Pediatric Otorhinolaryngology	International Journal of Audiology
Publication status	Accepted and published: Le Roux, T., Swanepoel, D., Louw, A., Vinck, B. & Tshifularo, M. (2015). Profound childhood hearing loss in a South African cohort: Risk profile, diagnosis and age of intervention. *International Journal of Pediatric Otorhinolaryngology,* 79(1), 8-14. doi: 10.1016/j.ijporl.2014.09.033	Accepted and published: Le Roux, T., Vinck, B., Butler, I., Cass, N., Louw, L., Nauta, L., Schlesinger, D., Soer, M., Tshifularo, M. & Swanepoel, D. (2016). Predictors of pediatric cochlear implantation outcomes in South Africa. *International Journal of Pediatric Otorhinolaryngology*, 84(5), 61-70. doi: 10.1016/j.ijporl.2016.02.025	Accepted and published: Le Roux, T., Vinck, B., Butler, I., Louw, L., Nauta, L., Schlesinger, D. & Swanepoel, D. (2017). Predictors of health-related quality of life in adult cochlear implant recipients in South Africa. *International Journal of Audiology,* 56(1), 16-23. doi: 10.1080/14992027.2016.1227482
Chapter in thesis	**3**	**4**	**5**

2.2 Research design and procedures

A restrospective cochort design was primarily used for Studies I, II and III. Cohort studies are also known as observational studies since there is no manipulation of any variable (Haynes & Johnson, 2009). Retrospective cohort studies recruit a group of participants and measure predictor variables from past data (Haynes & Johnson, 2009). For Studies II and III, cross-sectional outcome data were added to the retrospective dataset at the time of data-collection. Studies I, II and III also followed a descriptive research design, as the characteristics of an observed phenomenon was identified and described, without changing the situation under investigation (Leedy & Ormrod, 2010). Since this research had the purpose to explain and predict, quantitative data were collected for Studies I, II and III (Leedy & Ormrod, 2010).

Table 2.2 presents a summary of the study design, participant selection criteria, sampling method, sample size, data collection tools and material, and data collection procedures for each of the three studies.

Table 2.2 Research design and methods summary for Studies I to III

Study	I	II	III
Title	Profound childhood hearing loss in a South African cohort: Risk profile, diagnosis and age of intervention	Predictors of pediatric cochlear implantation outcomes in South Africa	Predictors of health-related quality of life in adult cochlear implant recipients in South Africa
Study design	Retrospective cohort design, descriptive research using quantitative data	Retrospective cohort design, cross-sectional outcome data were added to retrospective dataset at the time of data-collection, descriptive research using quantitative data	
Participant selection criteria	• multicenter study including pediatric (≤18 years) CI recipients from five participating CI programs in South Africa • pediatric CI recipients implanted between 1996 and 2013 (with 1996 being the most dated year of implantation for CI recipients turning 18 in the year of data collection – 2013) • PCEHL confirmed under the age of five years old	• multicenter study including pediatric (≤18 years) CI recipients from five participating CI programs in South Africa • all children (≤18 years), implanted between 1996 and 2013 (with 1996 being the most dated year of implantation for CI recipients turning 18 in the year of data collection – 2013) with a minimum of six months implant use at the time of data-collection and with data available on at least one outcome measure • no case selection occurred and children from the complete range of educational and communication environments were included	• multicenter study including adult (>18 years) CI recipients from four participating CI programs in South Africa • adult (>18 years) CI recipients, implanted between 1991 and 2013 (participating CI teams that have been in existence for the longest time were started in 1991) with available cross-sectional HRQoL outcome data • adult CI recipients with pre- and post-lingual onset hearing loss were included • a minimum of 12 months implant use at the time of data collection • only adult CI recipients who were proficient in English were requested to complete the HRQoL questionnaire
Participant sampling method	Non-probability purposive sampling (Beins, 2009)		
Sample size	264 pediatric CI recipients	301 pediatric CI recipients	100 adult CI recipients

Data collection tools and material	A retrospective review of the patient files of pediatric CI recipients at five participating CI programs was conducted. An electronic database was developed to organize and capture retrospective data in a consistent format amongst the participating programs. Retrospective data collected included demographical information, case history questionnaires containing documented risk factors, diagnostic test procedures conducted, diagnosis (type, onset and degree of hearing loss), as well as the age of caregiver suspicion, initial diagnosis and intervention.	A retrospective review of the patient files of pediatric CI recipients at five participating CI programs was conducted. An electronic database was developed to organize and capture retrospective data in a consistent format amongst the participating programs. Retrospective data included demographical, CI and hearing loss data, as well as family and risk factor data. Cross-sectional outcome data were added to the database at the time of data collection, including: • auditory performance: *Categories of Auditory Performance* (CAP) – Appendix A • speech production: *Speech Intelligibility Rating* (SIR) – Appendix B • communication mode • educational placement	A retrospective review of the patient files of adult CI recipients at four participating CI programs was conducted. An electronic database was developed to organize and capture retrospective data in a consistent format amongst the participating programs. Retrospective data included demographical and clinical characteristics of the study sample, as well as risk, family, educational and employment factors. Cross-sectional outcome data were added to the database at the time of data collection: • HRQoL: *Nijmegen Cochlear Implant Questionnaire* (NCIQ) – Appendix C An information letter accompanied each NCIQ questionnaire, together with an informed consent form (Appendix D). Only adult CI recipients who were proficient in English were requested to complete the questionnaire.
Data collection procedure	Data capturers were identified and trained for each participating CI program. All data capturers had an Audiology background and were directly or indirectly involved with the CI recipients at the respective CI programs.	Data capturers were identified and trained for each participating CI program. All data capturers had an Audiology background and were directly or indirectly involved with the CI recipients at the respective CI programs.	Data capturers were identified and trained for each participating CI program. All data capturers had an Audiology background and were directly or indirectly involved with the CI recipients at the respective CI programs.

	Patient registers were reviewed at each of the five participating CI programs in order to locate pediatric CI recipients who were South African residents, and for whom PCEHL was confirmed under the age of five years old. The clinical files of the children who complied with these criteria were drawn from the filing cabinets at each participating CI program and then reviewed retrospectively The datasheets were designed to ensure that data were captured consistently and uniformly, with fixed response categories (selection options) for most variables (except continuous variables). Frequent data entry spot checks were performed and all datasheets were meticulously checked for data capturing errors by the researcher. Data were captured within an eight month period and all data collection procedures were overseen by the researcher.	All pediatric CI recipients who met the inclusion criteria were identified at each of the five participating CI programs. Clinical files of 301 eligible children were reviewed retrospectively. The datasheets were designed to ensure that data were captured consistently and uniformly, with fixed response categories (selection options) for most variables (except continuous variables). Frequent data entry spot checks were performed and all datasheets were meticulously checked for data capturing errors by the researcher. Cross-sectional outcome data in terms of auditory performance (CAP scores), speech production (SIR scores), communication mode and educational placement were added to the database at the time of data collection. CAP and SIR scores were allocated by experienced audiologists/ speech-language therapists involved in the rehabilitation of the children at the respective CI programs. These professionals also provided the outcome data on the communication mode and educational placement of the implanted children. Data were captured within an eight month period and all data collection procedures were overseen by the researcher.	Clinical files of 334 adult CI recipients were reviewed retrospectively at the four participating CI programs. The datasheets were designed to ensure that data were captured consistently and uniformly, with fixed response categories (selection options) for most variables (except continuous variables). Frequent data entry spot checks were performed and all datasheets were meticulously checked for data capturing errors by the researcher. At the time of data collection, the NCIQ was distributed to all adult CI recipients at the participating CI programs by email. In order to increase the response rate of completed questionnaires, the NCIQ was also handed to adult CI recipients who were seen for consultations during the data collection period at the respective CI programs. The NCIQ was completed electronically or in hard copy as a self-assessment of HRQoL by individual CI recipients themselves at home or during consultations at the various CI programs. This cross-sectional HRQoL data were then added to the electronic database at the time of data collection. Data were captured within an eight month period and all data collection procedures were overseen by the researcher.

2.3 Research context

At the time of data-collection, there were eight independant CI programs throughout South Africa. All eight programs were approached to participate in this multicenter research study, from which five programs agreed to participate. Four programs are situated in the Gauteng Province (University of Pretoria Cochlear Implant Unit, Johannesburg Cochlear Implant Program, Chris Hani Baragwanath Academic Hospital Cochlear Implant Program, Steve Biko Academic Hospital Cochlear Implant Program), while the remaining program is in the Free State Province (Bloemfontein Cochlear Implant Program). Two of these CI programs function solely within the private health care system (University of Pretoria Cochlear Implant Unit and Johannesburg Cochlear Implant program), while Bloemfontein Cochlear Implant Program is part of the private health care systems, but also offer government funding for CI recipients. Chris Hani Baragwanath Academic Hospital Cochlear Implant Program and Steve Biko Academic Hospital Cochlear Implant Program are complete public sector driven CI programs. The ratio of private health care versus public health care CI recipients was 92.4% to 7.6% for the sample in Study I, 95% to 5% for the sample in Study II and 96% to 4% for the sample in Study III respectively.

All participating CI programs are made up of multidisciplinary teams. Involved professionals are suitably qualified, registered with relevant professional bodies including the *South African Cochlear Implant Group* (SACIG) and the Health Professional Council of South Africa (HPCSA). These multidisciplinary teams are responsible for the long-term management of CI recipients, according to the outlined protocols for pre- and post-operative assessment and long-term management of CI recipients in South Africa as stipulated by SACIG (South African Cochlear Implant Group, 2011).

2.4 Ethical considerations

The research project was approved by the Postgraduate Committee of the Faculty of Humanities of the University of Pretoria on 16 October 2012, and by the Research Ethics Committee of the Faculty of Humanities of the University of Pretoria on 25 October 2012 (Appendix E). Permission was obtained from the team coordinators of each participating CI program to participate and contribute data to this multicenter research (Appendix F).

Medical and health care research is subject to ethical standards that promote respect for all human beings and protect their health and rights (South African National Health Act, 2007). The current research was conducted within the framework of general ethical principles for social research (Beins, 2009) and the ethical guidelines set out in the South African National Health Act (2007). The individual principles presented in these documents are listed and discussed below in Table 2.3 as they were applied to the current research.

Table 2.3 Ethical principles applied to formulation of research design, participant selection and data collection and analysis procedures
(South African National Health Act, 2007; Beins, 2009)

Principle	Application to research
Any form of health research conducted in South Africa which involves the participation of human subjects, must be relevant both to the overall health and developmental needs of the people of the Republic and the individual needs of those who suffer from the disease and or concerns of the study.	The rationale for this research was carefully considered in order to contribute to the overall needs of individuals with severe-profound hearing loss who eventually received CIs. Furthermore this research aimed to contribute to accurate prognostic information that is required for evidence-based pre-operative counselling and post-operative intervention services for CI recipients throughout South Africa.
Participants' rights to privacy and confidentiality should be protected at all times. The confidentiality of records that could identify participants should also be protected.	When the data required for this research were received from the participating CI teams, all identifying information was excluded and data were presented anonymously for the purpose of data-analysis. Only the researcher and the data-analyst had access to this combined dataset. Also, participant confidentiality was ensured as data were reported using a alphanumeric code. The identity of the participant represented by this code was unknown, even to the researcher.
Persons on whom research is to be conducted have the right to be informed of the purpose of the research, methods and procedures to be followed or used during the research, potential or real harm and risks involved in participation and the extent to which confidentiality and privacy will be maintained.	Since this research followed mainly a retrospective research design, no active participation was required from pediatric and adult CI recipients. Written consent was not a prerequisite, since it was not possible to obtain individual written consent from 635 CI recipients, with retrospective data dating back to 1991. Consequently, each CI participant included in the combined dataset's right to privacy was protected at all times by treating data with strict confidetiality. The coordinators of the participating CI programs signed a letter of consent, stating that they give permission that the specific data required for the purposes of this research, will anonymously be made available to the researcher and that they wil act as custodians of their CI program's data (Appendix F). In exception to the retrospective data captured for Studies I - III, Study III required cross-sectional HRQoL outcome data that was obtained from adult CI recipients by completing the NCIQ questionnaire at the time of data-collection. An information letter and informed consent form accopanied each questionnaire (Appendix D). This was the

	only cross-sectional data that written consent was required for.
It should be ensured that the selection, recruitment and inclusion/ exclusion of research participants are just and fair.	Adult and pediatric CI recipients from the complete range of demographical, educational and communication environments were included.
The rights, safety and wellbeing of participants are the most important considerations in research and should prevail over interest of science and society. Foreseeable risks and inconveniences should be weighed against the anticipated benefit for participants and society. Only if the anticipated benefits justify the risks, a study should be initiated and continued.	There were no risks involved for the participants of this research, and due to the retrospective nature of this research study, participants were not exposed to unusual stress, embarrassment or loss of self-esteem.
A researcher conducting research involving human subjects is obliged to submit their research proposals for approval to an accredited research ethics committee.	Institutional ethics committee approval was obtained by the Research Ethics Committee of the Faculty of Humanities of the University of Pretoria (Appendix E) before data collection commenced. This research was the original work of the researcher and where secondary material was used, it was carefully acknowledged and referenced in accordance with specified requirements (Appendix G).

2.5 Statistical analysis

Table 2.4 provides an overview of the types of statistical analyses that were conducted for Studies I, II and III respectively. Due to the retrospective nature of the study, patient files were not all complete for every variable considered. Results were therefore based on the available data for each variable.

Table 2.4 Statistical analysis summary for Studies I to III

Study	I	II	III
Title	Profound childhood hearing loss in a South African cohort: Risk profile, diagnosis and age of intervention	Predictors of pediatric cochlear implantation outcomes in South Africa	Predictors of health-related quality of life in adult cochlear implant recipients in South Africa
Study design	Retrospective cohort design, descriptive research using quantitative data	Retrospective cohort design, cross-sectional outcome data were added to retrospective dataset at the time of data-collection, descriptive research using quantitative data	
Description of variables for prediction analysis		Outcome variables included auditory performance (CAP scores), speech production (SIR scores), mode of communication (oral/ non-oral), educational placement (mainstream/ non-mainstream). Explanatory variables included demographical and hearing loss factors, CI factors, family factors and risk factors (see Table 4.3).	Outcome variables included overall HRQoL (total NCIQ score), basic sound perception, advanced sound perception, speech production, self-esteem, activity limitations, social interactions. Explanatory variables included demographic and related factors, hearing loss factors, CI factors and risk factors (see Table 5.3).
Statistical analyses	Descriptive statistics were utilized to define the study population in terms of demographics, risk profile, diagnosis and degree of permanent childhood hearing loss, age of hearing loss suspicion and diagnosis and age of intervention.	Descriptive statistics were utilized to define the study population in terms of demographical, CI and hearing loss characteristics, as well as risk and family profiles. From these characteristics, 20 suspected predictive factors were identified (see Table 4.3). For the purpose of variable selection for regression modelling, bivariate data analyses were undertaken to determine the existence of a possible association between a potential predictor and a categorical outcome variable, in two categories using the Pearson Chi-Square test.	Descriptive statistics were utilized to define the study population in terms of demographic and clinical characteristics as well as risk, family, educational and employment profiles. From these characteristics, 22 suspected predictive factors were identified (see Table 5.3) Data from the NCIQ was scored and analyzed according to the specifications outlined in Hinderink et al. (2000). Scores for each of the six subdomains of the

		For the main prediction analysis, two types of regression were used: 1. For continuous outcome variables (auditory performance and speech production), linear regression models in the form of multiway analysis of variance were constructed to investigate the influence of categorical predictors on the mean CAP and SIR scores. 2. Log linear models were constructed for categorical outcome variables (communication mode and educational placement). An index for each category of a predictor was calculated as the exponent of the regression coefficient of that category, obtained from the log linear model. The odds for any combination of categories of predictors were found by multiplication of the overall mean odds (the exponent of the intercept term in the log odds model) with the indices of the specified categories. Based on these odds the probability for non-oral communication or non-mainstream educational placement was estimated by dividing the odds outcome by the factor (1 + odds).	NCIQ were computed as well as an overall HRQoL average percentage score. Multiple linear regression analysis was used for the prediction of HRQoL outcomes in adult CI recipients. Regression models were constructed to investigate the influence of categorical and continuous predictors on HRQoL percentage scores.

CHAPTER 3

PROFOUND CHILDHOOD HEARING LOSS IN A SOUTH AFRICAN COHORT: RISK PROFILE, DIAGNOSIS AND AGE OF INTERVENTION

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3.1 Abstract

Objective: To describe profound childhood hearing loss in a South African population of pediatric cochlear implant recipients in terms of risk profile, and age of diagnosis and intervention.

Methods: A retrospective review of patient files for 264 pediatric cochlear implant recipients from five cochlear implant programs was conducted. Data were captured from 264 eligible subjects, of which all were implanted between 1996 and 2013 and PCEHL was confirmed under the age of five years old. Data collected included demographical information, risk factors from case histories, diagnostic test procedures conducted, diagnosis (type, onset and degree of hearing loss) and documented ages of caregiver suspicion, initial diagnosis and intervention.

Results: Risk factors for permanent childhood hearing loss were present in 51.1% of cases, with the most prevalent risks being NICU admittance (28.1%), family history of childhood hearing loss (19.6%) and prematurity (15.1%). An associated syndrome was diagnosed in 10% of children and 23.5% presented with at least one additional developmental condition. Hearing loss for most (77.6%) children was confirmed as congenital/early onset, while 20.3% presented with postnatal onset of hearing loss. ANSD was diagnosed in 5% of children, with admittance to NICU (80%) and hyperbilirubinemia (50%) being the most prevalent risk factors for these cases. Hearing loss was typically diagnosed late (15.3 months), resulting in delayed initial hearing aid fitting (18.8 months), enrollment in early intervention services (19.5 months) and eventual cochlear implantation (43.6 months).

Conclusion: Most prevalent risk factors in profound childhood hearing loss were admittance to NICU, family history and prematurity. Diagnosis and intervention was typically delayed predisposing this population to poorer outcomes.

3.2 Introduction

Congenital or early onset permanent bilateral hearing loss affect an estimated 798 000 newborns annually (Olusanya et al., 2008). At least 90% of these reside in developing countries around the world, implying that almost 2000 infants with hearing loss are born daily in developing world regions (Swanepoel et al., 2009). Based on an estimated incidence of six per 1000 live births, 180 000 infants with permanent hearing loss are born annually in sub-Saharan Africa alone (Olusanya, 2008; Swanepoel & Storbeck, 2008). Profound hearing loss prevalence in developing regions is largely unknown with only a few previously

reported estimates (Arslan & Genovese, 1996; Berruecos, 2000; A. Smith, 2008; Zeng, 1995). Although comprehensive population studies for Africa do not exist, available reports suggest that the prevalence of profound hearing loss is higher than the estimated 20-30% of children with permanent childhood hearing loss in the developed world (Kral & O'Donoghue, 2010; Olusanya, 2008; Saunders & Barrs, 2011; Westerberg et al., 2008).

The lifelong consequences of permanent congenital and early onset hearing loss (PCEHL) are well documented (Calderon, Bargones, & Sidman, 1998; Olusanya, Ruben, & Parving, 2006; Swanepoel, 2008; World Health Organization (WHO), 2010) however, these consequences are exacerbated for children and their families when a profound degree of hearing loss is diagnosed. These include the lack of development of spoken language which results in restricted learning, literacy and educational achievements, as well as later employment opportunities (Kral & O'Donoghue, 2010; Mohr et al., 2000). Profound hearing loss also results in a considerable cost for both the child and society (Mohr et al., 2000) with the costs expected to be even higher in developing countries (Saunders & Barrs, 2011). Early auditory stimulation during periods of maximal receptiveness is therefore critical for this population, since congenital/early onset profound hearing loss alters the functional properties of the auditory system and impairs cortical development (Fallon, Irvine, & Shepherd, 2008; Kral & O'Donoghue, 2011; Mohr et al., 2000; Sharma, Gilley, Dorman, & Baldwin, 2007).

Unfortunately it is estimated that less than 10% of the more than 1 million babies born annually in South Africa will have their hearing screened, implying that children with hearing loss will most likely miss out on necessary early auditory stimulation (Meyer et al., 2012; Statistics South Africa, 2011, 2013; Theunissen & Swanepoel, 2008). Within the public health care system, which serves approximately 85% of the South African population (Blecher &

Harrison, 2006), less than 7.5% of hospitals offered any infant hearing screening services when surveyed in 2008 (Theunissen & Swanepoel, 2008). Slightly better coverage is provided in the private health care system, with 53% of obstetric units offering some form of screening, but only 14% offering universal newborn screening (Meyer et al., 2012). As a result, the average age of hearing loss diagnosis in South Africa has been reported to be between 23 to 44.5 months (Butler et al., 2013; Swanepoel et al., 2013; Van der Spuy & Pottas, 2008) in contrast to the recommended age of 3 months (Joint Committee on Infant Hearing, 2007).

Despite recent reports on early hearing detection services in the public and private health care sectors of South Africa (Meyer et al., 2012; Theunissen & Swanepoel, 2008) information on the status of intervention in terms of amplification and enrollment into early intervention programs is limited (Swanepoel et al., 2009). Contextual data on profound childhood hearing loss, in particular, is non-existing. A report from the Western Cape province on a representative sample of 54 children with hearing loss, most (61%) with severe to profound hearing loss, indicated the average age of initial hearing aid fitting and enrolment in early intervention to be 28 and 31 months respectively (Van der Spuy & Pottas, 2008). A survey conducted amongst speech therapy and audiology departments within public sector hospitals in South Africa reported that within a sample of 76 children aged 18 months or younger that were fitted with hearing aids 12 months prior to the survey, less than 7% received hearing aids by the age of 6 months, as recommended (Health Professions Council of South Africa, 2006; Joint Committee on Infant Hearing, 2007; Theunissen & Swanepoel, 2008). As a result of limited early hearing detection and intervention (EHDI) programs and poor data capturing and management amongst existing programs (Meyer et al., 2012; Swanepoel et al., 2013) the prevalence and nature of PCEHL

in South Africa is largely unknown along with the associated risk profiles. Except for a series of etiological surveys of children in schools for the deaf dating back to the 1970s and early 80s (Sellars & Breighton, 1983), no data have been available to describe the risk profile of PCEHL in South Africa. At the time of these early etiological reports (Sellars & Beighton, 1978; Sellars & Breighton, 1983; Sellars, Groeneveldt, & Beighton, 1976), diagnostic categories of hearing loss did not include auditory neuropathy spectrum disorder (ANSD). Also, with the advent of newborn hearing screening (NHS) the risk profiles for PCEHL were expanded and described more accurately (Olusanya, 2011). This was not accounted for in these early South African reports (Sellars & Beighton, 1978; Sellars & Breighton, 1983; Sellars et al., 1976). Only in a recent report was the nature of hearing loss and associated risk profile described with consideration of ANSD for a population of infants and children diagnosed at a pediatric referral clinic in South Africa (Swanepoel et al., 2013). More than half of the diagnosed children (56%) presented with sensorineural hearing loss, with 50% being of a profound degree. ANSD was diagnosed in 21% of the cases, suggesting a larger prevalence for populations from developing contexts such as sub-Saharan Africa, as has previously been reported. This is attributed to an increased incidence of environmental, maternal and child health related risk factors predisposing ANSD (Olusanya & Somefun, 2009; Swanepoel, 2010).

