Wideband Acoustic Immittance Measures as part of a Newborn Hearing Screening

Program in Canadian First Nations and Metis, Caucasian and Other Ethnicity Neonates

by

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Abstract

Purpose: There are few data on the prevalence of Otitis Media (OM) in neonates of all ethnicities, especially First Nations and Metis (FNAM) neonates, at birth. There is a need to diagnose type of hearing loss at the time of Newborn Hearing Screening (NHS) to determine prevalence and to refer neonates for timely assessment and intervention. Wideband Acoustic Immittance (WAI) is a viable tool that can aid in the diagnosis of conductive hearing loss (CHL) at time of hearing screening.

Design: This cross-sectional study examined the application of WAI measures (Wideband Absorbance (WBA) at Ambient and Tympanometric Peak Pressure (TPP), and Admittance Phase (Yφ) as part of a regular NHS protocol. NHS pass/fail rates, likely diagnoses and WAI measurements in FNAM newborns were compared to newborns of other ethnicities. 213 neonates (426 ears) were recruited from the Royal University Hospital in Saskatoon, Saskatchewan. 382 ears met the inclusion criteria: 42 FNAM, 212 Caucasian, 48 Other Ethnicities, and 80 Undeclared Ethnicity.

Results: FNAM neonates had a significantly higher NHS fail rate than Caucasian neonates. The WBA of FNAM neonates was significantly lower than that of neonates of other ethnicities in both NHS pass and fail conditions. WBA was significantly lower for neonates who failed the test battery and who failed Transient Evoked Otoacoustic Emission (TEOAE) testing. The difference in WBA at peak pressure was larger than the difference at ambient pressure for neonates who passed or failed a NHS test battery. Yφ was significantly lower in neonates who passed the test battery and who had a likely diagnosis of normal hearing.

Conclusions: WBA and Yφ are effective in distinguishing ears with likely CHL from normal hearing ears. Pressurized WBA may be more effective than ambient WBA and Yφ is a promising measure in the diagnosis of CHL.

FNAM neonates have a higher NHS fail rate and a greater prevalence of likely CHL. WBA of FNAM neonates is lower than that of other ethnicities. Further research is needed to determine if lower WBA in FNAM neonates indicates a greater prevalence of OM or a difference in middle ear anatomy.

Lay Summary

The goal of Newborn Hearing Screening (NHS) Programs is to treat hearing loss by the time a child is 6 months old. Early treatment gives a child access to sound in the developing months which allows them to develop speech and improve learning outcomes. Early diagnosis is necessary to achieve early treatment. Fluid in the middle ear prevents an early diagnosis of sensorineural hearing loss and long-term fluid can cause a conductive hearing impairment that also affects speech and learning. First Nations and Metis children have a higher prevalence of chronic middle ear fluid. This study added Wideband Absorbance (WBA), a method of sending sound at the eardrum and measuring how much is absorbed, to a NHS protocol to diagnose middle ear fluid at birth. This study also documented prevalence of middle ear fluid and looked at the differences in Wideband Absorbance in newborns of different ethnicities.

Preface

This thesis is based on work conducted at the Royal University Hospital by Dr. Navid Shahnaz, Dr. Charlotte Douglas, and myself, Lareina Abbott. I contributed to the identification of the research question and methodology with great guidance from Dr. Navid Shahnaz of UBC. Training on the newborn ward of the RUH was under the guidance of Dr. Charlotte Douglas and her Newborn Hearing Screening team. I was responsible for the collection of the data, collection of the consent, and the writing of the thesis. Statistical analysis was performed under guidance of Dr. Navid Shahnaz. Dr. Tony Herdman and Sasha Brown were thesis committee members who provided great input to the writing of this paper.

Ethics approval was sought from UBC Clinical Research Ethics Board by Dr. Navid Shahnaz and myself, Lareina Abbott. The UBC ethics certificate of expedited approval is UBC CREB Number: H17-00437. Ethics approval was also sought from the Saskatoon Health Region by Dr. Navid Shahnaz, Dr. Charlotte Douglas, and myself, Lareina Abbott. The ethics certificate of approval is number Bio 17-75. Both certificates were under the project title, "Investigating the Screening Outcome for a Novel Hearing Screening Protocol in Neonatal Intensive Care Unit (NICU) and Well-baby Unit infants."

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List of Abbreviations

AA – Australian Aborigine

AABR – Automated auditory brainstem response

ABR – Auditory brainstem response

AC – Air conduction

AD – Auditory dys-synchrony

AN – Auditory neuropathy

ANOVA – Analysis of variance

ASR – Acoustic stapedial reflex

AOM – Acute otitis media

AUROC – Area under the receiver operating curve

BBN – Broadband noise

BC – Bone conduction

BCEHP – British Columbia Early Hearing Program

CHL – Conductive hearing loss

COM – Chronic otitis media

dB - Decibels

daPa - Decapascal

DPOAE – Distortion product otoacoustic emission

EHDI – Early hearing detection and intervention

EHF – Extended high frequency

ENT – Ear nose throat physician

FNAM – First Nations and Metis

GG – Greenhouse-Geiser

HFT – High frequency tympanometry

Hz – Hertz

KHz – Kilohertz

LiSN-S – Listening in Spacialized Noise

ME – Middle ear

MEMR – Middle ear muscle reflex

MLD – Masking level difference

NH – Normal hearing

NHS – Newborn hearing screening

NICU – Neonatal intensive care unit

OAE – Otoacoustic emission

OM – Otitis media

OME – Otitis media with effusion

PA – Power absorption

PCHI – Permanent childhood hearing impairment

SNHL – Sensorineural hearing loss

SPL – Sound pressure level

SRT – Speech reception threshold

TEOAE – Transient evoked otoacoustic emission

TPP – Tympanometric peak pressure

WAI – Wideband acoustic immittance

WBA – Wideband absorbance

WBR – Wideband reflectance

WHO – World Health Organization

Yφ– Admittance Phase

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Dedication

To Jason Lewis and Zoe Lewis

Chapter 1: Introduction

All children learn language along a similar timeline, with their language maturation coinciding with their biological maturation (Hickerson, 2000). However, the human brain does not come equipped with a native language, but rather has an innate ability to learn language. Noam Chomsky theorized a "Universal Grammar" that gives the child a template onto which the language of their environment is superimposed