Children with profound hearing losses are known to be identified at earlier ages and are predisposed to enter early intervention services earlier than children with less severe degrees of hearing loss (Durieux-Smith et al., 2008). However, the initiation of early intervention services are often delayed in the resource limited settings such as sub-Saharan Africa, where poor healthcare infrastructure, the lack of audiological services and widespread poverty impede the attainment of developed world benchmarks for

intervention (Joint Committee on Infant Hearing, 2007; Olusanya, 2012; Swanepoel & Storbeck, 2008; Van der Spuy & Pottas, 2008).

It can be expected that the risk profile for children with profound hearing loss may show marked distinctions from children with less severe degrees of hearing loss. Profound childhood hearing loss is more than just a sensory loss, since central nervous system consequences of congenital deafness are aggravated with an increase in degree of hearing loss (Kral & O'Donoghue, 2010). Also, approximately 30% of children with a profound hearing loss are reported to have an additional disability, with cognitive impairment and neurodevelopmental disabilities being the most common (Chilosi et al., 2010; Naarden et al., 1999). Since the epidemiological profile of PCEHL differs across various regions of the world and since risk factors have been reported mostly for school-aged children (Olusanya, 2011), profiling the risk factors for profound hearing loss in younger children is an important epidemiological endeavor, especially in developing countries (Olusanya, 2011).

Recently reported findings from Swanepoel et al. (2013) provide preliminary data on the nature of hearing loss and associated risk profiles for a small sample of infants with hearing loss in South Africa. However, data pertaining to additional developmental conditions and intervention was not available for this sample population. The current study therefore investigates profound childhood hearing loss in a South African population of pediatric cochlear implant recipients considering associated risk profiles, the diagnosis of hearing loss and age of intervention.

3.3 Method

Approval from the institutional ethics committee was obtained before data collection was initiated.

3.3.1 Study population

There are currently eight independant cochlear implant programs throughout South Africa. All eight programs were approached to participate in this multicenter study, from which five programs committed to participation. Four programs are situated in the Gauteng Province, while the remaining program is in the Free State Province. A retrospective review of the patient files of pediatric cochlear implant recipients at these participating five programs was conducted. Data captured within a 8 month period resulted in a dataset of 264 eligible pediatric cochlear implant recipients, of which all were implanted between 1996 and 2013 and PCEHL was confirmed under the age of five years old. The children included in this study sample were diagnosed with PCEHL at various diagnostic audiology clinics throughout South Africa. When candidacy for cochlear implantation was confirmed, the children were referred to the nearest cochlear implant program for assessment. Once approved and implanted, a comprehensive patient file was opened for each child, containing records of their pre-operative case history and diagnostic audiological assessment data.

3.3.2 Procedures

Patient registers were reviewed at each of the five participating cochlear implant programs in order to locate pediatric cochlear implant recipients who were South African residents, and for whom PCEHL was confirmed under the age of five years old. The clinical files of the children who complied with these criteria were drawn from the filing cabinets at each participating cochlear implant program and then reviewed retrospectively. Data capturers were identified and trained for each participating cochlear implant program. An electronic database was developed to organize and capture the data in a consistent format amongst the participating programs. Data collected included demographical information, case history

questionnaires containing documented risk factors, diagnostic test procedures conducted, diagnosis (type, onset and degree of hearing loss), as well as the age of caregiver suspicion, initial diagnosis and intervention.

3.3.3 Data processing and analysis

A commercially available statistical software package (IBM SPSS version 21) was utilized to analyze the obtained data. The central tendency parameters and the degree of variation of the captured variables were calculated using descriptive statistics. For the capturing of pre-operative behavioral pure tone and Auditory Steady State Response (ASSR) threshold data, when a "no response" was indicated in the clinical file at a respective frequency, the threshold was captured as 120 dBHL. The minimum diagnostic criteria considered for ANSD were the presence of oto-acoustic emissions and/or a response for a cochlear microphonic between 80 and 90 dB nHL, with the absence of or severely abnormal Auditory Brainstem Response (ABR) waves (Berlin et al., 2010).

3.4 Results

3.4.1 Demographics

The study population of 264 children were all approved for cochlear implantation and showed an even gender distribution (50.4% male and 49.6% female). Only 7.6% of children were public health care patients compared to 92.4% private health care patients. Ethnical category was distributed as 66.2% White, 20.5% Black, 7.6% Indian/Asian and 5.7% Colored. Just more than half (50.8%) of the children's home languages was Afrikaans, 40.7% was English and 5.6% was an African language (n=248). Most children (95.4%) had normal

hearing parents, while both parents had hearing loss in 2.5% of the cases and one parent had hearing loss in 0.8% of the cases (n=241).The majority of children (73.8%) were communicating orally and received either auditory/oral or auditory/verbal style education. The current communication mode for 6% of the children was South African Sign Language, while 13.1% used Total Communication and the remaining 7.2% alternative manual modes of communication (n=252).

3.4.2 Risk profile

A total of 23 children (10%) were diagnosed with a syndrome (Table 3.1), with Waardenberg syndrome being the most prevalent (5.2%; n=12/229). Of the total sample, 23.5% (n=55/234) presented with at least one additional developmental condition (Table 3.1). The most frequently occurring conditions for this population were visual impairment (8.5%; n=20/234).

Table 3.1 Presence of syndromes and additional developmental conditions

Syndrome	***% (n)***
Waardenberg Syndrome	5.2 (12/229)
Ushers Syndrome	1.3 (3/229)
Pierre Robin Syndrome	0.9 (2/229)
Leopard Syndrome	0.9 (2/229)
Additional developmental conditions	***% (n)***
Visual impairment	8.5 (20/234)
Mobility impaired	3.0 (7/234)
Cerebral palsy	5.6 (13/234)
Autism	2.1 (5/234)
Apraxia	1.7 (4/234)
Cleft lip and/or palate	1.3 (3/234)

Within the sample of children diagnosed with ANSD specifically, 58.3% (n=7/12) presented with at least one additional developmental condition. Most occurring conditions for this population was documented as visual impairment (16.7%; n=2/12) and cerebral palsy (16.7%; n=2/12).

Birth type was specified to be normal delivery in 40% of the cases and caesarian section in 60% of the cases (n=80). Average birth weight was 2543.2g (range: 710 - 4100, 902.6 SD; n=91) and average gestation age was 37 weeks (range: 24 - 42, 4.7 SD; n=128). Prenatal, natal and postnatal risk factors are listed in Table 3.2.

Table 3.2 Risk factor prevalence for profound childhood hearing loss (n=264)

	Total population *n=264*	**ANSD *n=12***
Risk factors	***% (n)***	***% (n)***
Pre-natal risk factor		
Family history of permanent childhood hearing loss	19.6 (40/204)	10 (1/10)
Rubella	5.5 (12/219)	20 (2/10)
Cytomegalovirus	3.2 (7/219)	-
Twin/ triplet	3.2 (7/219)	10 (1/10)
Syphilis	0.5 (1/219)	-
Toxoplasmosis	0.5 (1/219)	-
Natal risk factor		
Admittance to NICU	28.1 (43/153)	80 (8/10)
Prematurity (<34 weeks gestation)	15.1 (33/219)	40 (4/10)
Low birth weight (<2500g)	8.7 (19/219)	10 (1/10)
Extremely low birth weight (<1500g)	5.5 (12/219)	10 (1/10)
Birth asphyxia	1.8 (4/219)	-
Maternal hypertensive disorder in pregnancy	1.8 (4/219)	10 (1/10)
Rupture of membranes	0.9 (2/219)	10 (1/10)
Rh incompatibility	0.9 (2/219)	10 (1/10)
Birth trauma	0.5 (1/219)	-
Post-natal risk factor		
Neonatal jaundice/ hyperbilirubinemia	10.5 (23/219)	50 (5/10)
Blood transfusion	2.3 (5/219)	20 (2/10)
Meningitis	10.0 (22/219)	-
Viral infection (unspecified)	5.0 (11/219)	10 (1/10)
Mumps	0.9 (2/219)	-
Measles	0.5 (1/219)	-
Tuberculosis	0.5 (1/219)	-

Admittance to neonatal intensive care unit (NICU) was recorded as the most prevalent risk factor for 28.1% of the population (n=43/153). However, only a smaller subset of data were available pertaining to duration of NICU stay, indicating that 90.2% (n=37/41) of children were admitted to NICU for longer than 5 days. More than half (51.1%; n=112/219) of the study sample presented with one or more risk factors, while 48.9% (n=107/219) presented with no associated risk factors for hearing loss (Table 3.3). The occurrence of natal (23.3%; n=51/219) and postnatal (34.7%; n=76/219) risk factors were more evident than pre-natal (12.3%; n=27/219) risk factors.

Table 3.3 Occurrence of risk factors in children with profound hearing loss (n=264)

	PRE-NATAL risk factors *% (n)*	**NATAL risk factors** *% (n)*	**POST-NATAL risk factors** *% (n)*	**TOTAL** *% (n)*
Available data	83.0 (219/264)	83.0 (219/264)	83.0 (219/264)	83.0 (219/264)
No risk factors	87.7 (192/219)	76.7 (168/219)	65.3 (143/219)	48.9 (107/219)
Risk factors present	12.3 (27/219)	23.3 (51/219)	34.7 (76/219)	51.1 (112/219)
1 risk factor present	11.9 (26/219)	13.7 (30/219)	29.2 (64/219)	28.8 (63/219)
2 risk factors present	0.5 (1/219)	7.3 (16/219)	4.1 (9/219)	11.0 (24/219)
3 or more risk factors	-	2.3 (5/219)	1.4 (3/219)	11.4 (25/219)

3.4.3 Diagnosis and degree of permanent childhood hearing loss

Hearing loss for most (77.6%) children was confirmed as congenital/early onset, while 8.5% presented with progressive hearing loss, 11.8% with sudden hearing loss and 2% with unknown onset of hearing loss (n=246). The vast majority of children (95%) presented with SNHL (n=228/240) and 5% presented with ANSD (n=12/240). From the 264 clinical files that were reviewed for this study, no pre-operative hearing data were available for 60 (22.7%) children. The remaining 204 files contained pre-operative pure tone thresholds for 144 children (70.6%). Only the ears with comprehensive threshold data available at all required frequencies (0.5; 1; 2 and 4 kHz) were included. The mean pure tone average (PTA) air-conduction threshold (average of 0.5; 1; 2 and 4 kHz) for 197 ears was 108.6 dBHL (range: 90.0 - 120 dBHL; 9.2 SD). Available pre-operative behavioral audiological data confirmed a profound (>90 dBHL) degree of hearing loss in all ears with available data.

In line with the national cochlear implant evaluation protocol (South African Cochlear Implant Group, 2011) all children (n=264) underwent diagnostic electrophysiological assessment pre-operatively and these original diagnostic test results were only available for 95 (36%) children. The files of these children were reviewed for ABR and ASSR test results

specifically. The files of fifty (52,6%) children contained both ABR and ASSR test results, while 24 files (25.3%) contained only ABR test results and 21 files (22.1%) only ASSR test results (n=95). Pre-operative click-ABR threshold data were available for a total of 141 ears. A "no response" was obtained at the maximum output of the equipment (90 dBnHL) for 138 ears (97.9%), while for the remaining 3 ears (2.1%), an average click ABR threshold of 86.7 dBnHL (range: 80 - 90 dBnHL; 5.8 SD) was obtained (n=141). ASSR thresholds were available for 71 children and only the ears with comprehensive threshold data available at all required frequencies (0.5; 1; 2 and 4 kHz) were included. In a total of 119 ears the average ASSR threshold (determined for 0.5; 1; 2 and 4 kHz) was 112.0 dBHL (range: 90 – 120 dBnHL; 9.0 SD). Available pre-operative electrophysiological audiological data confirmed on average a profound (>90 dBHL) degree of hearing loss in all ears with available data.

3.4.4 Age of hearing loss suspicion and diagnosis

Data on whether newborn hearing screening (NHS) was conducted was available for only 85 children, of whom it was indicated that NHS was not done for 72.9% of them. Within the group of children with a confirmed congenital/early onset hearing loss (n= 191), only 64 caregivers reported the age at which they suspected the presence of the hearing loss for the first time (Table 3.4). The average age of diagnosis was 15.3 months (9.3 SD), with a delay of 5.3 months between suspicion and diagnosis of the hearing loss. The majority of children (94%) presented with a pre-lingual hearing loss (n=249).

Table 3.4 Age of congenital/early onset hearing loss suspicion and diagnosis

	Age at suspicion (months) *n*=64	Age at diagnosis (months) *n*=121	Delay from suspicion to diagnosis (months) *n*=61
Mean	11.3	15.3	5.3
S.D.	7.8	9.3	5.5
Max	36.0	45.0	27.0
Min	1.0	0.5	0

3.4.5 Age of intervention

Age of intervention was determined for children with confirmed congenital/early onset hearing loss (n=191/246). For this group the average age at implantation was 43.6 months (31.2 SD), with a delay of more than two years (24.7 months; 27.1 SD) between diagnosis and implantation (Table 3.5). Ages of initial hearing aid fitting and initial enrollment in early intervention services were available for 108 and 36 children, respectively (Table 3.5). Early intervention services, being either home- or centre-based, refer to any type of habilitative, rehabilitative or educational program provided to children with hearing loss and their parents (Joint Committee on Infant Hearing, 2007). On average, initial hearing aid fitting occurred at the age of 18.8 months (10.7 SD), 2.6 months (4.9 SD) after diagnosis. The average age of initial enrollment in early intervention services was 19.5 months (27.1 SD), with a delay of 3.2 months (6.7 SD) between initial hearing aid fitting and enrollment in early intervention services.

Table 3.5 Ages at initial hearing aid fitting, cochlear implantation and initial enrolment in early intervention services *(HA = hearing aid; CI = cochlear implantation; EI = early intervention)*

	Age at initial HA fitting (months) *n*=108	Delay from diagnosis to fitting (months) *n*=101	Age at CI (months) *n*=186	Delay from diagnosis to CI (months) *n*=116	Age at initial enrolment in EI (months) *n*=36	Delay from initial HA fitting to EI services (months) *n*=31
Mean	18.8	2.6	43.6	24.7	19.5	3.2
S.D.	10.7	4.9	31.2	27.1	12.6	6.7
Max	51.0	33.0	188.0	164.1	60.0	27.0
Min	1.0	0	6.0	3.0	2.0	0

3.5 Discussion

The risk profile of South African children with profound hearing loss in this study showed the most prevalent risks to be NICU admittance (28.1%), family history of childhood hearing loss (19.6%) and prematurity (15.1%). Occurrence of natal (23.3%) and postnatal (34.7%) risk factors were more common than pre-natal (12.3%) risk factors. NICU stay for longer than five days is considered as one of the most common risk factors for childhood hearing loss (Swanepoel et al., 2013; Young, Reilly, & Burke, 2011). Data on the duration of NICU stay for this study was only available for 41 children. Of this smaller subset, admittance to NICU for longer than 5 days was indicated for 90.2% of children (n=37/41). For the cohort of children diagnosed with ANSD, admittance to NICU was also indicated as the most prevalent (80%) risk factor. NICU admittance is an established risk factor for ANSD (Joint Committee on Infant Hearing, 2007; Korver, van Zanten, Meuwese-Jongejeugd, van Straaten, & Oudesluys-Murphy, 2012) as indicated in a Nigerian study where over half (54.5%) the children diagnosed with ANSD were admitted to hospital for serious illness within the neonatal period (Olusanya et al., 2008).

Caesarian section constituted more than half (60%) of the births in the study sample. Whilst unusually high South Africa is known for high rates of caesarian births. Caesarian births in South Africa has been reported to constitute 21% of births in general and 43.1% of births amongst White women (Department of Health, 2003). With 66% of the current sample being White this is likely to have increased the number of represented caesarian sections. Furthermore, the influence of malpractice litigation and a higher prevalence of high-risk pregnancies in this sample are also likely to have led to the high caesarian section rate for the study sample (R. Ching, 2006).

The second most common risk factor for the total sample was family history of permanent childhood hearing loss, revealing a higher prevalence (19.6%) than previously reported for developing contexts. In a Nigerian sample of children from schools for the deaf, family history of permanent childhood hearing loss was indicated as an associated perinatal factor for 6.9% children (Olusanya & Okolo, 2006).

Neonatal jaundice/hyperbilirubinemia was indicated as the most common postnatal risk factor (10.5%) for the sample population, with a further 2.3% of children requiring a subsequent blood transfusion. Two separate Nigerian studies indicated a prevalence of 4.9% in a sample of children diagnosed with SNHL (Lasisi, Ayodele, & Ijaduola, 2006) and 13.5% in a cohort of children with severe-profound hearing loss (Olusanya & Okolo, 2006). Hyperbilirubinemia has been associated as the most commonly reported risk factor for ANSD, varying between 30 to 70% (Berlin et al., 2010; Beutner, Foerst, Lang-Roth, Von Wedel, & Walger, 2007; T. Ching, Day, et al., 2013; Kirkim, Serbetcioglu, Erdag, & Ceryan, 2008). The current study had 50% of ANSD cases presenting with hyperbilirubinemia as a

risk factor similar to a recent report from South Africa in which half of the ANSD cases (n=5/10) also presented with hyperbilirubinemia (Swanepoel et al., 2013).

Meningitis occurred in 10% of the total study sample and was recorded as the second most prevalent postnatal risk factor. Bacterial meningitis is the most common cause of acquired SNHL in infants and children and accounts for about 6% of all cases of SNHL in the pediatric population (Fortnum & Davis, 1993; R. J. H. Smith, Bale, & White, 2005). Among developing countries the incidence of meningitis is the highest in Africa, mainly in sub-Saharan Africa, often referred to as the sub-Saharan meningitis belt (Pitkaranta et al., 2007). Meningitis prevalence ranging from 7.8% to 22% was reported for children with permanent hearing loss from Nigeria (Lasisi et al., 2006; Somefun, Lesi, Danfulani, & Olusanya, 2006). In Angola, severe-profound permanent hearing loss was diagnosed in 30% of children with acute bacterial meningitis (Pitkaranta et al., 2007).

One in every ten children in the current study also presented with an associated syndrome, with Waardenburg syndrome constituting 52% of these cases. Within a sample of pediatric cochlear implant recipients, Young et al. (2011) also reported 9.5% of children presenting with a syndrome. Waardenburg syndrome however, constituted only 10.8% of these cases. A previous South African etiological survey dating back three decades (Sellars & Breighton, 1983) reported 6.6% of children with confirmed severe-profound hearing loss presenting with a syndrome, with Waardenburg syndrome being represented by 43.8% of cases. For the present study the most common additional developmental conditions were indicated as visual impairment (8.5%) and cerebral palsy (5.6%). This corresponds to a UK epidemiological study (Fortnum, Marshall, & Summerfield, 2002) where visual impairment was reported in 5.4 to 7.5% and cerebral palsy in 2.5 to 3.6% of children with profound

hearing loss. Additional developmental conditions were particularly common in cases of ANSD for whom more than half (58%) had at least one additional developmental condition. This increased incidence of additional disabilities is typically reported for children with ANSD (T. Ching, Day, et al., 2013).

Up to 25% of bilateral childhood hearing losses reportedly have a postnatal onset (Weichbold, Nekahm-Heis, & Welzl-Mueller, 2006). In the current study population 20.3% of children presented with a postnatal onset with 8.5% having a late onset progressive hearing loss and 11.8% having sudden hearing loss. ANSD was diagnosed in 5% of the cases which compares to previous reports where the prevalence of ANSD in children ranged from 4.1 to 14% (Foerst et al., 2006; Walton, Gibson, Sanli, & Prelog, 2008; Young et al., 2011). For developing countries such as India and Egypt, the reported prevalence ranges are 13.4 to 14% (Mittal et al., 2012; Sanyelbhaa Talaat, Kabel, Samy, & Elbadry, 2009) and reports available for sub-Saharan Africa suggest an even higher prevalence. In Nigeria the reported prevalence ranges between 10.3 to 15.9% (Olusanya & Somefun, 2009) and in South Africa an even higher prevalence of 21.4% was recently reported (Swanepoel et al., 2013). In the current cohort of children with PCEHL the prevalence of ANSD is lower than expected and may be attributed in part to the majority of the research sample (92.4%) being private health care patients. In South Africa, perinatal risk factors are more likely to occur in public health care patients, since adequate health care are known to be more accessible for private patients (Saloojee & Pettifor, 2005). Therefore, children in this study were less exposed to environmental, maternal and child health related risk factors that predispose ANSD in populations from the developing world (Olusanya & Somefun, 2009; Swanepoel, 2010). Also, since this cohort include children being diagnosed with profound PCEHL over the past 18 years, it is possible that the diagnosis of ANSD was not differentiated from SNHL in earlier

years, given that the first report on auditory neuropathy dates back to 1996 (Starr, Picton, Sininger, Hood, & Berlin, 1996) and accurate diagnosis of the disorder only followed in subsequent years. The first documented diagnosis of ANSD in the current study cohort dates back to 2007 which corresponds to the first ANSD diagnosis in a recently reported retrospective study from South Africa (Swanepoel et al., 2013).

In the current study, PCEHL was typically diagnosed late (15.3 months, 9.3 SD) resulting in delayed initiation of intervention. On average, caregivers suspected hearing loss by 11.3 months of age, with a delay of 5.3 months until eventual diagnosis. In spite of the age of parental suspicion corresponding with a Nigerian sample (Olusanya, Luxon, & Wirz, 2005), this study's results indicate ages of suspicion and diagnosis much earlier than recent South African reports (Butler et al., 2013; Swanepoel et al., 2013; Van der Spuy & Pottas, 2008). Children with profound hearing losses are however known to be identified at earlier ages than children with less severe degrees of hearing loss, since the symptoms of profound hearing loss are more apparent and may prompt parents to seek audiological evaluation sooner (Durieux-Smith et al., 2008). This could be a reason for earlier suspicion, diagnosis and intervention within this study sample, in contrast to former South African reports that included children with degrees of hearing loss ranging from mild to profound. In spite of earlier diagnosis, NHS was not done for 72.9% of children (n=62/85), reflecting the current EHDI status in South Africa where NHS services are offered in only a few hospitals in both the public and private health care sectors (Meyer et al., 2012; Theunissen & Swanepoel, 2008). With recent South African reports on infant hearing loss mainly focusing on screening and diagnosis, limited information is available on ages of intervention (Swanepoel et al., 2009). In the current study, earlier ages of intervention in terms of initial hearing aid fitting and initiation of early intervention services was reported in comparison to a study sample

from the Western Cape (Van der Spuy & Pottas, 2008). For children not benefitting from acoustic amplification, early access to sound through early cochlear implantation has been widely advocated (Fitzpatrick, Johnson, & Durieux-Smith, 2011; Kral & O'Donoghue, 2010; Tait, De Raeve, & Nikolopoulos, 2007). Nonetheless, the average age of implantation for children with a congenital/early onset hearing loss in this study exceeded three and a half years of age, indicating a delay of more than two years from diagnosis to implantation. Cochlear implants are not provided by the South African National Department of Health and caregivers of children requiring cochlear implantation need to have adequate finances or access to funding from a private medical aid to be able to acquire this technology (Kerr et al., 2012). In 2010 the total average costs for a child for the first five and ten years post implantation was determined to be 298 961 ZAR and 455 225 ZAR respectively (Kerr et al., 2012), with the current USD/ZAR conversion rate being 1 USD to 11.21 ZAR. Since implant systems are manufactured outside of South Africa and imported for use, these costs may fluctuate as a result of exchange rate changes (Kerr et al., 2012). Also, as a result of the weakening ZAR against the USD the past few years, implantable devices have become more expensive. With the average monthly income level of South African citizens in 2010 being only 2 800 ZAR (Statistics South Africa, 2010), it is clear that funding constraints as well as a lack of prompt referral to specialized cochlear implantation services are likely contributing factors to late implantation. Since age of implantation rather than age of diagnosis is considered as the primary predictor of language outcomes in implanted children (Nicholas & Geers, 2006), effort should be made to identify factors contributing to delayed cochlear implantation. The current study population, consisting of predominantly White (66.2%) Afrikaans speaking (50.8%) children from the private health care system (92.4%) is a representative sample of pediatric cochlear implant recipients in South Africa. This sample is

not however, representative of the larger South African population reflecting the general disparities in health care access across ethnicities. Current population estimates indicate that 79.8% of the population is of African ethnicity with 74.9% speaking an African first language (Statistics South Africa, 2011, 2013). Also, only 15% of the population are covered by private health care financing, while the majority (85%) of the population rely on public health care for health services (Blecher & Harrison, 2006). The demographic distribution of the study sample highlights the persistent health care inequalities for advanced interventions such as cochlear implants in South Africa with previously disadvantaged people groups still marginalized. Despite the selective nature of this South Africa study sample (i.e. more privileged) critical periods for intervention, prior to 12 months of age, are not realized for children with profound hearing loss (Joint Committee on Infant Hearing, 2007; Olusanya, 2011; Pimperton & Kennedy, 2012; Yoshinaga-Itano, 2004).

3.6 Conclusion

The most prevalent associated risks for profound PCEHL in South Africa included NICU admittance, family history of childhood hearing loss, prematurity, hyperbilirubinemia and meningitis. Profound hearing loss was typically sensorineural with a congenital onset and a 5% prevalence of ANSD. Diagnosis of PCEHL was delayed, resulting in deferred ages for initial hearing aid fitting, enrollment in early intervention services, and eventual cochlear implantation. Even though average ages for intervention were earlier than previously reported in South Africa, necessary early auditory stimulation required for optimal outcomes for children with profound PCEHL, is not typically realized.

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CHAPTER 4

PREDICTORS OF PEDIATRIC COCHLEAR IMPLANTATION OUTCOMES IN SOUTH AFRICA

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4.1 Abstract

Objective: To identify and describe predictors of pediatric cochlear implantation outcomes in a South African population.

Methods: A retrospective study of 301 pediatric cochlear implant (CI) recipients from five cochlear implant programs was conducted and cross-sectional outcome data were added at the time of data collection. Twenty potential prognostic factors were identified from the retrospective dataset, including demographical, CI, risk and family factors. Regression analyses were performed to identify predictor variables that influence outcomes in terms of auditory performance (CAP scores), speech production (SIR scores), communication mode and educational placement.

Results*:* Although implanted children within this sample did not have equal opportunity to access a second implant, bilateral implantation was strongly predictive of better auditory

performance and speech production scores, an oral mode of communication and mainstream education. NICU admittance/ prematurity were associated with poorer auditory performance and speech production scores, together with a higher probability for non-oral communication and non-mainstream education. The presence of one or more additional developmental condition was predictive of poorer outcomes in terms of speech production and educational placement, while a delay between diagnosis and implantation of more than one year was also related to non-mainstream education. Ethnicities other than Caucasian were predictive of poorer auditory performance scores and a lower probability for mainstream education.

Conclusion: An extensive range of prognostic indicators were identified for pediatric CI outcomes in South Africa. These predictive factors of better and poorer outcomes should guide pediatric CI services to promote optimal outcomes and assist professionals in providing evidence-based informational counselling.

4.2 Introduction

In recent years, significant improvement has been demonstrated in pediatric cochlear implant (CI) outcomes due to technological advances, earlier implantation and earlier intervention (Amirsalari et al., 2012; Birman et al., 2012; Kral & O'Donoghue, 2011). Speech and language skills comparable to normal hearing children can be achieved in some pre-lingually deaf children implanted within the first year of life, as indicated by recent reports (T Ching et al., 2009; Niparko et al., 2010; Wie, 2010). Understandably, expectations for pediatric cochlear implantation are high (Birman et al., 2012). However, outcomes vary as

multiple internal and external factors have the potential to affect clinical outcomes (Black et al., 2014; Tyc Ching, Crowe, & Martin, 2010; Hawker et al., 2008). As a result many pediatric cases present with sub-optimal outcomes. In order to counsel families pre-operatively about the range of possible outcomes and to plan for post-implantation intervention, accurate prognostic information is required (Black et al., 2011; Graham O'Brien et al., 2012).

Indications for pediatric cochlear implantation are becoming more complex with an increase in bilateral implantation and a growing number of children with less severe hearing losses being implanted (Black et al., 2011; Dettman et al., 2004; Fitzpatrick et al., 2009; Sparreboom et al., 2012; Tait et al., 2010). Also, children with multiple medical conditions resulting from prematurity or perinatal etiologies are more likely to be considered as candidates, expanding the criteria for implantation even more (Teagle, 2012). Consequently the number of pediatric cochlear implantation surgeries has increased significantly since 1990 (Özdemir et al., 2013), which necessitates a clear understanding of potential threats to overall outcomes in this population (Black et al., 2014).

In a recent systematic literature review on prognostic indicators in pediatric CI surgery, Black et al. (2011) identified only four factors influencing pediatric CI outcomes consistently, namely age at implantation, presence of inner ear malformations, as well as occurrence of meningitis and Connexin 26 GJB2 gene-related deafness. Firstly, early implantation is indisputably considered as a strong positive predictor of expressive and receptive language skills, as confirmed by a plethora of published studies (Black et al., 2014; Boons, Brokx, Dhooge, et al., 2012; Govaerts et al., 2002; Habib et al., 2010; Manrique et al., 2004; May-Mederake, 2012; Nicholas & Geers, 2007; Svirsky et al., 2004; Zwolan et al., 2004). Secondly, inner ear malformations are strongly associated with pediatric CI outcomes in terms of

speech perception and expressive language skills, with children who have more severe cochlear malformations (e.g. cochlear dysplasia and common cavity) performing worse than children with less severe malformations (e.g. incomplete partition or enlarged vestibular aqueduct) (Black et al., 2014; Broomfield et al., 2010; Eisenman et al., 2001; Kim et al., 2006; Rachovitsas et al., 2012). Thirdly, despite the fact that the central effects associated with meningitis may impact language learning potential (Francis et al., 2004), children with postmeningitic hearing loss do appear to benefit from CIs in terms of auditory receptive abilities, provided they receive an implant early (Nikolopoulos et al., 2006). However, for children with ossified cochleae as a result of meningitis, speech perception is frequently poorer than children with non-ossified cochleae (El-Kashlan et al., 2003). Lastly, Connexin 26 GJB2-related deafness in children with CIs appear to have lesser impacts predicting better speech intelligibility, speech discrimination and communication abilities when compared to implanted children with other etiologies of hearing loss (Gérard et al., 2010; Sinnathuray, Toner, Clarke-Lyttle, et al., 2004; Sinnathuray, Toner, Geddis, et al., 2004).

Many other prognostic factors are described in literature, but only anecdotally, mostly due to small sample sizes (Black et al., 2011). Likewise, emerging trends in pediatric cochlear implantation such as multiple disabilities, family influences and the impact of prematurity still require further evaluation as prognostic indicators (Black et al., 2014). The presence of additional disabilities negatively effects the language development of implanted children (Birman et al., 2012; Boons, Brokx, Dhooge, et al., 2012; Gérard et al., 2010; Rajput et al., 2003). Yet outcomes after cochlear implantation for these children with associated disabilities, even if variable, show a positive evolution in speech perception, communication abilities, social engagement and quality of life (Berrettini et al., 2008; Kral & O'Donoghue, 2011). Problematic family environments are significantly associated with poorer speech and

language outcomes (Black et al., 2014; Holt et al., 2012). Then again, family factors such as a high socioeconomic level (Geers et al., 2003; Gérard et al., 2010; Niparko et al., 2010), sufficient parental involvement in the rehabilitation process (Boons, Brokx, Dhooge, et al., 2012; Sarant et al., 2008; Spencer, 2004) and higher levels of maternal education (Cupples et al., 2014) are all related to improved language outcomes. Prematurity is considered as an anecdotal prognostic factor often described in pediatric CI literature, but has not been consistently proven (Black et al., 2012). The same holds for other likely etiological factors or risk indicators associated with permanent childhood hearing loss, such as neonatal intensive care unit (NICU) admittance, low birth weight and assisted ventilation (Joint Committee on Infant Hearing, 2007).

In recent years there has been increasing interest in outcomes of bilateral cochlear implantation, since it has become the standard of care for children with severe to profound hearing loss in developed countries (Sarant et al., 2014; Tait et al., 2010). The benefits of bilateral implantation in children are well documented in terms of improved localization (Lovett et al., 2010; Sparreboom et al., 2010; Van Deun et al., 2009) and enhanced speech recognition in quiet (Scherf et al., 2007; Zeitler et al., 2008) and in noise (Litovsky et al., 2006; Lovett et al., 2010; Van Deun et al., 2010) when compared to listening with a unilateral CI. Also recently confirmed, children with bilateral CIs have significantly better language outcomes compared to children with unilateral CIs (Boons, Brokx, Frijns, et al., 2012; Sarant et al., 2014). However, there is still a lack of evidence regarding the effect of bilateral cochlear implantation on broader outcomes such as literacy, academic skills and overall quality of life, particularly concerning long-term outcomes (Johnston et al., 2009; Sarant et al., 2014; Sparreboom et al., 2010).

Prognostication is considered as a key component in pediatric cochlear implantation. Parents will only be able to set evidence-based and achievable expectations for their children if they are guided by professionals who are able to discern the factors that will exert an adverse effect on outcomes (Black et al., 2012; Kral & O'Donoghue, 2011). Given the paucity of proven prognostic factors in pediatric cochlear implantation (Black et al., 2012), this current work aims to identify possible predictors of outcomes and to investigate the prognostic significance of these factors, in a large caseload of pediatric CI recipients in South Africa. Since the first multichannel cochlear implantation took place in South Africa in 1986, more than 1500 individuals has been implanted at nine respective CI programs (Kerr et al., 2012; South African Cochlear Implant Group, 2015). Therefore, this study also provides a broad depiction of the current status of pediatric cochlear implantation in South Africa and reports on an extensive range of prognostic indicators identified in an unselected group of pediatric CI recipients.

4.3 Materials and methods

A retrospective study of 301 pediatric CI recipients was conducted. Institutional ethics committee approval was obtained before data collection commenced.

4.3.1 Study population

Five South African CI programs participated in this multicenter study, from which four programs are situated in the Gauteng Province (University of Pretoria Cochlear Implant Unit, Johannesburg Cochlear Implant Program, Chris Hani Baragwanath Academic Hospital Cochlear Implant Program, Steve Biko Academic Hospital Cochlear Implant Program) and

one program in the Free State Province (Bloemfontein Cochlear Implant Program). Patient files of pediatric CI recipients at participating programs were reviewed retrospectively and cross-sectional outcome measures were added during an eight month data collection period. All children (≤18 years), implanted between 1996 and 2013 with a minimum of six months implant use at the time of data-collection and with data available on at least one outcome measure, were considered as eligible participants for this study. No case selection occurred and children from the complete range of educational and communication environments were included. The final sample consisted of 301 children, including eight (2.7%) children who were non-users of their CI devices (n=301). Of the total sample, 190 (63.1%) children were implanted unilaterally and 111 (36.9%) were implanted bilaterally at the time of data collection (n=301). All bilateral implants were performed sequentially, except for two children who were implanted simultaneously (2/111, 1.8%). The mean interval between first and second implant was 35 months (range: 1 - 156 months; 34.6 SD; n=107). Characteristics of the study population are presented in Table 4.1. Most children (94%) were implanted with Cochlear© devices and 18 children (6%) with Med-el© devices (n=301). With the exception of 13 children (5.3%), all children had a fully inserted electrode array in at least one cochlea (n=243). Nine children (9/301, 3%) had explant/re-implant procedures of their 1st/only implant, while four children (4/111, 3.6%) with bilateral implants were reimplanted in their 2nd ear. Of the children implanted unilaterally, most (81.8%, 108/132) used bimodal amplification. Less than a third of the children (29%, 77/265) made use of assistive listening devices. Almost all children had normal hearing parents (96.4%, 268/278).

Table 4.1 Characteristics of study population

Demographics	***% (n)***	**Hearing loss and CI characteristics**	***% (n)***
Gender		**Onset of hearing loss**	
Male	52.5 (158/301)	Congenital/ early onset	73.2 (188/257)
Female	47.5 (143/301)	Progressive	10.9 (28/257)
		Sudden	14.4 (37/257)
		Unknown	1.6 (4/257)
Ethnic category		**Age at diagnosis of hearing loss (months):**	
Caucasian	61.8 (186/301)	Congenital/ early onset (n=122)	
Black	24.3 (73/301)	Mean (SD)	16.1 (10.0)
Indian/ Asian	8.6 (26/301)	Range	1 - 60
Coloured	5.3 (16/301)	Post-natal (sudden/progressive) onset (n=51)	
		Mean (SD)	30.8 (31.2)
		Range	3 - 180
Home language		**Age at implantation (months):**	
Afrikaans	46.4 (129/278)	Congenital/ early onset (n=187)	
English	42.8 (119/278)	Mean (SD)	45.6 (32.5)
African language	4.0 (11/278)	Range	5 - 188
Other	6.8 (19/278)	Post-natal (sudden/progressive) onset (n=65)	
		Mean (SD)	64.9 (42.5)
		Range	9 – 193
Health sector		**Delay from diagnosis to implantation (months) in 1st ear** (n=188)	
Private	95.0 (286/301)		
Public	5.0 (15/301)	Mean (SD)	28.7 (28.5)
		Range	0.6 - 164.1
South African citizen		**Type of hearing loss**	
Yes	91.7 (276/301)	Sensory-neural	96.5 (275/285)
No	8.3 (25/301)	Auditory Neuropathy Spectrum Disorder	3.5 (10/285)

4.3.2 Description of variables

Regression modelling was performed to determine prognostic factors that will influence outcomes in terms of auditory performance (CAP scores), speech production (SIR scores), communication mode and educational placement.

Outcome variables

Both “auditory performance” and “speech production” were used as continuous outcome variables in this study. Auditory performance was rated by the Categories of Auditory

Performance (CAP) (Archbold, Lutman, & Marshall, 1995) - a language- and age-independent hierarchical scale of auditory receptive abilities. The CAP has 8 categories, ranging from 0 (unaware of environmental sounds) to 7 (use of telephone with a familiar person). A revised version, referred to as the CAP_R (Stacey, Fortnum, Barton, & Summerfield, 2006) was used, in which a ninth category was added (use of telephone with an unfamiliar person). The Speech Intelligibility Rating (SIR) (Allen, Nikolopoulos, & O'Donoghue, 1998) was used for the assessment of speech production to classify children's speech production according to one of five hierarchical categories, ranging from Category 1 (connected speech is unintelligible) to Category 5 (connected speech is intelligible to all listeners). Validity, reliability and inter-tester reliability of both the CAP and SIR scales has been confirmed (Allen, Nikolopoulos, Dyar, & O'Donoghue, 2001; Archbold, Lutman, & Nikolopoulos, 1998; Philips et al., 2009).

The research also included "communication mode" and "educational placement" as categorical outcome variables. Children's mode of communication included oral communication, South African Sign Language (SASL), total communication, and other alternative modes of manual communication (such as informal gestures or augmentative communication devices). Oral communication refers to the use of spoken language, with primary reliance on auditory cues for communication (Budenz et al., 2013). The children in this study, who were communicating orally, received auditory-oral or auditory-verbal style intervention. SASL is a system of manual communication using visual gestures and signs used by the Deaf community in South Africa, while total communication implies the combined use of oral speech, a formal sign language system, speech reading and audition for communication (Johnson, 2012). Educational placement of implanted children involved mainstream schooling (normal hearing educational setting), school for the Deaf (SASL mode

of communication), school for the hard of hearing (oral mode of communication), special school (following either a mainstream or adapted special syllabus), home school, or no school if children did not attend school for some reason (e.g. placement challenges as a result of multiple disabilities) or were too young to attend school.

Explanatory variables

The collected retrospective data included demographical, CI and hearing loss data (Table 4.1), as well as family and risk factor data (Table 4.2). From this retrospective dataset, 20 potential prognostic factors were identified and defined as categorical variables in two-way categories. These categorical predictors are presented in Table 4.3 in terms of biographical and hearing loss factors (gender, ethnicity, age of diagnosis of hearing loss), CI factors (choice of ear for first implant, age at implant, delay from diagnosis to implant, bilateral implantation), family factors (family history of permanent childhood hearing loss, parental marital status, highest educational qualification of father, highest educational qualification of mother, employment status of mother) and risk factors (additional developmental conditions, prenatal risk factors, admittance to NICU, prematurity, natal risk factors, post-natal risk factors, meningitis, risk factors in general).

Table 4.2 Risk and family factor prevalence

Syndromes and additional developmental conditions identified	*% (n)*	Risk factors identified	*% (n)*	Family factors identified	*% (n)*
Syndromes		**Prenatal risk factor**		Family history of permanent childhood hearing loss	20.1 (44/219)
Any syndrome diagnosed (including syndromes listed below)	9.5 (24/252)	Rubella	6.2 (14/225)		
		Cytomegalovirus	3.6 (8/225)		
		Twin/triplet	3.1 (7/225)	Parental marital status	
		Syphilis	0.4 (1/225)	Married	74.2 (196/264)
Waardenberg Syndrome	5.2 (13/252)	Toxoplasmosis	0.4 (1/225)	Divorced	15.9 (42/264)
Ushers Syndrome	1.2 (3/252)			Single	8.7 (23/264)
Pierre Robin Syndrome	0.8 (2/252)			Partner, not married	1.1 (3/264)
Leopard Syndrome	0.8 (2/252)				
				Parental hearing status	
				Both hearing	96.4 (268/278)
				One/both hearing loss	2.5 (7/278)
Additional developmental conditions		**Natal risk factor**			
		Admittance to NICU	26.9 (43/160)	Communication mode of mother	
1 or more condition present	24.4 (64/262)	Prematurity (≤34 weeks gestation)	13.9 (32/230)	Oral	97.8 (266/272)
Visual impairment	7.6 (20/262)	Low birth weight (<2500g)	9.1 (21/230)	Sign Language	1.5 (4/272)
Cerebral palsy	5.3 (14/262)	Extremely low birth weight (<1500g)	4.8 (11/230)	Total communication	0.7 (2/272)
ADHD	4.6 (12/262)	Birth asphyxia	1.7 (4/230)		
Mobility impaired	3.1 (8/262)	Maternal hypertensive disorder in pregnancy	1.3 (3/230)	Communication mode of father	
Learning disabilities	2.7 (7/262)			Oral	97.5 (274/281)
Autism	1.9 (5/262)	Rupture of membranes	1.3 (3/230)	Sign Language	1.4 (4/281)
Apraxia	1.9 (5/262)	Birth trauma	0.9 (2/230)	Total communication	1.1 (3/281)
Developmental motor delay	1.5 (4/262)	Rh incompatibility	0.4 (1/230)		
Epilepsy	1.1 (3/262)			Highest educational qualification: mother	
Cleft lip and/or palate	1.1 (3/262)			Tertiary qualification (University)	40.4 (38/94)
				Tertiary qualification (other)	19.1 (18/94)
				Matric completed	33.0 (31/94)
				High school (Grade 8-11)	7.4 (7/94)

Postnatal risk factor	
Meningitis	13.6 (31/228)
Neonatal jaundice/ hyperbilirubinemia	7.9 (18/228)
Blood transfusion	1.8 (4/228)
Viral infection (unspecified)	5.3 (12/228)
Ototoxic drugs	3.1 (7/228)
Mumps	0.9 (2/228)
Measles	0.4 (1/228)
Tuberculosis	0.4 (1/228)

Highest educational qualification: father	58.5 (48/82)
Tertiary qualification (University)	15.9 (13/82)
Tertiary qualification (other)	23.2 (19/82)
Matric completed	2.4 (2/82)
High school (Grade 8-11)	
Mother employment status	76.6 (98/128)
Employed	23.4 (30/128)
Not employed	
Father employment status	99.3 (146/147)
Employed	0.7 (1/147)
Not employed	

Table 4.3 Suspected prognostic factors

Prognostic factors	Two-way categories	*% (n)*
Biographic and hearing loss factors		
Gender	Male	52.5 (158/301)
	Female	47.5 (143/301)
Ethnic category	Caucasian	61.8 (186/301)
	Other	38.2 (115/301)
Age of diagnosis of hearing loss (congenital/early onset only)	Early diagnosis (<36 months)	93.4 (114/122)
	Late diagnosis (≥ 36 months)	6.6 (8/122)
Cochlear implant factors		
1st ear left/ right	Left	35.8 (106/296)
	Right	64.2 (190/296)
Age at implant 1st ear (congenital/early onset only)	Early implantation (<36 months)	49.2 (92/187)
	Late implantation (≥36 months)	50.8 (95/187)
Delay from diagnosis to 1st implant	<12 months	29.3 (55/188)
	≥12 months	70.7 (133/188)
Bilateral implant (including only cases with at least 6 month experience with bilateral implant)	Yes	29.0 (87/301)
	No	71.0 (214/301)
Family factors		
Family history of permanent childhood hearing loss	Yes	20.1 (44/219)
	No/ unsure	79.9 (175/219)
Parental marital status	Married	74.2 (196/264)
	Single/ divorced	25.8 (68/264)
Highest educational qualification: Mother	High school	40.4 (38/94)
	Tertiary education	59.6 (56/94)
Highest educational qualification: Father	High school	25.6 (21/82)
	Tertiary education	74.4 (61/82)
Mother employment status	Employed	76.6 (98/128)
	Not employed	23.4 (30/128)
Risk factors		
Additional developmental conditions		
	Yes (1 or more)	24.4 (64/262)
Admittance to NICU	None	75.6 (198/262)
	Yes	26.9 (43/160)
Prematurity (≤34 weeks gestation)	No	73.1 (117/160)
	Yes	13.9 (32/230)
Prenatal risk factors	No	86.1 (198/230)
	Yes (1 or more)	15.6 (35/225)
Natal risk factors	None	84.4 (190/225)
	Yes (1 or more)	23.5 (54/230)
Post-natal risk factors	None	76.5 (176/230)
	Yes (1 or more)	36.4 (83/228)
Meningitis	None	63.6 (145/228)
	Yes	13.6 (31/228)
Risk factors present (pre-natal, natal, post-natal combined)	No	86.4 (197/228)
	Yes (1 or more)	55.6 (133/239)
	None	44.4 (106/239)

4.3.3 Data collection

All pediatric CI recipients who met the inclusion criteria were identified at each of the five participating CI programs. After data capturers were identified and trained for each participating program, the clinical files of all eligible children were reviewed retrospectively. An electronic database was developed for the capturing of the retrospective data (Table 4.1; Table 4.2) amongst the participating programs. Cross-sectional outcome data in terms of auditory performance, speech production, communication mode and educational placement were added to the database at the time of data collection. CAP and SIR scores were allocated by experienced audiologists/ speech-language therapists involved in the rehabilitation of the children at the respective CI programs. These professionals also provided the outcome data on the communication mode and educational placement of the implanted children.

4.3.4 Statistical analysis

Simple descriptive statistics were utilized to define the study population in terms of demographical, CI and hearing loss characteristics (Table 4.1), as well as risk and family profiles (Table 4.2). From these characteristics, 20 suspected prognostic factors were identified (Table 4.3).

For age of hearing loss diagnosis and age at implantation, only the children with congenital/ early onset hearing loss were considered and categorized into either an early diagnosis/implantation (<36 months) or late diagnosis/ implantation (≥36 months) category.

For bilateral implantation, only the children who had at least 6 months experience with their bilateral implant at the time of data collection were considered as bilateral implant users (78.4%, 87/111).

Children were categorized into performance groups for auditory receptive abilities (CAP scores). Thus, a low score was defined as CAP category 0-4 and a high score as CAP category 5-8. Children's speech intelligibility was also categorized into performance groups according to SIR scores, indicating whether a child's connected speech is intelligible or not to a listener who concentrates and lip-reads. SIR category 1-2 was defined as a low score and SIR category 3-5 as a high score. Furthermore, children's hearing age with a CI (i.e. length of device use from the day of initial stimulation of 1st implant) at the time of the scoring of the CAP and SIR was defined in months and is hence referred to as hearing age at CAP/SIR. Children's mode of communication was described as being either oral or non-oral, with non-oral referring to children utilizing SASL, total communication or any alternative mode of manual communication. For educational placement children were divided in 2 groups: mainstream education and non-mainstream education.

For the purpose of variable selection for regression modelling, bivariate data analyses were undertaken to determine the existence of a possible association between a potential predictor (Table 4.3) and a categorical outcome variable, in two categories using the Pearson Chi-Square test. The p-values of the Pearson chi-square test on these 2x2 tables appear in Table 4.4.

Table 4.4 Predictors having a possible association with outcome variables

Potential predictors	**CAP score** (in two categories)	**SIR score** (in two categories)	**Communication mode**	**Educational placement**
Ethnic category (n=301)	0.095*	0.031**	0.096*	0.015**
Age at implant 1st ear (congenital/early onset hearing loss only) n=187	-	-	-	0.054**
Delay from diagnosis to 1st implant (n=188)	-	-	-	0.005**
Bilateral implantation (n=301)	0.000**	0.000**	0.000**	0.000**
Highest educational qualification of mother (n=94)	-	-	-	0.005**
Additional developmental conditions (n=262)	-	0.002**	0.027**	0.002**
Admittance to NICU (n=160)	0.002**	0.022**	0.008**	0.037**
Prematurity (≤34 weeks gestation) (n=230)	0.053*	-	-	-
Natal risk factors (n=230)	0.005**	0.058*	0.011**	0.072*
Post-natal risk factors (n=228)	0.003**	0.078*	0.085*	-
Meningitis (n=228)	0.066*	-	-	-
Risk factors present (in general) (n=239)	0.003**	-	0.031**	0.036**

**possible significance (0.05 < p < 0.1); **significance (p < 0.05)*

For the main prediction analysis, two types of regression were used: for continuous outcome variables (auditory performance and speech production), linear regression models in the form of multiway analysis of variance were constructed to investigate the influence of categorical predictors on the mean auditory performance (CAP scores) as well as the mean speech production (SIR scores).

Log linear models were constructed for categorical outcome variables (communication mode and educational placement) to model the log odds of children's mode of communication to be non-oral and the log odds of educational placement to be non-

mainstream in terms of the categorical predictors. An index for each category of a predictor can be calculated as the exponent of the regression coefficient of that category, obtained from the log linear model. The odds for any combination of categories of predictors can be found by multiplication of the overall mean odds (the exponent of the intercept term in the log odds model) with the indices of the specified categories. Based on these odds the probability for non-oral communication or non-mainstream educational placement was estimated by dividing the odds outcome by the factor (1 + odds).

Throughout the process two factors were additionally forced into the models. For the linear regression models, the hearing age at CAP/SIR factor (being either ≤36 months or ≥37 months) was added. The onset of hearing loss (being either congenital/ early onset or post-natal) was forced into both the linear regression models, as well as in the log linear models to ensure that a clear distinction was made statistically between children with congenital/ early onset (pre-lingual) hearing loss and children with post-natal (sudden or progressive) onset hearing loss.

4.4 Results

4.4.1 General clinical and outcome profile

The demographical, hearing loss and CI profile of the study sample are presented in Table 4.1. CAP and SIR scores were obtained for 240 children at the time of the study (240/301 or 79.7%). Overall, most children (164/240 or 68.3%) achieved high CAP scores (category 5-8), while 76 children (76/240 or 31.7%) achieved low CAP scores (category 0-4). For the total sample, high SIR scores (category 3-5) were attained by 171 children (171/240 or 71.2%),

with 69 children (69/240 or 28.8%) attaining low SIR scores (category 1-2). Average hearing age at CAP/SIR for this study sample was 67.4 months (range: 6 - 88 months; 43.6 SD; n=236). This hearing age at CAP/SIR was divided into two groups: children with a hearing age with CI of ≤36 months (73/236 or 30.9%) and children with a hearing age with CI ≥37 months (163/236 or 69.1%). Taking this hearing age with CI into account, for children wearing their implants ≥37 months, high CAP scores (128/163 or 78%) and high SIR scores (128/163 or 78%) were achieved for even more children.

Data on children's current mode of communication were obtained for 96.3% (290/301) of the total sample. Most children (74.5%, 216/290) were oral communicators, while 13.1% (38/290) utilized TC and 6.2% (18/290) used SASL. The remaining 6.2% (18/290) were using other alternative modes of manual communication. All children who were not oral communicators were grouped together as non-oral communicators (25.5%, 74/290).

For almost the entire sample (99%, 298/301), data were available on the educational placement of children. Just more than half of the children were in mainstream schools (52.3%, 156/298), while 15.1% (45/298) were in schools for the deaf (SASL mode of communication) and 7.4% (22/298) were in schools for the hard-of-hearing (oral mode of communication). A significant proportion of children (17.4%, 52/298) attended special schools where in half of the cases (50%, 26/52) a mainstream syllabus was followed and the other half of the cases (50%, 26/52) an adapted special syllabus was followed. Fourteen children (4.7%, 14/298) did not go to school, and another 9 children (3%, 9/298) were home-schooled. All children not attending mainstream schools were grouped together as being placed in non-mainstream education (47.7%, 142/298).

4.4.2 Linear regression analysis: auditory performance (CAP scores) and speech production (SIR scores)

Only the predictor variables that appeared to be associated with the outcome variables in the bivariate analysis were included in the regression models (Table 4.4). For the linear regression models, all associated predictor variables with a significance level of $p < 0.1$, as well as the two forced factors, were randomly fed into the model. During the model building process, the best predictors of the two continuous outcome variables (CAP and SIR scores) were identified.

The two resulting linear regression models showing the best predictors of outcomes in terms of auditory performance (model 1) and speech production (model 2) are presented in Table 4.5.

Table 4.5 Linear regression analysis results

Model	Outcome variables	Explanatory variables	DF*	Sum of Squares	F Value	Pr > F** (P value)	R^2
1	Auditory performance (CAP)	Bilateral implantation Prematurity Hearing age at CAP/SIR & ethnic category interaction	5	202.221	14.39	<0.0001	0.28
2	Speech production (SIR)	Bilateral implantation Additional developmental conditions Hearing age at CAP/SIR & NICU interaction	5	113.083	14.81	<0.0001	0.26

**DF: Degrees of freedom; **Pr>F: p-value of the F-test (with F-test testing the significance of the model)*

Both linear regression models (model 1 and 2) were highly significant (p = < 0.0001) and present with determination coefficients (R^2) of 28% and 26% respectively, giving an indication that less than 30% of the variation in the outcomes observed in the data were accounted for by the models. Accordingly, 72% of the variation in auditory performance outcomes and 74% of the variation in speech production outcomes was not explained by the selected factors in the linear regression models.

The boxplots in Figure 4.1 illustrate bilateral implantation, prematurity and ethnicity as predicting factors for the auditory performance outcome (regression model 1). It shows that children implanted unilaterally have significantly lower average CAP scores (minus 2 units) compared to children who are implanted bilaterally (p = 0.0003). The same results are observed for the prematurity factor where on average children born prematurely (≤34 weeks gestation) also score 2 CAP units lower (p = 0.0075). A third factor that was identified in model 1 was the interaction between the hearing age at CAP/SIR and ethnic category for the group of children with a hearing age with CI ≥37 months , showing a lower average CAP score (minus 2 units) for children with “other” ethnicities when compared to Caucasian children (p < 0.0001).

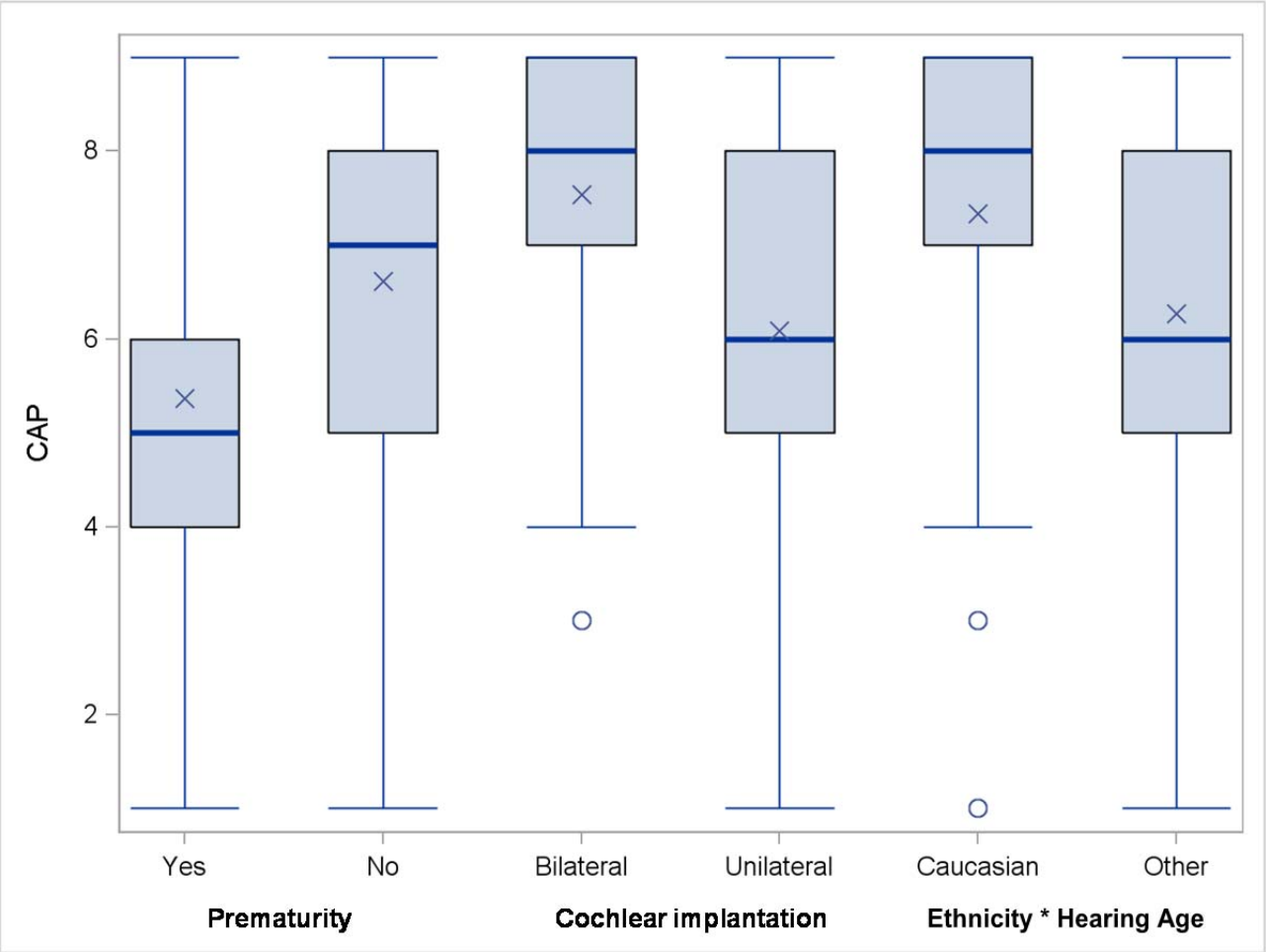

Figure 4.1 Bilateral implantation, prematurity and ethnicity*hearing age as predictors of auditory performance (CAP scores) n=193

The box plots represent the smallest observation, lower quartile, median (bold line), mean (x), upper quartile, largest observation, and outliers (>1.5 times interquartile range) (○). * interaction

The identified relevant predictors for speech production (regression model 2) (Table 4.2), illustrated by the boxplots in Figure 4.2, show that children with bilateral implants are expected to have an average SIR score of 5, compared to an average score of 3 for children with unilateral implants (p = 0.0038). Secondly, children with additional developmental conditions are expected to have a lower average SIR score of 3 when compared to children without any additional developmental conditions (average SIR score of 4) (p = 0.0002).

Lastly, the hearing age at CAP/SIR and NICU admittance interaction shows that for children with a hearing age with CI ≥37 months, those who were admitted to the NICU have lower SIR scores (minus 2.5 units) than those who did not have a history of NICU admittance (p = < 0.0001).

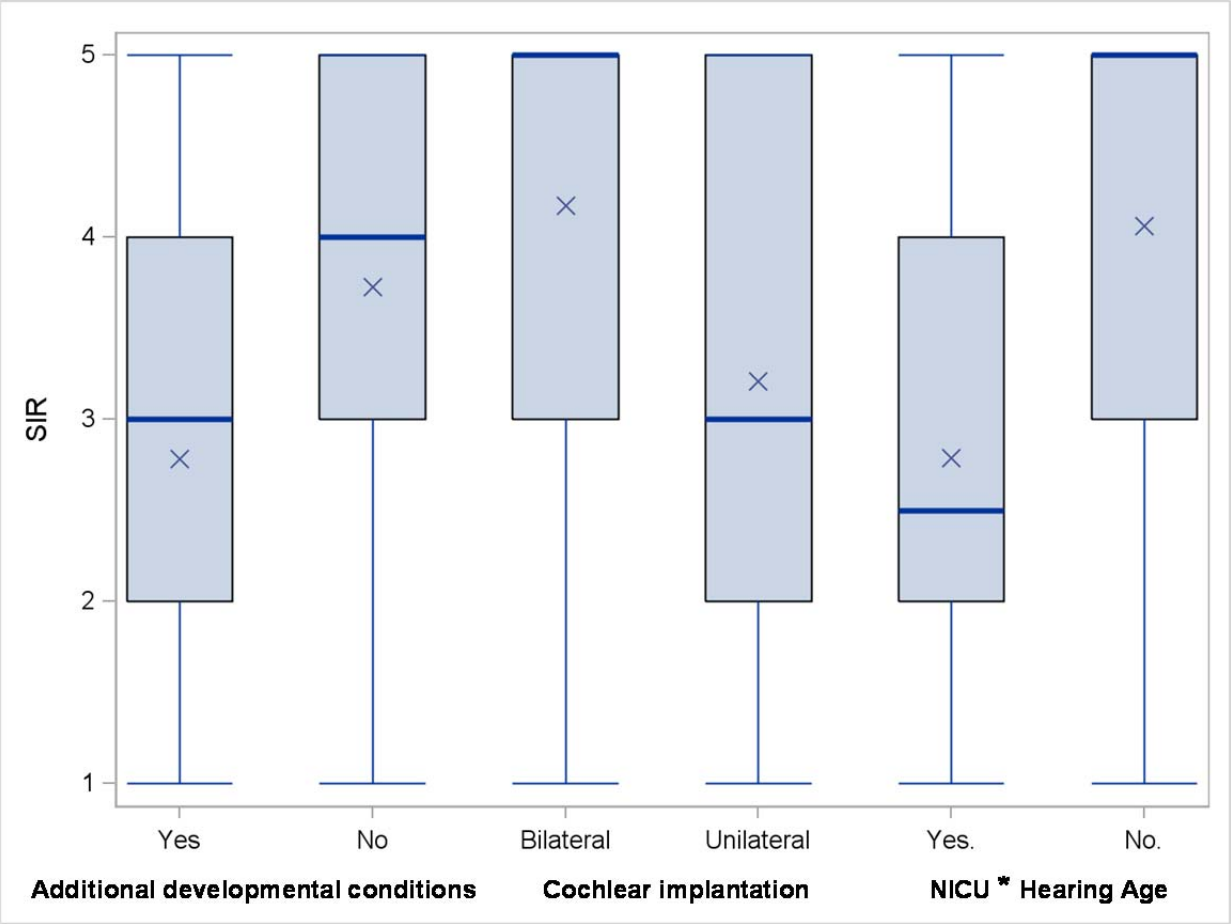

Figure 4.2 Bilateral implantation, presence of additional developmental conditions and admittance to NICU*hearing age as predictors of speech production (SIR scores) n=213

The box plots represent the smallest observation, lower quartile, median (bold line), mean (x), upper quartile, largest observation. *interaction

4.4.3 Log linear analysis: non-oral mode of communication and non-mainstream educational setting

Log linear modelling is used to determine the influence of a set of categorical explanatory factors on a categorical outcome. The cell frequencies within a combination of categories of predictors must be large enough. Therefore only a limited number of predictor variables in the categorical modelling can be considered for the sample sizes of n=139 and n=151 for the two odds models. In this study, only the predictor variables that were significantly associated with the categorical outcome variables were included ($p < 0.05$) (Table 4.4). Log linear model analysis was used to model the log of the odds to be a non-oral CI user (model 3) and the log of the odds to be a CI user in a non-mainstream educational setting (model 4). The statistical outcome of the log linear analysis is summarized in Table 4.6 in terms of indices. By using the indices, the odds to be non-oral and non-mainstream were calculated by multiplying the overall main effect (index of the intercept) with the indices of any combination of categories of predictors. The odds and percentage chance for models 3 and 4 are presented in Figure 4.3 and 4.4 respectively.

Table 4.6 Log linear analysis results (maximum likelihood estimates)

Model	Parameter (combined factors)	Categories	Estimate from log linear model	Index[a]
3	Overall mean odds		-1.2025	0.30
	Bilateral/ unilateral CI and natal risk factors	Bilateral CI	-0.3465	0.71
		Unilateral CI	0.3465	1.41
	Onset of HL, NICU admittance, risk factors (general) and additional developmental conditions	Congenital onset HL, NICU	0.5411	1.72
		Congenital onset HL, no NICU	-0.4027	0.67
		Post-natal onset HL	-0.1384	0.87
4	Overall mean odds		-0.0772	0.93
	Onset of HL, ethnicity, delay between diagnosis and implantation, bilateral/ unilateral implantation	Caucasian, congenital onset HL, <12 months, bilateral CI	-1.5484	0.21
		Post-natal onset HL	0.2921	1.34
		Other, congenital onset HL	0.6383	1.89
		Caucasian, congenital onset HL, >12 months, bilateral CI	-0.4461	0.64
		Caucasian, congenital onset HL, <12 months, unilateral CI	0.4095	1.51
		Caucasian, congenital onset HL, ≥12 months, unilateral CI	0.6546	1.92
	Additional developmental conditions and NICU admittance	Additional developmental condition, NICU	0.9102	2.49
		Additional developmental condition, no NICU	-0.1756	0.84
		No additional developmental condition	-0.7346	0.48

[a]*Index is the exponent of the estimate. An index lower than 1 indicates an odds (to be non-oral/ to be placed in non-mainstream education) that is lower than the average odds of 1 (low-risk category), while an index higher than 1 indicates an odds higher than average (high-risk category).*

For unilaterally implanted children with a congenital/ early onset hearing loss and a history of admittance to the NICU, there was a 42% probability to be a non-oral communicator, with the probability being almost half times less (22%) if children were not admitted to NICU (model 3, Figure 4.3). In contrast, should bilaterally implanted children with a congenital/ early onset hearing loss have a history of NICU admittance, the chance to be a non-oral communicator was less (27%). For children with a post-natal onset of hearing loss, those implanted unilaterally had a higher probability (27%) to be non-oral communicators, in contrast to children with bilateral implants (16%).

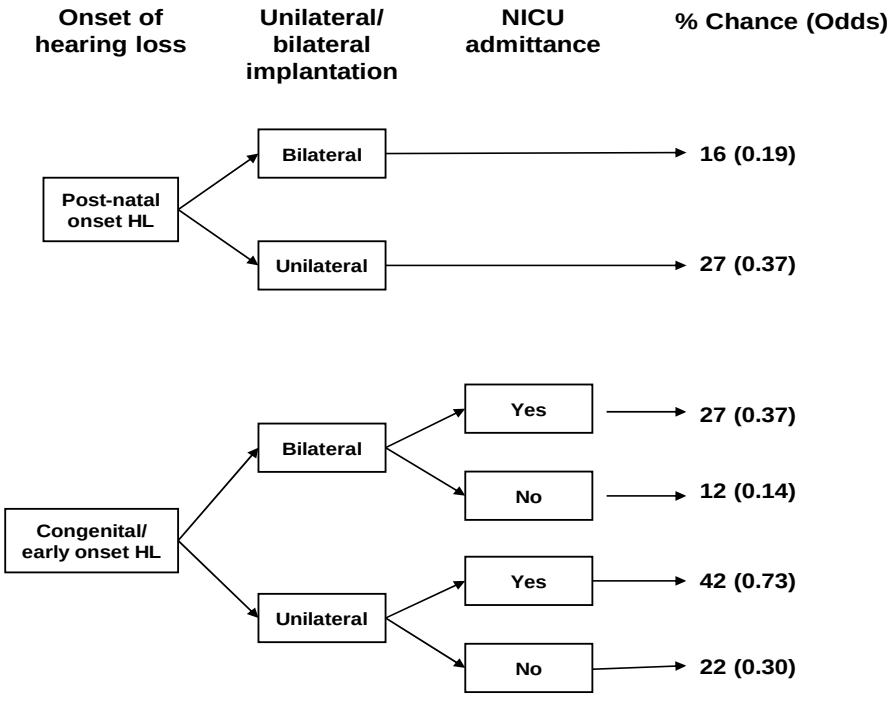

Figure 4.3 Associated probability predisposing non-oral mode of communication (model 3)
n=139

For model 4 (Figure 4.4), a very high probability for non-mainstream educational placement (82%) was indicated for Caucasian, unilaterally implanted children with a congenital/ early onset hearing loss, with a delay of more than one year between diagnoses and implantation, who presented with a history of NICU admittance and at least one additional developmental condition. Similarly a high chance for non-mainstream educational placement (81%) was indicated for all children with ethnicities other than Caucasian and a congenital/ early onset hearing loss, who were admitted to NICU and presented with at least one additional developmental condition. For Caucasian children with a congenital/ early onset hearing loss, with a delay of less than one year between diagnosis and implantation, who presented with a history of NICU admittance and the presence of at least one additional developmental condition, the difference in probability for non-mainstream education was significant between those implanted unilaterally (78%) and bilaterally (33%). Even if these children were not admitted to NICU, the difference in probability for unilateral implanted children (54%) and bilateral implanted children (9%) was still substantial. For children with a post-natal hearing loss, the probability to be placed in a non-mainstream educational setting were twice as high (76%) for those who were admitted to NICU and presented with at least 1 additional developmental condition, in contrast to those with no history of NICU admittance or additional developmental conditions (37%).

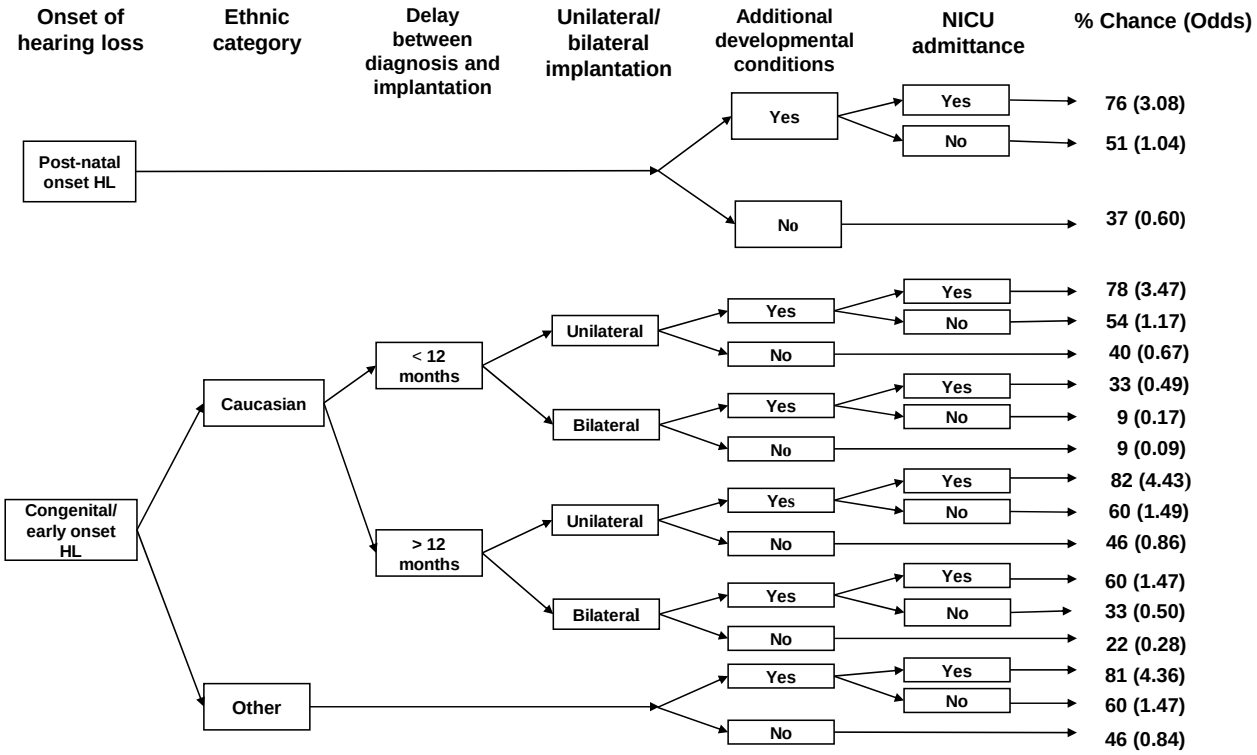

Figure 4.4 Associated probability predisposing non-mainstream educational setting (model 4) n=151

4.5 Discussion

A broad range of predictors for pediatric cochlear implantation outcomes in South Africa were identified. The vast majority of children (78%) implanted for more than three years achieved high CAP scores for auditory performance, and high SIR scores for speech production, suggesting they can understand spoken conversation with a familiar person and have connected speech that is intelligible for at least an experienced listener. Almost 75% of children in this study were oral communicators and more than half (56%) of children who used their implants for longer than three years were placed in mainstream educational settings. However, mainstream education as a measure of success in cochlear implantation

should be used with caution, since the emphasis should rather be on the appropriateness of education placement to each child's specific needs. Current educational policy in South Africa has the long-term goal to develop an inclusive education system, also for children with severe-profound hearing loss, which will address barriers to learning such as socio-economic barriers, language and communication and inflexible curriculums (Department of Education, 2001). Nonetheless, various persistent challenges, such as disparities in resourcing inclusive education across provinces and limited access to specialist support in public ordinary schools, currently impede the progress that is being made towards an inclusive education system (Department of Education, 2015).

Predictive factors for pediatric CI outcomes in this study were bilateral implantation, admittance to the NICU, prematurity, additional developmental conditions, ethnicity and the delay between diagnosis and implantation. Clear distinction was made in the statistical analysis of data between children with congenital/ early onset (pre-lingual) hearing loss and children with post-natal (sudden/progressive) onset hearing loss. This distinction is important when a heterogeneous caseload is considered, since it is expected that children with post-lingual onset hearing loss will mostly perform well after cochlear implantation as a result of more mature auditory pathways and early foundations for speech and language (Ahmad et al., 2012; Gray, Jones, & Court, 2003; Nicholas & Geers, 2007; Sharma, Dorman, & Spahr, 2002).

Bilateral implantation was a strong predictor for better auditory performance and speech production scores, and was associated with a lower probability for a non-oral mode of communication and a non-mainstream educational setting. Scherf at al.(2009) also used the CAP as outcome measure in a group of 35 children with bilateral CIs, showing that after

three years of bilateral implant use, higher CAP scores were obtained for significantly more children than before their second implant. Although the positive effect of bilateral implantation on spoken language development has recently been demonstrated (Boons, Brokx, Frijns, et al., 2012; Sarant et al., 2014), the influence of bilateral implantation on speech production remains to be demonstrated (Sparreboom et al., 2010). The strong association between bilateral implantation and the increased ability of children to produce intelligible speech in the current study, could be the direct result of the improved auditory input from a second CI, since speech perception and speech production skills are highly correlated with each other (Geers, Strube, Tobey, Pisoni, & Moog, 2011).

Evidence for bilateral cochlear implantation affecting educational outcomes is lacking (Johnston et al., 2009; Sparreboom et al., 2010). The current study provides preliminary evidence that children with bilateral CIs, in at least a subgroup of Caucasian children with congenital/ early-onset hearing loss, have a lower associated probability for non-mainstream education, compared to those children with unilateral CIs. Also, the probability for non-oral communication was greater for unilaterally implanted children, irrespective of onset of hearing loss. However, it is imperative that the association between bilateral implantation and better outcomes in this study should be viewed against the background that implanted children in South Africa do not have equal opportunity to access a second CI. With 95% of this sample representing the private health care sector, family financial resources remains to be a significant determining factor for bilateral implantation in South Africa, implying that a bilateral CI will only be accessible to children who's caregivers have adequate finances. As a result, it is more likely that unilaterally implanted children from affluent families, who communicates orally and already functions in mainstream educational environments, would be considered for bilateral implantation.

NICU admittance was associated with poorer speech production scores and a higher probability for non-oral communication and non-mainstream school placement, while prematurity was associated with lower auditory performance scores. To the authors' knowledge, NICU admittance, together with prematurity, has not yet been demonstrated as prognostic factors in pediatric CI. Robertson et al. (2009) reported that in a group of 1279 children admitted to NICU because of extreme prematurity, 3.1% presented with permanent childhood hearing loss, of whom 73% had more than one other major developmental disability. The outcomes of NICU graduates with permanent childhood hearing loss who eventually receive CIs are likely to be affected by the increased incidence of additional developmental conditions. NICU admittance and prematurity are therefore risk factors for poorer CI outcomes, likely related to the comorbidities that accompany these perinatal developmental challenges.

The presence of one or more additional developmental condition was found to be strongly predictive of poorer speech production scores, and was associated with a higher probability for non-mainstream education. It is estimated that 30 to 40% of children with profound deafness have additional disabilities (Birman et al., 2012; Cruz, Vicaria, Wang, Niparko, & Quittner, 2012; van Wieringen & Wouters, 2015), which is slightly higher than the 24% prevalence in this study population. In an outcome study of 119 three year old children with hearing loss and additional disabilities, of whom 29% were CI users, speech intelligibility ratings revealed relatively poor outcomes, with a mean rating of 4.2 on a scale from 1 to 6, where 1 represents 100% intelligibility (Cupples et al., 2014). Not only does the presence of additional developmental conditions negatively impact language development in pediatric CI recipients (Birman et al., 2012; Boons, Brokx, Dhooge, et al., 2012; Rajput et al., 2003) but

it may also prevent them from reaching their full potential cognitively, socially and educationally (Cupples et al., 2014).

Ethnicity was found to be a predictor of auditory performance and educational placement, with ethnicities other than Caucasian achieving lower auditory performance scores and having a higher associated probability for non-mainstream education. Not only in South Africa, but all over the world many areas of healthcare are replete with evidence of socioeconomic status and ethnicity related disparities, with pediatric cochlear implantation being no exception (Kirkham et al., 2009; Stern, Yueh, Lewis, Norton, & Sie, 2005; Tobey, Geers, Brenner, Altuna, & Gabbert, 2003). The current study population consisted of predominantly Caucasian (62%) children from the private health care system (95%), speaking either Afrikaans (46%) or English (43%). This sample could be considered as representative of pediatric CI recipients in South Africa and reflects the current health care inequalities for advanced interventions such as CIs. However, this sample does not represent the larger South African population, with 79.8% of the population being of African ethnicity, 74.9% speaking an African first language and 85% relying on public health care for health services (African, 2000; Blecher & Harrison, 2006; Statistics South Africa, 2011). Ethnicity as a prognostic indicator in this study is most likely a proxy for social and health inequality.

A delay between diagnosis and implantation of more than 12 months was strongly associated with a higher probability of non-mainstream school placement in at least a subgroup of Caucasian children with congenital/ early-onset hearing loss. With the recent emphasis on early access to sound through early implantation, late implantation is now defined as more than 12 months after diagnosis of hearing loss (Fitzpatrick, Ham, &

Whittingham, 2015). Early implantation during periods of optimal neural plasticity maximizes early auditory experience and leads to more age-appropriate speech and language skills (T. Ching, Dillon, et al., 2013; Leigh, Dettman, Dowell, & Briggs, 2013; Sharma et al., 2002), which may also increase the likelihood for mainstream education from earlier ages onwards. Likely contributing factors for this delay between diagnosis and implantation include funding constraints, lack of prompt referral to specialized CI services, parental barriers such as delayed/missed appointments, complex medical conditions, family indecision and geographical location (Armstrong et al., 2013; Fitzpatrick et al., 2015; le Roux, Swanepoel, Louw, Vinck, & Tshifularo, 2015).

Within this relatively large dataset, various factors were identified to be predictive of outcomes, however the determination coefficients of the linear regression models were less than 30% and do not account for two-thirds of the remaining variation in auditory performance and speech production outcomes. This implies that both outcomes are in reality determined by many more single or interacting factors not included in the different models used herein.

Unlike many other studies, age of implantation was not confirmed as a prognostic factor for this dataset. A possible explanation for this could be the fact that this study examined outcomes at a single point in time, rather than longitudinally, as also reported by other studies (Geers et al., 2003; Percy-Smith, Cayé-Thomasen, Breinegaard, & Jensen, 2010). It might be that some of the advantages for early implantation are more evident at younger ages, becoming less apparent when children become older.

4.6 Conclusion

Bilateral implantation was a strong predictor of better auditory performance and speech production outcomes, and was strongly related to an oral communication mode and mainstream education. However, since family financial resources remains a decisive factor for bilateral implantation in South Africa, not all implanted children in this dataset had the opportunity to access a second CI. NICU admittance/ prematurity were predictive of poorer auditory performance and speech production outcomes, together with a higher probability for non-oral communication and non-mainstream education. The presence of one or more additional developmental conditions was associated with poorer outcomes in terms of speech production and educational placement, with a delay between diagnosis and implantation of more than 12 months also being associated with non-mainstream schooling. Ethnicity was validated to be predictive of auditory performance outcomes and educational setting, with ethnicities other than Caucasian having lower auditory performance outcomes and a lower probability for mainstream education. The challenges associated with multicenter retrospective data collection in this study, such as unsystematic, missing and inconsistently recorded data, highlighted the need for the implementation of a shared data recording methodology across programs in South Africa. Only within such an agreed standardized framework, with universal standardized outcome measures, can compatible patient and outcome data be captured and utilized for the purpose of collaborative multicenter research (Black et al., 2014). Irrespective, findings from this study provide valuable guidance and understanding into the causes of variation of pediatric CI outcomes, and also contribute to evidence-based pediatric CI services that promote optimal outcomes.

4.7 Acknowledgements

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CHAPTER 5

PREDICTORS OF HEALTH-RELATED QUALITY OF LIFE IN ADULT COCHLEAR IMPLANT RECIPIENTS IN SOUTH AFRICA

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5.1 Abstract

Objective: To identify and describe predictors of health-related quality of life (HRQoL) outcomes for adult cochlear implant (CI) recipients in South Africa.

Design: A retrospective study of adult CI recipients was conducted and cross-sectional HRQoL outcome data were added at the time of data-collection, using the Nijmegen Cochlear Implant Questionnaire. Twenty-two potential predictive factors were identified from the retrospective dataset, including demographic, hearing loss, CI and risk related factors. Multiple regression analyses were performed to identify predictor variables that influence HRQoL outcomes.

Study sample: The study sample included 100 adult CI recipients from four CI programs, implanted for at least 12 months.

Results*:* History of no tinnitus prior to CI, bilateral implantation and mainstream schooling were strongly predictive of better overall HRQoL outcomes. Factors such as age, age at implant, gender, onset of hearing loss, duration of CI use and presence of risk factors did not predict HRQoL scores.

Conclusion: A range of significant prognostic indicators were identified for HRQoL outcomes in adult CI recipients. These predictors of HRQoL outcomes can guide intervention services' informational counselling.

5.2 Introduction

Cochlear implantation is a well-established intervention for individuals with severe-profound sensorineural hearing loss who obtain no or insufficient benefit from acoustic amplification. With the broadening of implantation criteria, increased numbers of adult patients are being implanted at advanced ages and with less severe hearing losses (Olze et al., 2011). Cochlear implantation does not only affect the hearing, speech perception and speech production abilities of a patient, but it also has a broader impact on social functioning, daily activities and self-esteem (Hinderink et al., 2000; Hirschfelder et al., 2008) In recognizing the need to measure and objectify the benefits or limitations of medical interventions on an individuals' social, emotional and physical well-being, the term quality of life (QoL) has been defined (Loeffler et al., 2010). QoL is a broad ranging concept, referring to an individual's perception of his/her position in life, affected in a multifaceted

way by psychological state, level of independence, social relationships, personal beliefs and physical health (World Health Organization, 1998). More specifically, this general health status of patients, often referred to as health-related quality of life (HRQoL), has been recognized as a more comprehensive measure of medical intervention outcomes (Mo et al., 2005).

In order to capture cochlear implant (CI) patient outcomes more holistically, the functional impact of permanent hearing loss and consequent treatment on personal well-being should be assessed through HRQoL measures (Capretta & Moberly, 2015; Zaidman-zait, 2010). In recent years, in addition to standard speech perception testing, HRQoL has become a widespread outcome measure to quantify and monitor CI outcomes. Significant improvement between pre- and post-implantation HRQoL scores was documented for unilaterally implanted post-lingually (Chung et al., 2012; Damen et al., 2007; Hinderink et al., 2000; Hirschfelder et al., 2008; Klop et al., 2008; Mo et al., 2005; Olze et al., 2011), as well as pre-lingually (Klop et al., 2007; Straatman et al., 2014) deafened adult CI recipients. Similarly, HRQoL measures revealed a positive effect of implantation for unilaterally implanted post-lingually deafened elderly patients (Orabi et al., 2006; Sanchez-Cuadrado et al., 2013; Vermeire et al., 2005) and also adult patients implanted for single-sided deafness (Arndt et al., 2011; Vermeire & Van De Heyning, 2009). Recent studies also demonstrate improved HRQoL for bilateral sequential cochlear implantation compared to unilateral implantation (Härkönen et al., 2015; King et al., 2014; Olze et al., 2012).

Various factors have been identified as predictors of improved outcomes in adult CI recipients in terms of speech recognition performance, including better pre-operative speech recognition, shorter duration of deafness, higher educational level, oral mode of

communication during childhood, progressive hearing loss, earlier age at implantation and positioning of electrode arrays closer to the modiolar wall (Caposecco et al., 2012; Friedland et al., 2010; Hirschfelder et al., 2008; Holden et al., 2013; Klop et al., 2008; Leung et al., 2005). Yet, these factors do not necessarily contribute to broader HRQoL outcomes (Capretta & Moberly, 2015) and as a result, identifying patient factors that predict outcomes in terms of HRQoL is of specific interest. This prognostic information is not only required for the planning of post-implantation intervention, but also to counsel potential CI recipients pre-operatively about the range of possible outcomes (Black et al., 2011).

A significant association between speech perception testing outcomes and HRQoL scores have been indicated in several studies (Cohen, Labadie, Dietrich, & Haynes, 2004; Damen et al., 2007; Francis, Chee, Yeagle, Cheng, & Niparko, 2002; Hirschfelder et al., 2008; Vermeire et al., 2005). However, this association could not be replicated by a number of studies (Capretta & Moberly, 2015; Hinderink et al., 2000; Maillet, Tyler, & Jordan, 1995; Mo et al., 2005; Straatman et al., 2014), arguably due to the fact that subjective perceptions of benefit from a CI could not be linked directly to the objective performance level on speech perception testing (Hinderink et al., 2000). It is therefore possible that the effect of cochlear implantation on HRQoL may outweigh the improvements in hearing as measured during speech perception testing (Loeffler et al., 2010).

Various other factors having an influence on HRQoL outcomes in adult CI recipients have been investigated, with some factors being inconclusive among studies. While no correlation was found between duration of deafness and HRQoL scores by a number of studies (Capretta & Moberly, 2015; Cohen et al., 2004; Hawthorne et al., 2004; Hirschfelder et al., 2008; Mo et al., 2005; Olze et al., 2011), Maillet et al. (1995) indicated that the longer

the duration of deafness, the less improvement in HRQoL is perceived. An association between younger age and better HRQoL scores was found by Chung et al. (2012) and Klop et al. (2008), whereas numerous other studies could not confirm this association (Capretta & Moberly, 2015; Hirschfelder et al., 2008; Vermeire et al., 2005). Hawthorne et al. (2004) indicated that HRQoL outcomes depend on socio-economic status, with CI recipients in the top socio-economic tertile obtaining greater gains in HRQoL scores. Study results from Hirschfelder et al. (2008) showed a significant positive correlation between duration of CI use and HRQoL scores, while Capretta and Moberly (2015) found that duration of CI use, socio-economic status, reading ability, vocabulary size and cognitive status did not consistently predict HRQoL scores. The findings of Olze et al. (2011) revealed that a high level of tinnitus impairment is associated with lower HRQoL scores before and after CI and confirmed negative correlations between HRQoL and stress, depression and anxiety.

CI performance and HRQoL outcomes vary among adult patients and are influenced by a wide variety of multifactorial predictors. Accurate pre-operative predictions of these outcomes would enable clinicians to counsel patients to such an extent that they will be able to make informed judgements of the personal benefits they might receive from implantation (A. Summerfield & Marshall, 1995). However, in spite of the recent focus to assess the broader personal impact of permanent hearing loss and cochlear implantation in patients, the multifaceted nature of HRQoL as an outcome measure requires further study to explore relative significance of different interacting factors (Klop et al., 2008). Given the current paucity of proven prognostic factors for HRQoL in CI recipients, this study aimed to identify predictors of HRQoL and to investigate the prognostic significance of these factors in an unselected caseload of adult CI recipients in South Africa.

5.3 Method

Institutional ethics committee approval was obtained prior to the commencement of data collection.

5.3.1 Study population

Four CI programs participated in this multicenter study. Three programs are situated in the Gauteng Province (University of Pretoria Cochlear Implant Unit, Johannesburg Cochlear Implant Program, Chris Hani Baragwanath Academic Hospital Cochlear Implant Program), and the remaining program is situated in the Free State Province (Bloemfontein Cochlear Implant Program). Patient files of 334 adult (>18 years) CI recipients were reviewed retrospectively at these four participating programs as part of a larger national outcomes study. During the data collection period, the Nijmegen Cochlear Implant Questionnaire (NCIQ) was distributed by e-mail or handed to adult CI recipients who were seen for consultation at the participating CI programs. Only adult CI recipients who were proficient in English were requested to complete the questionnaire. A third (113/344; 33%) of the adult CI recipients returned the questionnaires. Experience with a CI of at least 12 months was specified as the only inclusion criteria. Returned questionaires were then inspected to confirm completeness of answers and CI experience of at least 12 months. Thirteen of the 113 subjects who completed the NCIQ were excluded: five subjects' questionnaires could not be used for data-analysis due to incomplete answers and a further eight subjects completed the NCIQ questionnaire, but did not have at least 12 months experience with a CI. The final study sample consisted of 100 adult CI recipients who were implanted with multichannel CIs between 1991 and 2013. All subjects were implanted for at least 12 months and were active users of their CIs.

Demographic and clinical characteristics of the study population are presented in Table 5.1. Most subjects (70%) were implanted unilaterally, while 30 (30%) were implanted bilaterally at the time of data collection (n=100). All bilateral implants were performed sequentially, with the interval between first and second implant ranging from 0.1 to 15.5 years (mean= 5.3 years; 4.3 SD; n=30). With the exception of five subjects (5.5%, 5/91), all subjects had a fully inserted electrode array in at least one cochlea. Explant/re-implant procedures of their 1st/only implant were necessary for four (4%) subjects (n=100). Most of the subjects implanted unilaterally (81.2%, 56/69) used bimodal amplification and only 18 (18.6%, 18/97) made use of assistive listening devices. The study sample were primarily oral communicators (93%), with the exception of seven subjects (7%) who used total (mixed oral and manual) communication (n=100).

Table 5. 1 Characteristics of study population

Demographic characteristics	***% (n)***	**Clinical characteristics**	***% (n)***
Gender		**Onset of hearing loss**	
Male	58 (58/100)	Pre-lingual onset	35.0 (35/100)
Female	42 (42/100)	Post-lingual onset	62.0 (62/100)
		Unknown	3.0 (3/100)
Age at study (years) (n=100)		**Rapidity of onset of hearing loss**	
Mean (SD)	44.7 (16.7)	Congenital/ early onset	30.9 (30/97)
Range	19.4–83.4	Progressive	56.7 (55/97)
		Sudden	12.4 (12/97)
Employment status		**Age at diagnosis of hearing loss**	
Employed	67.4 (64/95)	Pre-lingual onset hearing loss (in months) (n=23)	
Retired	14.7 (14/95)	Mean (SD)	18.0 (8.1)
Unemployed/ not working	7.4 (7/95)	Range	3-35
Current educational/ training setting	8.4 (8/95)	Post-lingual onset hearing loss (in years) (n=55)	
		Mean (SD)	21.6 (17.6)
		Range	3-65
Highest educational qualification		**Age at implantation (years)**	
Secondary education (Grade 12) completed	47.3 (43/91)	Total sample (n=100)	
		Mean (SD)	36.9 (18.6)
Tertiary qualification (University)	29.7 (27/91)	Range	3.3–74.9
Tertiary qualification (other)	18.7 (17/91)	Pre-lingual onset hearing loss (n=35)	
Primary/ high school (< Grade 12)	4.4 (4/91)	Mean (SD)	25.9 (15.6)
		Range	3.3–67.6
		Post-lingual onset hearing loss (n=62)	
		Mean (SD)	43.1 (44.5)
		Range	4.4–74.9
Mode of communication		**Duration of CI use (years)** (n=100)	
Oral	93.0 (93/100)	Mean (SD)	7.7 (5.0)
Total communication (mixed)	7.0 (7/100)	Range	1.0–21.9
South African citizen		**Duration of hearing loss prior to CI (years)** (n=78)	
Yes	96 (96/100)	Mean (SD)	22.9 (16.8)
No	4 (4/100)	Range	0.3 –66.0
Health sector		**CI device**	
Private	96 (96/100)	Cochlear©	87 (87/100)
Public	4 (4/100)	Med-el©	10 (10/100)
		Advanced Bionics©	3 (3/100)

5.3.2 Description of variables

Outcome variables

The Nijmegen Cochlear Implant Questionnaire (NCIQ) was completed by adult CI recipients as a measurement of HRQoL. The NCIQ is a disease-specific, self-report questionnaire developed specifically for CI recipients (Hinderink et al., 2000). Three general domains are addressed in the NCIQ, namely: physical functioning (with "basic sound perception", "advanced sound perception" and "speech production" subdomains); psychological functioning (with "self-esteem" sub-domain) and social functioning (with "activity limitations" and "social interactions" subdomains). Each sub-domain consists of 10 questions, with answers depicted on a 5-point Likert scale, ranging from "never" to "always" (55 questions) or from "no" to "quite well" (5 questions). Should a question not apply to a CI recipient, a sixth answer ("not applicable") can be given. The subdomain scores range from 0 (never/ very poor) to 100 (always/ optimal). The NCIQ has become a standard outcome measure in evaluating the HRQoL in adult CI recipients (Loeffler et al., 2010). Validity, reliability and sensitivity to clinical changes have been confirmed for the NCIQ (Cohen et al., 2004; Damen et al., 2007; Damen, Pennings, Snik, & Mylanus, 2006; Hinderink et al., 2000; Hirschfelder et al., 2008; Krabbe, Hinderink, & van den Broek, 2000). For the data analysis, overall HRQoL (total NCIQ score), together with each of the six NCIQ subdomains (basic sound perception, advanced sound perception, speech production, self-esteem, activity limitations and social interactions) were considered as continuous outcome variables.

Explanatory variables

Data on demographic and clinical characteristics (Table 5.1), as well as risk, family, educational and employment factors (Table 5.2) of the study sample were collected

retrospectively. Twenty-two potential predictive factors were identified from this retrospective dataset and defined as either continuous or categorical variables. These predictors are presented in Table 5.3 in terms of demographic and related factors (gender, marital status, age at study, highest educational qualification, school type attended, employment status); hearing loss factors (onset of hearing loss, rapidity of onset of hearing loss, duration of hearing loss prior to CI, use of assistive listening device); CI factors (choice of ear for first/only implant, age at implantation, duration of CI use, bilateral implantation) and risk factors (additional disabilities, diagnosed ear disease, ear surgery prior to CI, tinnitus prior to CI, dizziness prior to CI, family history of permanent childhood hearing loss, pre-natal risk factors, post-natal risk factors). Supplementary Tables 5.2 and 5.3 are available in the online version of the journal.

Table 5.2 Risk, family, education and employment factor prevalence

Syndromes and additional developmental conditions identified	*% (n)*	Risk factors identified	*% (n)*	Family, educational and employment factors identified	*% (n)*
Syndromes		**Prenatal risk factor**		**Family factors**	
Any syndrome diagnosed (including syndromes listed below)	5.1 (5/89)	1 or more prenatal risk factor present	20.6 (20/97)		
		Family history of permanent childhood hearing loss	17.0 (16/94)	Marital status	
Ushers Syndrome	3.1 (3/89)			Married	47.5 (47/99)
Osteogenesis Imperfecta	1.0 (1/89)	Rubella	3.2 (3/94)	Single	47.5 (47/99)
Leopard Syndrome	1.0 (1/89)	Twin/triplet	1.1 (1/94)	Divorced	2.0 (2/99)
				Partner, not married	3.0 (3/99)
Additional disabilities		**Natal risk factor**			
1 or more condition present	10.4 (10/96)	1 or more natal risk factor present	6.5 (6/92)	**Educational and employment factors**	
Visual impairment	5.2 (5/96)	Birth trauma	3.3 (3/92)		
Cerebral palsy	2.1 (2/96)	Rh incompatibility	2.2 (2/92)	Highest educational qualification	
Learning disability	2.1 (2/96)	Prematurity	2.2 (2/92)	Secondary education (Grade 12) completed	47.3 (43/91)
Emotional/ behavioral disability	1.0 (1/96)	Anoxia	1.1 (1/92)	Tertiary qualification (University)	29.7 (27/91)
Epilepsy	1.0 (1/96)			Tertiary qualification (other)	18.7 (17/91)
		Postnatal risk factor		Primary/ high school (< Grade 12)	4.4 (4/91)
		1 or more postnatal risk factor present	33.7 (31/92)		
		Meningitis	8.7 (8/92)	Employment status	
		Noise exposure	7.6 (7/92)	Employed	67.4 (64/95)
		Trauma	5.4 (5/92)	Retired	14.7 (14/95)
		Viral infection (unspecified)	3.3 (3/92)	Unemployed/ not working	7.4 (7/95)
		Neonatal jaundice/ hyperbilirubinemia	3.3 (3/92)	Current educational/ training setting	8.4 (8/95)
		Measles	2.1 (2/92)		
		Mumps	2.1 (2/92)	School type attended	
		Neonatal jaundice with blood transfusion	1.1 (1/92)	Mainstream school	73.0 (65/89)
				School for the Deaf (Sign Language mode of communication)	11.2 (10/89)
		Neonatal jaundice Kernicterus	1.1 (1/92)		
		Ototoxic drugs: aminoglycosides	1.1 (1/92)	School for the hard-of-hearing (oral mode of communication)	11.2 (10/89)
		Ototoxic drugs: cerebral malaria treatment	1.1 (1/92)		
				Special school (mainstream syllabus)	3.4 (3/89)
				Alternative education: technical or apprentice	1.1 (1/89)

General otological risk factor	22.5 (20/89)
History of tinnitus prior to CI	15.7 (14/89)
Chronic middle-ear infection	15.7 (14/89)
History of dizziness prior to CI	13.5 (12/89)
History of ear surgery prior to CI	2.3 (2/89)
Meniere's disease	1.1 (1/89)
Otosclerosis	

Table 5.3 Suspected predictive factors

Explanatory variables	Categorical/ continuous description	*% (n)*
Demographic and related factors		
Gender	Male	58.0 (58/100)
	Female	42.0 (42/100)
Marital status	Married	47.5 (47/99)
	Single/ divorced/ partner, not married	52.5 (52/99)
Age at study (years)*	Mean (SD)	44.7 (16.7)
(n=100)	Range	19.4 – 83.4
Highest educational qualification	High school	51.6 (47/91)
	Tertiary qualification	48.4 (44/91)
School type attended	Mainstream	73.0 (65/89)
	Non-mainstream	27.0 (24/89)
Employment status	Employed	67.4 (64/95)
	Not employed	32.6 (31/95)
Hearing loss factors		
Rapidity of onset of hearing loss	Congenital/ early onset	30.9 (30/97)
	Post-natal (sudden and progressive)	69.1 (67/97)
Onset of hearing loss	Pre-lingual	36.1 (35/97)
	Post-lingual	63.9 (62/97)
Duration of hearing loss prior to CI* (n=78)	Mean (SD)	22.9 (16.8)
(time from diagnosis of hearing loss to cochlear implantation)	Range	0.3 – 66.0
Use of assistive listening device	Yes	18.2 (18/99)
	No	81.8 (81/99)
Cochlear Implant factors		
Choice of ear for 1st/ only implant	Left	41.0 (41/100)
	Right	59.0 (59/100)
Age at implantation (years)*	Mean (SD)	36.9 (18.6)
(n=100)	Range	3.3 – 74.9
Duration of CI use (years)*	Mean (SD)	7.7 (5.0)
(n=100)	Range	1.0 – 21.9
Bilateral implantation *(including only cases with at least 6 month experience with bilateral implant)*	Yes (bilateral)	24.0 (24/100)
	No (unilateral)	76.0 (76/100)
Risk factors		
Additional disabilities	Yes (1 or more)	10.4 (10/96)
	None	89.6 (86/96)
Diagnosed ear disease	Yes	20.2 (18/89)
(e.g. Meniere's disease, otosclerosis,	No	79.8 (71/89)
chronic middle-ear infection)		13.5 (12/89)
History of ear surgery prior to CI	Yes	86.5 (77/89)
	No	22.5 (20/89)
History of tinnitus prior to CI	Yes	77.5 (69/89)
	No	15.7 (14/89)

History of dizziness prior to CI	Yes	84.3 (75/89)
	No	17.0 (16/94)
Family history of permanent childhood hearing loss	Yes	83.0 (78/94)
	No/ uncertain	20.6 (20/97)
Presence of 1 or more pre-natal risk factor	Yes (1 or more)	79.4 (77/97)
	None	33.7 (31/92)
Presence of 1 or more post-natal risk factor	Yes (1 or more)	66.3 (61/92)
	None	

**continuous variables*

5.3.3 Data collection

An electronic database was developed to capture retrospective data from the clinical files of eligible adult CI recipients amongst the participating CI programs. At the time of data collection, the NCIQ was distributed to all adult CI recipients at the participating CI programs by email. Only CI recipients proficient in English were requested to complete the questionnaire. In order to increase the response rate of completed questionnaires, the NCIQ was also handed to adult CI recipients who were seen for consultations during the eight months data collection period at the respective CI programs. The NCIQ was completed electronically or in hard copy as a self-assessment of HRQoL by individual CI recipients themselves at home or during consultations at the various CI programs. This cross-sectional HRQoL data were then added to the electronic database.

5.3.4 Statistical analysis

Descriptive statistics was utilized to define the study population in terms of demographic and clinical characteristics (Table 5.1), as well as risk, family, educational and employment profiles (Table 5.2). Twenty-two suspected predictive factors were identified from these characteristics (Table 5.3).

The criterion used to differentiate between a pre-lingual and post-lingual onset of hearing loss in CI recipients was age of diagnosis of hearing loss before and after their third birthday, henceforth called pre-lingual and post-lingual onset respectively (De Graaf & Bijl, 2002). For three subjects the onset of hearing loss was unknown and they were omitted from the analyses. For bilateral implantation, only the subjects who had at least six months experience with their bilateral implant at the time of data collection were considered as bilateral implant users (80%, 24/30).

Answers to the 60 questions of the NCIQ were scored by transforming answer categories (1-5) as follows: 1=0, 2=25, 3=50, 4=75, and 5=100. Scores for each of the six subdomains of the NCIQ were computed by adding together the 10-item scores of each subdomain and dividing it by the number of completed questions (Hinderink et al., 2000). The response category “not applicable” as well as missing values were treated as not completed. Subjects exceeding the maximum number of three incomplete answers for each specific subdomain, were excluded (Hinderink et al., 2000). An overall HRQoL average percentage score was then also calculated for the six subdomains together.

Multiple linear regression analysis was used for the prediction of HRQoL outcomes in adult CI recipients. Regression models were constructed to investigate the influence of categorical and continuous predictors on HRQoL percentage scores.

5.4 Results

5.4.1 HRQoL outcome profile

Comprehensive post-operative NCIQ scores were obtained for 100 adult CI recipients. Table 5.4 presents the descriptive statistics for overall HRQoL and the six sub-domains of the NCIQ. Highest mean scores were obtained for the "advanced sound perception" (77%) and the "activity limitations" (71.5%) sub-domains. Lowest mean score was obtained for the "self-esteem" (57.9%) sub-domain.

Table 5.4 HRQoL scores depicted from NCIQ results (n=100)

Nijmegen Cochlear Implant Questionnaire	Mean (SD)	Median	Range
Total HRQoL score	66.1 (12.6)	65.7	30.4 – 90.4
NCIQ sub-domain			
Physical: Basic sound perception	64.1 (17.1)	67.5	19.4 – 97.5
Physical: Advanced sound perception	77.0 (15.9)	80.3	38.9 – 100
Physical: Speech production	59.6 (18.7)	60.0	12.5 – 100
Psychological: Self-esteem	57.9 (17.2)	60.0	12.5 – 85.0
Social: Activity limitations	71.5 (18.5)	75.0	25.0 – 100
Social: Social interactions	66.5 (11.4)	67.5	30.6 – 90.0

5.4.2 Multiple linear regression analysis: HRQoL

A multiple linear regression model was constructed for overall HRQoL outcomes. Twenty-two predictor variables (Table 5.3) were randomly fed into the model and the best predictors for overall HRQoL were then identified during the model building process. A similar analysis was then done for each of the six sub-domains of the NCIQ, but only revealed significant associations with the "advanced sound perception" sub-domain. Table 5.5 presents the multiple linear regression analysis results, showing the best predictors of

outcomes in terms of overall HRQoL and advanced sound perception. The simultaneous effect of the identified predictors was measured for these two outcomes and therefore the influence of a predictor is significant on the outcome in the presence of the other predictors.

Table 5.5 Multiple linear regression analysis results

Outcome variables	Predictors	p-value	df**	Sum of Squares	F Value	Pr > F*** (p value)	R^2****
Overall HRQoL (n=66)	Tinnitus prior to CI	0.0301	5	2084.52	3.40	0.0090	0.22
	Duration of hearing loss prior to CI*	0.0408					
	Bilateral implantation	0.0433					
	School type attended	0.0485					
	Additional disabilities	0.0544					
Advanced sound perception (n=70)	School type attended	0.0142	4	2673.16	3.87	0.0070	0.19
	Additional disabilities	0.0228					
	Employment status	0.0571					
	Duration of hearing loss prior to CI*	0.0922					

continuous variables; **df: Degrees of freedom; ***Pr>F: p-value of the F-test (with F-test testing the significance of the model); **R^2: determination coefficient*

Multiple linear regression results identified tinnitus, bilateral implantation, school type attended and additional disabilities as categorical predictors for the overall HRQoL outcome (Table 5.5). The boxplots in Figure 1 illustrate that patients with a history of tinnitus prior to CI have a significantly lower mean HRQoL score of 63% compared to the mean score of 69% of patients without a history of tinnitus (p=0.0301). The same results are observed for the bilateral implantation and school type attended factors, where on average patients with unilateral implants scored 6% lower than patients implanted bilaterally (p=0.0433), and

patients who did not attend mainstream schools scored 4% lower than those who attended mainstream schools (p=0.0485). Furthermore, this analysis indicates a suggestive, but not significant association between the additional disability factor and overall HRQoL outcomes. Patients without additional disabilities have a significant lower average HRQoL score (67%) compared to an average score of 75% for patients with additional disabilities (p=0.0544). Also, a regression coefficient of 0.17 was noted for the duration of hearing loss prior to CI continuous predictor (p=0.0408).

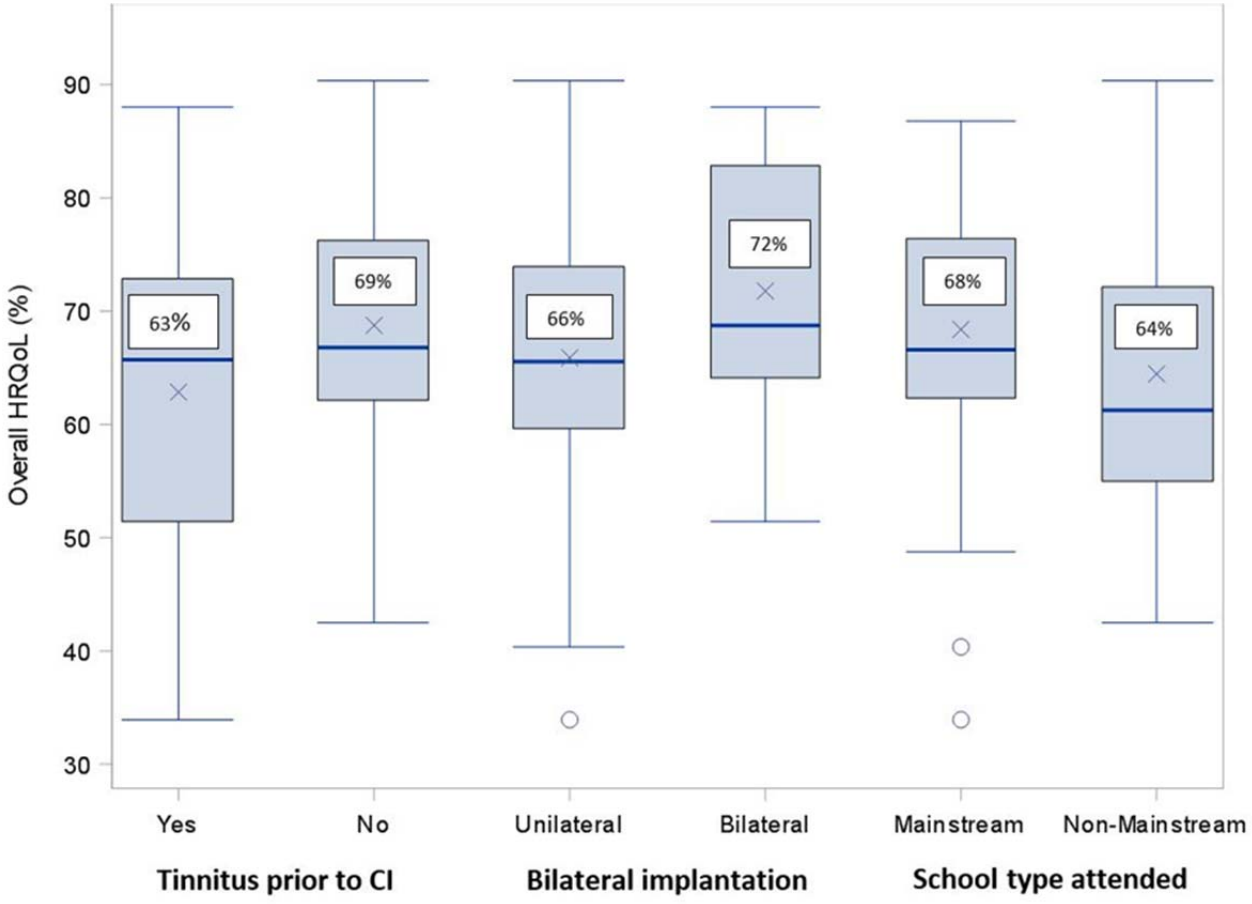

Figure 5.1 Tinnitus prior to CI, bilateral implantation and school type attended as predictors of overall HRQoL n=66

The box plots represent the smallest observation, lower quartile, median (bold line), mean (x) with percentage indicated in textbox, upper quartile, largest observation, and outliers (>1.5 times interquartile range) (○)

In a similar regression analysis, school type attended and additional disabilities were identified as categorical predictors for the advanced sound perception outcome, together with employment status (Table 5.5). Patients who attended mainstream schools have a significant higher average score for the advanced sound perception sub-domain of 80%, compared to a lower average score of 72% for patients who attended non-mainstream schools (p=0.0142). Patients without additional disabilities have a significant lower average score for advanced sound perception (77%) when compared to the average score of 86% for patients with additional disabilities (p=0.0228). This analysis shows marginal evidence to suggest that patients who are unemployed obtain a significant lower score of 72% for the advanced sound perception sub-domain when compared to patients who are employed with an average score of 79% (p=0.0571). Duration of hearing loss prior to CI was indicated as a continuous predictor for advanced sound perception, but with negligible significance (regression coefficient of 0.16; p=0.0992).

Linear regression models for both the overall HRQoL and advanced sound perception outcomes were highly significant ($p<0.01$) and present with determination coefficients (R^2) of 22% and 19% respectively. These determination coefficients indicate that less than 25% of the variation in the HRQoL outcomes observed in the data was accounted for by the specified models.

5.5 Discussion

The HRQoL outcomes in the unselected group of adult CI recipients in this study were significantly predicted by history of tinnitus prior to CI, bilateral implantation and school

type attended. History of tinnitus prior to CI was a strong predictor of poorer HRQoL outcomes overall. In spite of the dearth of available data on the HRQoL of patients with tinnitus before and after implantation (Olze et al., 2011), some evidence suggest that tinnitus is an important factor that significantly affects the HRQoL of CI patients. Using the *Glasgow Benefit Inventory* and the *Specific Questionnaire* as HRQoL measures, Ramos et al. (2013) found that better HRQoL scores were obtained by adult (>60 years) CI recipients that have never had tinnitus, with 88% of these adults being "remarkably satisfied" with their CI intervention. Olze et al. (2011) also utilized the NCIQ to evaluate HRQoL pre- and post-operatively in post-lingually deafened adults, showing that patients with high-level tinnitus had significantly lower NCIQ scores before and after CI. Additionally, in a study exploring the benefits of sequential implantation, positive changes in HRQoL were associated with improvements in hearing, but were counterbalanced by negative changes associated with worsening of tinnitus (Q. Summerfield et al., 2006). Even though data on the severity of tinnitus pre and post CI were not collected and could not be reported on, this study provides evidence that the presence of tinnitus prior to CI influences HRQoL outcomes with implications for the rehabilitation process.

Bilateral implantation was also strongly associated with better HRQoL outcomes. This finding confirms results from the prospective study of Härkönen et al. (2015) in which generic HRQoL questionnaires (the *Glascow Benefit Inventory* and the *15D* questionnaire) were used to indicate that sequential bilateral cochlear implantation improved HRQoL. Similarly, in a study where the additional benefit of a second CI was evaluated, Olze et al. (2012) indicated that HRQoL assessed with the NCIQ further increased after the second CI. With their novel HRQoL questionnaire that assesses physical and psychosocial benefits of sequential bilateral implantation, King et al. (2014) also demonstrated subjective

improvement in all measured domains after receiving a second CI. However, it should be noted that not all patients in this dataset had the opportunity to access a second CI, since financial resources currently remains a decisive factor for bilateral implantation in South Africa. It is therefore possible that the association between bilateral implantation and increased HRQoL outcomes could be related to socioeconomic factors as well. Irrespective, results from this study suggest that perceived improvements in hearing resulting from the addition of a second CI could be associated with better HRQoL outcomes.

Mainstream schooling, implying a normal hearing educational setting, was strongly predictive of better HRQoL outcomes overall and in the advanced sound perception sub-domain. Evidence suggest that deaf children perform better on measures of speech perception, receptive and expressive language when oral communication predominate their educational environment, potentially by placement in a mainstream classroom setting (Cosetti & Waltzman, 2012). This study provides preliminary evidence that a mainstream educational setting also predicts better overall HRQoL outcomes for adult CI recipients, possibly as a result of former integration in oral communication educational environments. Yet again, due to socioeconomic and geographical constraints it is possible that not all CI recipients from this dataset had equal access to supportive mainstream education. Nevertheless, better subjective ratings in terms of perceived advanced sound perception could still be expected from adult CI recipients who attended mainstream schools. In support of these results, Van Deun et al. (2009) indicated that in a group of sequentially implanted children, localization abilities were greatest in children who attended mainstream schools versus schools for the deaf.

Contrary to expectations, additional disabilities and duration of hearing loss prior to CI also yielded statistical significance as predictive factors in the regression analysis. Firstly, multiple disabilities were associated with better scores for total HRQoL and for the advanced sound perception sub-domain. With only 10% of the total study sample presenting with one or more additional disability, the results obtained for this association could not be generalized. However, it could be that these few cases with additional disabilities perceive the restorative effect of cochlear implantation and the consequent lessening of the total disability burden to be more significant than patients who only have deafness as an isolated disability. Secondly, longer duration of hearing loss prior to CI predicted better scores for overall HRQoL and for the self-esteem sub-domain. Duration of deafness / severe-to-profound hearing loss is generally considered as a more robust predictive factor in CI outcomes, since it implies the duration of auditory deprivation, which is known to be a critical predictor of implantation success. However, CI performance remains highly variable, even among patients with identical duration of deafness, signifying that clinical and HRQoL outcomes are determined by various other interacting factors (Giraud & Lee, 2007). Similar to the contradictory tendency observed in this study, Klop et al. (2008) and Ramos et al. (2013) also found a significant association between longer duration of deafness and better HRQoL outcomes, which accentuate the complex nature of HRQoL as an outcome measure.

Since this current study aimed to provide a broad overview of HRQoL outcomes, the range for duration of CI use in this diverse study sample was rather broad. However, this was accounted for by including duration of CI use as an explanatory variable in the regression analysis. In agreement with the study results of Capretta and Moberly (2015), duration of CI use did not influence HRQoL scores for this study sample. Furthermore, the factors identified to be predictive of HRQoL outcomes within this dataset accounted for less than

25% of the variation in HRQoL outcomes. This underscores the intricate and multifactorial influence of predictors on HRQoL outcomes.

5.6 Conclusion

History of no tinnitus prior to CI, bilateral implantation and mainstream schooling were strong predictors of better HRQoL outcomes in adult CI recipients. Other factors such as age, age at implant, gender, onset of hearing loss, duration of CI use and presence of risk factors did not consistently predict HRQoL scores. The importance of appropriate pre-operative counselling and post-implantation support and rehabilitation services for patients with tinnitus is underscored by the findings from this study. This work also contributes to a better understanding of factors influencing HRQoL outcomes enabling clinicians to provide evidence-based information counselling to adult CI patients and their families

5.7 Acknowledgements

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CHAPTER 6
GENERAL DISCUSSION, CLINICAL IMPLICATIONS AND CONCLUSION

Because of improved accessibility to sound and speech, language development progresses positively in children receiving CIs (Boons, Brokx, Dhooge, et al., 2012). For adult CI recipients, the improvement in hearing in terms of audiological performance is significant, with audiological monosyllabic and sentence tests showing a noticeable increase in open-set speech recognition after implantation (Fetterman & Domico, 2002; Hamzavi, Franz, Baumgartner, & Gstoettner, 2001; Loeffler et al., 2010). Despite these positive results, the large variability in pediatric and adult CI outcomes remains a significant concern (Boons, Brokx, Dhooge, et al., 2012; Holden et al., 2013). Outcomes vary and many CI cases present with sub-optimal outcomes as a result of a broad spectrum of adverse influences (Black et al., 2011).

Appropriate prognosis and pre-operative counselling is of paramount importance to the CI patient, professionals, parents and families to avoid unrealistic expectations and subsequent disappointment in cases where adverse influences are present (Black et al., 2011). Research evidence to date has not yet comprehensively identified specific prognostic indicators that reliably predict successful outcomes with a CI (Geers et al., 2003).

Given the paucity of proven prognostic factors for CI outcomes (Black et al., 2012), this current research aimed to identify predictors of pediatric CI outcomes related to speech production, auditory performance, communication mode and educational placement. The risk and intervention profiles of a sub-group of these pediatric CI recipients were also considered. Concerning adult CI recipients specifically, this work aimed to identify and

describe predictors of HRQoL outcomes. Furthermore, the prognostic significance of these predictive factors was investigated within a large caseload of pediatric and adult CI recipients in South Africa.

6.1 Overview of research findings

Study I described profound childhood hearing loss in a South African cohort of 264 pediatric CI recipients based on risk profile, and age of diagnosis and intervention. The most prevalent associated risks for profound PCEHL included NICU admittance (28.1%), family history of childhood hearing loss (19.6%), prematurity (15.1%), hyperbilirubinemia (10.5%) and meningitis (10%). Profound hearing loss was typically sensorineural with a congenital onset and a 5% prevalence of ANSD. Diagnosis of PCEHL was delayed, resulting in deferred mean ages for initial hearing aid fitting (18.8 months), enrollment in early intervention services (19.5 months), and eventual cochlear implantation (43.6 months). Even though average ages for intervention were earlier than previously reported in South Africa, necessary early auditory stimulation required for optimal outcomes for children with profound PCEHL, is not typically realized.

Within a sample of 301 pediatric CI recipients, an extensive range of prognostic indicators were identified for pediatric CI outcomes in South Africa in **Study II**. Bilateral implantation was strongly predictive of better auditory performance and speech production scores, an oral mode of communication and mainstream education. NICU admittance and prematurity were associated with poorer auditory performance and speech production scores, together with a higher probability for non-oral communication and non-mainstream education. The presence of one or more additional developmental condition was predictive of poorer

outcomes related to speech production and educational placement. Moreover, a delay between diagnosis and implantation of more than one year was also related to non-mainstream education. Ethnicities other than Caucasian were predictive of poorer auditory performance scores and a lower probability for mainstream education. This study also provided a broad depiction of the current status and outcomes of pediatric cochlear implantation in South Africa. Most children (78%) implanted for more than three years achieved high CAP scores for auditory performance, and high SIR scores for speech production. This result suggests that they do understand spoken conversation with a familiar person and have connected speech that is intelligible, at least for an experienced listener. Almost 75% of the children in this study were oral communicators and more than half (56%) of the children who used their implants for longer than three years were placed in mainstream educational settings. Findings from this study not only provide a broad overview of pediatric CI outcomes, but also add to the specific understanding of the causes of variation of outcomes within the South African context.

In **Study III**, a range of significant prognostic indicators were identified for HRQoL outcomes in a South African sample of 100 adult CI recipients. History of no tinnitus prior to CI, bilateral implantation and mainstream schooling were strongly predictive of better overall HRQoL outcomes. Other factors that did not predict HRQoL scores were age at study, age at implant, gender, the duration of CI use, onset of hearing loss and the presence of risk factors. The findings underscore the importance of appropriate pre-operative counselling, post-implantation support and rehabilitation services for patients with tinnitus. This study has thus contributed to a better understanding of factors influencing HRQoL outcomes which, in turn, could enable clinicians to provide evidence-based information counselling to adult CI patients and their families.

6.2 Clinical implications

- Despite of the fact that children with profound hearing loss are typically identified at earlier ages than children with less severe degrees of hearing loss (Durieux-Smith et al., 2008), results from Study I indicated that diagnosis of PCEHL was still delayed (15.3 months), resulting in deferred ages for intervention. Delayed diagnosis implies that the necessary early auditory stimulation required for optimal outcomes for children with profound PCEHL is not realized. Moreover, the majority (72.9%) of children in this study did not receive NHS , reflecting the current EHDI status in South Africa where NHS services are offered in only a limited number of hospitals in both the public and private health care sectors (Meyer et al., 2012; Theunissen & Swanepoel, 2008). With 92% of the study sample representing the private health care sector, outcomes of Study 1 highlight the need for improvement of the current status of NHS services in the private health care sector in South Africa. To increase coverage rates, NHS should be integrated with hospital-based birthing services in private health care settings (Meyer et al., 2012).

- The average age of cochlear implantation for pediatric CI recipients in Study I exceeded three and a half years of age, indicating a delay of more than two years from diagnosis to implantation. Possible contributing factors to late implantation cover as wide a range as funding constraints, lack of prompt referral to specialized CI services, parental barriers such as delayed or missed appointments, complex medical conditions, family indecision and geographical region (Armstrong et al., 2013; Fitzpatrick et al., 2015). In Study II, a delay between diagnosis and implantation of more than 12 months was specifically identified as a strong

predictor of non-mainstream school placement. Currently late implantation is being defined as more than 12 months after hearing loss diagnosis with an emphasis on early access to sound through early implantation (Fitzpatrick et al., 2015). Therefore, an effort should be made to identify and address context specific factors contributing to delayed cochlear implantation in South African. As a start, the lack of early referral to specialized CI services could be addressed by educating and updating referring audiologists in South Africa to recent referral criteria for pediatric and adult cochlear implantation.

- Pre-operative assessment and counselling are critical to the cochlear implantation process and depends largely on the CI team's ability to define and evaluate risk. Prognostication requires the ability to identify factors that will exert either positive or adverse effects on outcomes (Black et al., 2012). A broad range of prognostic indicators were identified in both Study II and Study III and these add to the existing body of proven evidence concerning prognostic factors that apply to pediatric and adult cochlear implantation. For the first time, prognostic factors unique to the South African context were identified. Knowledge and understanding of these specific factors would enable professionals from CI teams to provide appropriate pre-operative counselling to such an extent that the eventual outcomes of a particular CI patient equals or exceeds the pre-operative expectations of those involved in the process (Black et al., 2012).

- CI teams should prioritize prognostication to predict outcomes with certainty. This can only be achieved via an evidenced-based process that requires a disciplined and

detailed approach to data collection before, during and after cochlear implantation (Black et al., 2012). The challenges associated with retrospective data collection in all three studies presented in this thesis emphasize the critical need for the implementation of a uniform data recording methodology. This should not only apply to individual CI teams, but also across all CI programs in South Africa. Moreover, equally significant for accurate prognostication is compulsory and precise documentation of a pre-operative case history, as well as the systematic documentation of outcomes based on standardized outcome measures.

- In Study III, history of tinnitus prior to CI was indicated as a predictor of poorer HRQoL outcomes in adult CI recipients. This has implications for the rehabilitation process. Appropriate pre-operative counselling and post-implantation support and rehabilitation services for patients with tinnitus are critically important.

6.3 Study strengths and limitations

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

6.3.1 Study strengths

Study I was the first of its kind to describe the risk and intervention profiles of children with profound PCEHL in sub-Saharan Africa. Except for a series of etiological surveys of children in schools for the deaf dating back to the 1970s and early 1980s (Sellars & Breighton, 1983), data that describe the risk profile of profound PCEHL in South Africa were not available. Only recently, Swanepoel et al. (2013) provided preliminary data on the nature of hearing

loss and associated risk profiles for a small sample of infants with varying types and degrees of hearing loss in South Africa. However, data pertaining to additional developmental conditions and intervention was not available for the sample population in the study of Swanepoel et al. (2013), but was reported on in Study I.

Studies II and III were the first to report on predictors of pediatric and adult CI outcomes in South Africa. To date, no other published data that document the current status and outcomes of CIs in South Africa exists.

Pediatric CI recipients from the complete range of demographical, educational and communication environments that met the required age range (≤18 years) were included in the study sample for Study II. In contrast to other prediction studies (Boons, Brokx, Dhooge, et al., 2012; Geers et al., 2003; Sarant et al., 2014), children with multiple disabilities, abnormal cognitive abilities and those with sudden or progressive post-natal onset hearing losses were part of this unselected study sample. This ensured an unbiased an encompassing prediction of outcomes. In the statistical data analysis a clear distinction was made between children with congenital/ early onset hearing loss and children with sudden or progressive post-natal onset hearing loss. This distinction is important when a heterogeneous caseload is considered, since it is expected that most children with post-lingual onset hearing loss will perform well after cochlear implantation. This is seen as a result of their early foundation in speech and language and more mature auditory pathways (Ahmad et al., 2012; Gray et al., 2003; Nicholas & Geers, 2007; Sharma et al., 2002).

Statistical regression analyses were used for the prediction analyses in Studies II and III. A broad range of suspected predictive factors were identified from the retrospective dataset and included in the building of the regression models. Study I had 20 predictive factors and Study II had 22 predictive factors. As a result, numerous independent variables, not typically described in literature, were included in the regression models that investigated the possible influence of an extensive range of predictor variables.

In Study II, NICU admittance and prematurity emerged as strong predictors of poorer pediatric CI outcomes. To the authors' knowledge, these two factors have not yet been confirmed as prognostic factors in pediatric cochlear implantation nor documented in existing literature. Study II therefore makes a novel contribution when validating these two factors as prognostic indicators of pediatric CI outcomes. Similarly, and also not found anywhere else in literature, Study III provides preliminary evidence that a mainstream educational setting predicts better overall HRQoL outcomes for adult CI recipients.

6.3.2 Study limitations

Over the 22 year study period, a plethora of different outcome measures were used by the respective CI programs for pediatric and adult CI recipients. This made it impossible to draw inferences about outcomes and compare outcomes over time, as outcomes were also not documented at fixed, predetermined intervals. As an alternative, outcomes were measured cross-sectionally in Studies II and III and outcome data were added to the retrospective database. Furthermore, the time-scale during which CI recipients received their implants were between 1996 and 2013 for the pediatric CI recipients and between 1991 and 2013 for

the adult CI recipients. During this period of time, international Audiology practice has changed significantly and these changes were evident in South Africa too. For example, NHS and advanced objective electrophysiological diagnostic test procedures resulted in a general decrease of age of diagnosis and age at cochlear implantation worldwide. However, this was accounted for in Studies II and III where age at diagnosis of hearing loss and age at implantation were considered as potential prognostic factors in the regression analyses.

The evaluation of speech perception abilities pre- and post-implantation provides valuable clinical information about progress over time and is considered as a critical outcome measure in cochlear implantation. A wide range of standardized, age-appropriate speech perception outcome measures are required to evaluate a hierarchy of auditory skills. However, a persistent challenge within the South African context is the availability of standardized speech perception material for each of the 11 official languages. As a result, many CI recipients are tested with available speech perception material, and not necessarily with speech stimuli from their first or home language. Also, speech perception testing was not uniformly administered by the respective CI programs in this study (e.g. varying presentation intensities, live voice versus pre-recorded speech stimuli) and results were not captured at fixed intervals. Consequently, for the purpose of prediction in Studies II and III, retrospective speech perception scores were not considered as a reliable and valid outcome measure. However, in the absence of formal objective auditory perception measurements, the CAP was utilized in Study II as a language- and age-independent outcome measure for auditory performance as suggested by Beadle et al. (2005).

A challenging aspect of this retrospective review of clinical files for Studies I-III was the precision of data recording. In spite of the fact that the electronic database data collection tool was designed to capture data uniformly among CI programs, data were often difficult to find, disorganized and inconsistently recorded. This limitation calls for the implementation of a common data recording methodology across CI programs in South Africa. This would, in return, enhance collaborative multicenter research. The need for compatible data is particularly important to effectively collate data across programs in the case of low incidence conditions (Black et al., 2014). Hence the rather uncommon factors that occurred in this dataset, such as ANSD type hearing loss, Waardenberg syndrome and public healthcare could not be statistically validated as predictors of outcomes due to low numbers.

Five CI programs throughout South Africa participated in this multicenter study, resulting in a relatively large retrospective dataset of 301 pediatric and 334 adult CI recipients. Consequently the study sample for this research could be considered as reasonably representative of CI recipients in South Africa. However, with the vast majority of CI recipients representing only the private healthcare sector, this research sample is not representative of the larger South African population and results could not be generalized.

Determination coefficients of the linear regression models in Study II and Study III were respectively less than 30% for the pediatric dataset and less than 25% for the adult dataset, and do not account for two-thirds of the remaining variation in auditory performance and speech production outcomes for Study II and three quarters of the remaining variation in HRQoL outcomes in Study III. This implies that, in reality, outcomes are determined by many

more single or interacting factors that were not included in the different models. Since this research is based mainly on secondary data, many other relevant variables, such as family influences, socio-economic status and inner ear malformations are not included in the prediction analyses.

6.4 Future perspectives

Results of Study I indicated an average delay of more than two years from diagnosis to implantation for pediatric CI recipients, implying that pediatric CI candidates in South Africa typically miss out on the necessary early and optimal auditory stimulation required for age-appropriate speech and language development. Context specific factors contributing to delayed cochlear implantation in South Africa should be identified and evaluated in future studies.

Once compatible outcome data are systematically captured at fixed intervals among South African CI programs, similar prediction analyses as were done in Study I and Study II would be valuable to report on the evolution of outcomes and consistency of predictors over time.

As recent pediatric CI outcome prediction studies confirm, problematic family environments are significantly associated with poorer speech and language outcomes (Black et al., 2014; Holt et al., 2012). Examples of family factors known to relate to improved language outcomes are a high socio-economic level (Geers et al., 2003; Gérard et al., 2010; Niparko et al., 2010), sufficient parental involvement in the rehabilitation process (Boons, Brokx, Dhooge, et al., 2012; Sarant et al., 2008; Spencer, 2004) and higher levels of maternal

education (Cupples et al., 2014). Evaluation of the family's influence on pediatric CI outcomes should therefore be prioritized as an area for future research.

Since CIs positively influence psychosocial outcomes, exploring pediatric CI recipients' HRQoL as a result of implantation can be a useful way to ensure that CI outcomes are positive (Kumar, Warner-czyz, Silver, Loy, & Tobey, 2015). In spite of the recent focus to assess the broader impact of permanent hearing loss and cochlear implantation in CI recipients, published studies determining the possible influence of predictor variables on HRQoL outcomes in children are lacking (Kumar et al., 2015). Future studies in South Africa should identify and evaluate predictors of HRQoL outcomes for pediatric CI recipients.

In Study II, educational placement was considered as a categorical outcome measure (mainstream versus non-mainstream educational placement) for pediatric CI outcomes. Since Study II was the first to report on the current status and outcomes of pediatric cochlear implantation in South Africa, educational placement was considered to be a suitable, broad preliminary outcome measure. However, mainstream education as a measure of success in cochlear implantation should be used with caution, since the emphasis should rather be on the appropriateness of educational placement to each child's specific needs. Against the background of current challenges impeding progress towards achieving an inclusive education system for children with hearing loss in South Africa (Department of Education, 2015), future studies should investigate the appropriateness of educational placement for pediatric CI recipients in South Africa to address their distinctive educational needs.

In Study III, history of tinnitus prior to CI was indicated as a strong predictor of poorer HRQoL outcomes. Despite the dearth of available data on the HRQoL of patients with tinnitus before and after implantation (Olze et al., 2011), evidence presented suggests that tinnitus is an important factor that affects the HRQoL of CI patients significantly. Future studies should assess the severity of tinnitus in adult CI recipients using validated questionnaires before and after cochlear implantation at fixed intervals. This could assist in determining the effect of tinnitus on HRQoL outcomes over time.

6.5 Conclusion

The most prevalent associated risks for profound PCEHL in a South African cohort included NICU admittance, family history of childhood hearing loss, prematurity, hyperbilirubinemia and meningitis. Diagnosis of PCEHL was delayed, resulting in deferred ages for initial hearing aid fitting, enrollment in early intervention services, and eventual cochlear implantation.

Predictive factors for pediatric CI outcomes in a South African cohort were bilateral implantation, admittance to the NICU, prematurity, additional developmental conditions, ethnicity and the delay between diagnosis and implantation. Although implanted children within this South African sample did not have equal opportunity to access a second implant, bilateral implantation was strongly predictive of better auditory performance and speech production scores, an oral mode of communication, and mainstream education. NICU admittance and prematurity were associated with poorer auditory performance and speech production scores, together with a higher probability for non-oral communication and non-mainstream education. The presence of one or more additional developmental condition was predictive of poorer outcomes in terms of speech production and educational placement, while a delay between diagnosis and implantation of more than one year was

also related to non-mainstream education. Ethnicities other than Caucasian were predictive of poorer auditory performance scores and a lower probability for mainstream education.

A history of no tinnitus prior to CI, bilateral implantation and mainstream schooling were strong predictors of better HRQoL outcomes in adult CI recipients in a South African cohort. Other factors such as age, age at implant, gender, duration of CI use, onset of hearing loss and presence of risk factors did not consistently predict HRQoL scores.

This work contributes to a better understanding of factors influencing pediatric and adult CI outcomes in South Africa. This enables CI teams to provide evidence-based informational counselling to CI recipients and their families and to plan appropriately for post-implantation intervention.

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APPENDICES

APPENDIX A

Categories of Auditory Performance (CAP)

Categories of Auditory Performance (Archbold et al., 1995)

Revised version **(CAP_R)** (Stacey et al., 2006)

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

APPENDIX B

Speech Intelligibility Rating (SIR)

Speech Intelligibility Rating (SIR) (Allen et al., 1998)

Category	SIR description
5	Connected speech is intelligible to all listeners. The child is understood in easy everyday contexts.
4	Connected speech is intelligible to a listener who has little experience of a deaf person's speech (the listener does not need to concentrate unduly)
3	Connected speech is intelligible to a listener who concentrates and lip-reads (within a known context).
2	Connected speech unintelligible. Intelligible speech is developing in single words when context and lip reading cues are available.
1	Connected speech is unintelligible. Pre-recognizable words in spoken language, primary mode of communication may be manual.

APPENDIX C

Nijmegen Cochlear Implant Questionnaire (NCIQ)

NIJMEGEN COCHLEAR IMPLANT QUESTONNAIRE (Hinderink et al., 2010*)

Name: _____ **Date:** _____

Please answer the following 60 questions regarding the CI situation (use "not applicable" [N/A] only if none of the possibilities is applicable).

	Never	Sometimes	Regularly	Usually	Always	N/A
1. Can you hear background noises (toilet flushing, vacuum cleaner)?	☐	☐	☐	☐	☐	☐
2. Does your hearing impairment present a serious obstacle in your contact with persons with normal hearing?	☐	☐	☐	☐	☐	☐
3. Are you able to whisper if you have to?	☐	☐	☐	☐	☐	☐
4. Do you feel at ease in company despite your hearing impairment?	☐	☐	☐	☐	☐	☐
5. Can you hold a conversation in a quiet environment (with or without lip-reading) with one person?	☐	☐	☐	☐	☐	☐
6. Does your hearing impairment present a serious problem during your work or studies?	☐	☐	☐	☐	☐	☐
7. Can you hear the footsteps of other persons in your house (eg, in the hall or on the stairs)?	☐	☐	☐	☐	☐	☐
8. Does your hearing impairment present a serious problem in your contact with deaf persons?	☐	☐	☐	☐	☐	☐
9. Are you able to shout if you need to?	☐	☐	☐	☐	☐	☐
10. Does it bother you that you are hard of hearing?	☐	☐	☐	☐	☐	☐
11. Are you able to hold a conversation with 2 or more persons in a quiet environment (with or without lip-reading)?	☐	☐	☐	☐	☐	☐
12. Does your hearing impairment present a serious problem in traffic?	☐	☐	☐	☐	☐	☐
13. Can you hear your own telephone or doorbell ringing?	☐	☐	☐	☐	☐	☐
14. Does your hearing impairment present a serious problem when you are with a group of persons (hobbies, sport, holidays)?	☐	☐	☐	☐	☐	☐
15. Are you able to make yourself understood to strangers without using hand gestures?	☐	☐	☐	☐	☐	☐
16. Do you become irritated if you cannot follow a conversation?	☐	☐	☐	☐	☐	☐
17. When you are in a busy shop, can you understand the shop assistant?	☐	☐	☐	☐	☐	☐
18. Does your hearing impairment present a serious problem during leisure-time activities?	☐	☐	☐	☐	☐	☐

	Never	Sometimes	Regularly	Usually	Always	N/A
19. Can you hear (not feel) the front door slam when you are busy at home?	☐	☐	☐	☐	☐	☐
20. Does your hearing impairment present a serious problem in your contact with the persons you live with (family/partner)?	☐	☐	☐	☐	☐	☐
21. Are you able to adapt your voice to different situations (noisy environment, quiet environment)?	☐	☐	☐	☐	☐	☐
22. Do you avoid speaking to strangers?	☐	☐	☐	☐	☐	☐
23. Are you able to enjoy music?	☐	☐	☐	☐	☐	☐
24. Does your hearing impairment present a serious problem for functioning in the home?	☐	☐	☐	☐	☐	☐
25. Are you able to hear cars approaching in traffic?	☐	☐	☐	☐	☐	☐
26. Are you left aside in company because of your hearing impairment?	☐	☐	☐	☐	☐	☐
27. Can strangers hear from your voice that you are deaf or hearing-impaired?	☐	☐	☐	☐	☐	☐
28. Do you ask other persons to speak more loudly or clearly if they are speaking too softly or unclearly?	☐	☐	☐	☐	☐	☐
29. Are you able to recognize certain melodies in music?	☐	☐	☐	☐	☐	☐
30. Does your hearing impairment present a serious problem when you are shopping?	☐	☐	☐	☐	☐	☐
31. Can you hear soft noises (key falling, microwave beeping)?	☐	☐	☐	☐	☐	☐
32. Do you go places where your hearing impairment might present a serious handicap?	☐	☐	☐	☐	☐	☐
33. Can you make yourself understood to acquaintances without using hand gestures?	☐	☐	☐	☐	☐	☐
34. Do you feel anxious when talking to strangers?	☐	☐	☐	☐	☐	☐
35. Are you able to recognize certain rhythms in music?	☐	☐	☐	☐	☐	☐
36. Does your hearing impairment present a serious problem when watching television?	☐	☐	☐	☐	☐	☐
37. Can you hear (not feel) someone approaching you from behind?	☐	☐	☐	☐	☐	☐
38. Does your hearing impairment present a serious hindrance in your contact with persons who live in your neighbourhood?	☐	☐	☐	☐	☐	☐
39. How often does it annoy you that persons can hear from your voice/speech that you have a hearing problem?	☐	☐	☐	☐	☐	☐
40. Can you understand strangers without lip-reading?	☐	☐	☐	☐	☐	☐
41. Does your hearing impairment present a serious problem at parties (eg, birthdays)?	☐	☐	☐	☐	☐	☐

42.Can you hear (not necessarily understand) persons talking on the radio?	☐	☐	☐	☐	☐	☐
43.Does your hearing impairment present a serious problem when you are with friends?	☐	☐	☐	☐	☐	☐
44.Can you make contact easily with other persons despite your hearing problem?	☐	☐	☐	☐	☐	☐
45.Can you hear the difference between a man's voice, a women's voice, and a child's voice?	☐	☐	☐	☐	☐	☐
46.Does your hearing impairment present a serious problem when dealing with formal matters (insurance, solicitor, municipal office)?	☐	☐	☐	☐	☐	☐
47.Can you hear when someone calls you?	☐	☐	☐	☐	☐	☐
48.Does your hearing impairment present a serious problem in your contacts with family members?	☐	☐	☐	☐	☐	☐
49.Are there situations in which you would feel happier if you were not hearing-impaired?	☐	☐	☐	☐	☐	☐
50.Do you feel it tiring to listen (with or without lip-reading)?	☐	☐	☐	☐	☐	☐
51.Does your hearing impairment present a serious problem when you go out or on trips?	☐	☐	☐	☐	☐	☐
52.Can you hear voices from another room (eg, children playing, baby crying)?	☐	☐	☐	☐	☐	☐
53.When you are in a group, do you feel that your hearing impairment keeps persons from taking you seriously?	☐	☐	☐	☐	☐	☐
54.Does your hearing impairment undermine your self-confidence?	☐	☐	☐	☐	☐	☐
55.Does your hearing impairment prevent you from sticking up for yourself (at work, in relationships)?	☐	☐	☐	☐	☐	☐

Please note: the answer categories for the following 5 questions are changed

	No	Poor	Fair	Good	Quite Well	N/A
56.Are you able to make your voice sound angry, friendly or sad?	☐	☐	☐	☐	☐	☐
57.Can you control the pitch of your voice (high, low)?	☐	☐	☐	☐	☐	☐
58.Can you control the volume of your voice?	☐	☐	☐	☐	☐	☐
59.Can you make your voice sound "natural" (so that it does, not sound like a deaf person's voice)?	☐	☐	☐	☐	☐	☐
60.Are you able to hold a simple telephone conversation?	☐	☐	☐	☐	☐	☐

* Hinderink, J.B; Krabbe, P.F. & Van den Broek, P. 2000. Development and application of a health-related quality-of-life instrument for adults with cochlear implants: The Nijmegen cochlear implant questionnaire. *Otolaryngology: Head and Neck Surgery*, 123: 756-76

APPENDIX D

Information letter and informed consent

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA
Denkleiers • Leading Minds • Dikgopolo tša Dihlalefi

Faculty of Humanities
Department of Communication Pathology

May 2014

Dear cochlear implant recipient/ parent of cochlear implant recipient,

RE: Research project - Cochlear implants in South Africa: Clinical profile and outcomes

We are researchers at the Department of Communication Pathology, University of Pretoria who are conducting research in the field of cochlear implants. The main aim of our study is to describe the clinical profile and outcomes of paediatric and adult cochlear implantation in South Africa. This multi-centric study will attempt to collect clinical and outcome data of all cochlear implant recipients in South Africa. A part of our study will focus specifically on the quality of life outcomes of paediatric and adult cochlear implant recipients. In order to determine this, participants will be required to complete a questionnaire entitled: *Nijmegen Cochlear Implant Questionnaire* (Hinderink et al., 2000).

Researcher: Mrs Talita le Roux

Study leader: Professor Bart Vinck

Design and procedure:

This study will follow a *prospective cohort design* (descriptive research, collecting quantitative data). It is requested that each adult participant/ cochlear implant recipient complete the questionnaire on quality of life (attached). For children under the age of 18 years, it is requested that one of the parents/ primary caregiver completes the questionnaire. The questionnaire can be completed in hard copy and returned to the participant's cochlear implant program. Alternatively, the questionnaire can be completed electronically and participants can e-mail the completed questionnaire to their cochlear implant program.

Confidentiality:

Identifying data will not to be disclosed and all the information obtained will be handled with strict confidentiality. When data is combined from the various cochlear implant programs, all identifying information would be omitted and participants will be assigned an identifying code which will be used for data processing. Anonymity of all participants will be guaranteed at all times.

Risks:

There are no risks associated with this study.

Expected contribution:

This study will contribute to provide data and empirical comparison to demonstrate the effectiveness of current service delivery within the South African context, as well as the efficiency of cochlear implantation within the developing world. Accordingly, evidence based practice would be ensured and preliminary data would be gathered on the currents status of cochlear implants in South Africa.

Release of findings:

The results of this research study will be published in accredited academic journals, as well as in a summative research report.

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bart.vinck@up.ac.za
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talita.leroux@up.ac.za

If you agree to participate in this study, you are requested to sign this letter of consent.

Please do not hesitate to contact us for further information.

Thank you in advance for your time and co-operation.

Yours sincerely,

Mrs Talita le Roux
Researcher

Professor Bart Vinck
Study leader
Head of the University of Pretoria Cochlear Implant Unit (UP CIU)
Head of the Department of Communication Pathology

WRITTEN CONSENT TO PARTICIPATE IN RESEARCH STUDY

Herewith I, _____ (cochlear implant recipient/ parent of a cochlear implant recipient) *agree to complete the attached questionnaires on quality of life.* I have received the necessary information about this study and have had the opportunity to ask questions regarding this project.

_____

Signature of participant

Date: _____

APPENDIX E

Ethical approval letter

Postgraduate Research Ethics Committee,

Faculty of Humanities, University of Pretoria

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Humanities
Office of the Deputy Dean

29 October 2012

Dear Prof Vinck

Project:	**Cochlear implants in South Africa: clinical profiles and outcomes**
Researcher:	**TE le Roux**
Supervisor:	**Prof B Vinck**
Department:	**Communication Pathology**
Reference number:	**01289055**

I am pleased to be able to tell you that the above application was **approved (with comment)** by the **Postgraduate Committee** on 16 October 2012 and by the **Research Ethics Committee** on 25 October 2012. 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.

The Committee requests you to convey this approval to the researcher.

We wish you success with the project.

Sincerely

Prof John Sharp
Chair: Postgraduate Committee &
Research Ethics Committee
Faculty of Humanities
UNIVERSITY OF PRETORIA
e-mail: john.sharp@up.ac.za

APPENDIX F

Information letter and informed consent from team coordinators of participating cochlear implant programs

Johannesburg Cochlear Implant Program

University of Pretoria Cochlear Implant Unit

Bloemfontein Cochlear Implant Program

Steve Biko Academic Hospital Cochlear Implant Program

Chris Hani Baragwanath Academic Hospital Cochlear Implant Program

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Faculty of Humanities
Department of Communication Pathology

Attention: Mrs Leone Nauta

Coordinator of the Johannesburg Cochlear Implant Program (JCIP)

June 2012

Dear Mrs Nauta,

RE: Multi-centric research initiative - Cochlear implants in South Africa: Clinical profile and outcomes

As discussed personally with a core group of your team, we are researchers at the Department of Communication Pathology, University of Pretoria who are conducting research in the field of cochlear implants. The main aim of our study is to describe the clinical profile and outcomes of paediatric and adult cochlear implantation in South Africa. This multi-centric study will attempt to collect clinical and outcome data of all cochlear implant recipients in South Africa.

Researcher/ PhD student: Mrs Talita le Roux

Study leader: Professor Bart Vinck

Design and procedure:

This study will follow a *retrospective cohort design* (descriptive research, collecting quantitative data). All paediatric and adult cochlear implant recipients from the 8 independent cochlear implant programs in South Africa will be included in the study. Existing patient files, clinical records and existing databases will be reviewed in order to obtain the necessary information to determine the outcomes for this study. An electronic database will be designed and implemented at all cochlear implant programs in order to systematically document and track the required data for this study.

Confidentiality:

Identifying data will not to be disclosed and all the information obtained from the clinical files and records will be handled with strict confidentiality. When data is combined from the various cochlear implant programs, all identifying information would be omitted and participants will be assigned an identifying code which will be used for data processing. Anonymity of all participants will be guaranteed at all times.

Risks: There are no risks associated with this study.

Expected contribution:

This study will contribute to provide data and empirical comparison to demonstrate the effectiveness of current service delivery within the South African context, as well as the efficiency of cochlear implantation within the developing world. Accordingly, evidence based practice would be ensured and preliminary data would be gathered on the currents status of cochlear implants in South Africa.

Release of findings:

The results of this research study will be published in accredited academic journals, as well as in a summative research report. Team coordinators from the participating cochlear implant programs will take responsibility to oversee the process of retrospective data collection from cochlear implant recipients in their individual programs. Team coordinators would be co-authors to subsequent publications.

University of Pretoria
PRETORIA 0002
Republic of South Africa

Tel: 012 420 2355
Fax: 012 420 3517

bart.vinck@up.ac.za
www.up.ac.za
talita.leroux@up.ac.za

In order to conduct this study, clinical and outcome data from all paediatric and adult cochlear implant users from the Johannesburg Cochlear Implant Program will be gathered, together with the data from all other cochlear implant programs in South Africa. If permission for this is granted from you as the team coordinator, you are requested to sign this letter of consent.

Please do not hesitate to contact us for further information.

Thank you in advance for your time and co-operation.

Yours sincerely,

Mrs Talita le Roux
Researcher/ PhD student

Professor Bart Vinck
Study leader
Head of the University of Pretoria Cochlear Implant Unit (UP CIU)
Head of the Department of Communication Pathology

PERMISSION FOR THE USE OF INFORMATION OF COCHLEAR IMPLANT RECIPIENTS FROM THE JOHANNESBURG COCHLEAR IMPLANT PROGRAM

Herewith I, Mrs Leone Nauta give permission that the information of cochlear implant recipients from the Johannesburg Cochlear Implant Program may be used for the multi-centric research project titled: *Cochlear implants in South Africa: Clinical profile and outcomes.* I have received the necessary information about this study and have had the opportunity to ask questions regarding this project. I will oversee the data-collection process at our cochlear implant program and will make the data pertaining to this study specifically available to the researcher for subsequent multi-centric publications.

Mrs Leone Nauta

Coordinator: Johannesburg Cochlear Implant Program

Date: 30/7/2012

In order to conduct this study, clinical and outcome data from all paediatric and adult cochlear implant users from the University of Pretoria Cochlear Implant Unit will be gathered, together with the data from all other cochlear implant programs in South Africa. If permission for this is granted from you as the team coordinator, you are requested to sign this letter of consent.

Please do not hesitate to contact us for further information.

Thank you in advance for your time and co-operation.

Yours sincerely,

Mrs Talita le Roux
Researcher/ PhD student

Professor Barry Vinck
Study leader
Head of the University of Pretoria Cochlear Implant Unit (UP CIU)
Head of the Department of Communication Pathology

PERMISSION FOR THE USE OF INFORMATION OF COCHLEAR IMPLANT RECIPIENTS FROM THE JOHANNESBURG COCHLEAR IMPLANT PROGRAM

Herewith I, Mrs Nicolize Cass give permission that the information of cochlear implant recipients from the University of Pretoria Cochlear Implant Unit may be used for the multi-centric research project titled: *Cochlear Implants in South Africa: Clinical profile and outcomes.* I have received the necessary information about this study and have had the opportunity to ask questions regarding this project. I will oversee the data-collection process at our cochlear implant program and will make the data pertaining to this study specifically available to the researcher for subsequent multi-centric publications.

Mrs Nicolize Cass

Coordinator: University of Pretoria Cochlear Implant Unit

Date: 2012/07/24

In order to conduct this study, clinical and outcome data from all paediatric and adult cochlear implant users from the Bloemfontein Cochlear Implant Program will be gathered, together with the data from all other cochlear implant programs in South Africa. If permission for this is granted from you as the team coordinator, you are requested to sign this letter of consent.

Please do not hesitate to contact us for further information.

Thank you in advance for your time and co-operation.

Yours sincerely,

Mrs Tallta le Roux
Researcher/ PhD student

Professor Bart Vinck
Study leader
Head of the University of Pretoria Cochlear Implant Unit (UP CIU)
Head of the Department of Communication Pathology

PERMISSION FOR THE USE OF INFORMATION OF COCHLEAR IMPLANT RECIPIENTS FROM THE BLOEMFONTEIN COCHLEAR IMPLANT UNIT

Herewith I, Dr Inn Butler give permission that the information of cochlear implant recipients from the Bloemfontein Cochlear Implant Program may be used for the multi-centric research project titled: *Cochlear Implants in South Africa: Clinical profile and outcomes.* I have received the necessary information about this study and have had the opportunity to ask questions regarding this project. I will oversee the data-collection process at our cochlear implant program and will make the data pertaining to this study specifically available to the researcher for subsequent multi-centric publications.

Dr Inn Butler

Coordinator: Bloemfontein Cochlear Implant Program

Date: 10/7/2012

In order to conduct this study, clinical and outcome data from all paediatric and adult cochlear implant users from the Steve Biko Academic Hospital Cochlear Implant Program will be gathered, together with the data from all other cochlear implant programs in South Africa. If permission for this is granted from you as the head of the team, you are requested to sign this letter of consent.

Please do not hesitate to contact us for further information.

Thank you in advance for your time and co-operation.

Yours sincerely,

Mrs Talita le Roux
Researcher/ PhD student

Professor Bart Vinck
Study leader
Head of the University of Pretoria Cochlear Implant Unit (UP CIU)
Head of the Department of Communication Pathology

PERMISSION FOR THE USE OF INFORMATION OF COCHLEAR IMPLANT RECIPIENTS FROM THE STEVE BIKO ACADEMIC HOSPITAL COCHLEAR IMPLANT PROGRAM

Herewith I, **Prof Tshifularo** give permission that the information of cochlear implant recipients from the Steve Biko Academic Hospital Cochlear Implant Program may be used for the multi-centric research project titled: *Cochlear implants in South Africa: Clinical profile and outcomes.* I have received the necessary information about this study and have had the opportunity to ask questions regarding this project. I will oversee the data-collection process at our cochlear implant program and will make the data pertaining to this study specifically available to the researcher for subsequent multi-centric publications.

Professor Tshifularo

Head: Steve Biko Academic Hospital Cochlear Implant Program

Date: 17.04.13.

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

MEDICAL ADVISORY COMMITTEE
CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

PERMISSION TO CONDUCT RESEARCH

Date: 12 April 2013

TITLE OF PROJECT: Cochlear implants in South Africa: clinical profiles and outcomes

UNIVERSITY: Pretoria

Principal Investigator: TE le Roux

Department: Communication Pathology

Supervisor (If relevant): Prof B Vinck

Permission Head Department (where research conducted): Yes

Date of start of proposed study: April 2013
Date of completion of data collection: April 2014

The Medical Advisory Committee recommends that the said research be conducted at Chris Hani Baragwanath Hospital. The CEO /management of Chris Hani Baragwanath Hospital is accordingly informed and the study is subject to:-

- Permission having been granted by the Committee for Research on Human Subjects of the University of the Witwatersrand.
- the Hospital will not incur extra costs as a result of the research being conducted on its patients within the hospital
- the MAC will be informed of any serious adverse events as soon as they occur
- permission is granted for the duration of the Ethics Committee approval.

.....
Recommended
(On behalf of the MAC)
Date: 12 April 2013

.....
Approved/Not Approved
Hospital Management
Date: 15/04/13

APPENDIX G

Plagiarism declaration

UNIVERSITY OF PRETORIA

FACULTY OF HUMANITIES

RESEARCH PROPOSAL & ETHICS COMMITTEE

DECLARATION

Full name: **Talita le Roux**

Student Number: **01289055**

Degree/Qualification: **D. Phil (Communication Pathology)**

Title of thesis/dissertation/mini-dissertation:

PREDICTORS OF COCHLEAR IMPLANT OUTCOMES IN SOUTH AFRICA

I declare that this **thesis** / dissertation / mini-dissertation is my own original work. Where secondary material is used, this has been carefully acknowledged and referenced in accordance with university requirements.

I understand what plagiarism is and am aware of university policy and implications in this regard.

SIGNATURE

2016.08.26

DATE

APPENDIX H

Proof of acceptance of articles

International Journal of Pediatric Otorhinolaryngology decision (Study I)

From: International Journal of Pediatric Otorhinolaryngology <pedot@elsevier.com>
Date: Tuesday, 30 September 2014 18:13
To: De Wet Swanepoel <dewet.swanepoel@up.ac.za>
Subject: Your Submission IJPORL-D-14-00419R1

Ms. Ref. No.: IJPORL-D-14-00419R1
Title: Profound childhood hearing loss in South Africa: Risk profile, diagnosis and age of intervention
International Journal of Pediatric Otorhinolaryngology

Dear Prof. De Wet Swanepoel,

I am pleased to tell you that your work has now been accepted for publication in International Journal of Pediatric Otorhinolaryngology.

You will receive further information from Elsevier regarding the publication process and proofs of your article very shortly.

When your paper is published on ScienceDirect, you want to make sure it gets the attention it deserves. To help you get your message across, Elsevier has developed a new, free service called AudioSlides: brief, webcast-style presentations that are shown (publicly available) next to your published article. This format gives you the opportunity to explain your research in your own words and attract interest. You will receive an invitation email to create an AudioSlides presentation shortly. For more information and examples, please visit http://www.elsevier.com/audioslides.

Interactive Case Insights: The journal encourages authors to complement their case reports and other articles of an educational nature with test questions that reinforce the key learning points. These author created questions are submitted along with the article (new or revised) and will then be made available in ScienceDirect alongside your paper. More information and examples are available (at http://www.elsevier.com/about/content-innovation/interactive-case-insights). Test questions are created online (at http://elsevier-apps.sciverse.com/GadgetICRWeb/verification). Create the test questions, save them as a file to your desktop, and submit them along with your (new or revised) manuscript through EES. That's it! For questions, please contact icihelp@elsevier.com

Thank you for submitting your work to this journal.

With kind regards,

Robert J. Ruben, MD
Editor-in-Chief
International Journal of Pediatric Otorhinolaryngology

International Journal of Pediatric Otorhinolaryngology decision (Study II)

From: "International Journal of Pediatric Otorhinolaryngology" <pedot@elsevier.com>
To: <talita.leroux@up.ac.za>, <gerhard.talita@gmail.com>
Date: 26/02/2016 01:08 AM
Subject: Your Submission IJPORL-D-15-01098R1

Ms. Ref. No.: IJPORL-D-15-01098R1
Title: PREDICTORS OF PEDIATRIC COCHLEAR IMPLANTATION OUTCOMES IN SOUTH AFRICA
International Journal of Pediatric Otorhinolaryngology

Dear Talita,

I am pleased to tell you that your work has now been accepted for publication in International Journal of Pediatric Otorhinolaryngology.

You will receive further information from Elsevier regarding the publication process and proofs of your article very shortly.

When your paper is published on ScienceDirect, you want to make sure it gets the attention it deserves. To help you get your message across, Elsevier has developed a new, free service called AudioSlides: brief, webcast-style presentations that are shown (publicly available) next to your published article. This format gives you the opportunity to explain your research in your own words and attract interest. You will receive an invitation email to create an AudioSlides presentation shortly. For more information and examples, please visit http://www.elsevier.com/audioslides.

Interactive Case Insights: The journal encourages authors to complement their case reports and other articles of an educational nature with test questions that reinforce the key learning points. These author created questions are submitted along with the article (new or revised) and will then be made available in ScienceDirect alongside your paper. More information and examples are available (at http://www.elsevier.com/about/content-innovation/interactive-case-insights). Test questions are created online (at http://elsevier-apps.sciverse.com/GadgetICRWeb/verification). Create the test questions, save them as a file to your desktop, and submit them along with your (new or revised) manuscript through EES. That's it! For questions, please contact icihelp@elsevier.com

Thank you for submitting your work to this journal.

With kind regards,

robert.ruben@einstein.yu.edu J. Family name, MD
Editor-in-Chief
International Journal of Pediatric Otorhinolaryngology

International Journal of Audiology (Study III)

From: International Journal of Audiology <onbehalfof+roeser+utdallas.edu@manuscriptcentral.com>
To: <talita.leroux@up.ac.za>, <gpleroux1@gmail.com>
Date: 19/08/2016 01:56 AM
Subject: International Journal of Audiology - Decision on Manuscript ID TIJA-2016-05-0159.R1

MS: "Predictors of health-related quality of life in adult cochlear implant recipients in South Africa"
MS#: TIJA-2016-05-0159.R1

Dear Mrs. le Roux:

Thank you for submitting your above listed revised manuscript. Based on the revisions made, it is a pleasure to accept it for publication in the International Journal of Audiology.

At this time, your manuscript is being sent to the publisher for final production. Page proofs will be sent to you during the production process. It is very important that you read your page proofs carefully and return them promptly so that your paper will be processed on schedule. Currently, it requires about 5-6 months for accepted papers to appear in a printed issue of the journal. However, the finished article will appear in electronic form and all readers will be notified through alerts that it is available shortly after you return your page proofs. The electronic posting represents a formal publication.

Thank you for your fine contribution. On behalf of the Editors of the International Journal of Audiology, we look forward to your continued contributions to the Journal. Of particular importance is that you consider accepting the offer to review papers for IJA if/when asked. Finding seasoned authors to review papers is a critically important component of the peer review process and your assistance in this area would be most appreciated.

Sincerely,

Ross J. Roeser, PhD
Editor-in-Chief
International Journal of Audiology
roeser@utdallas.edu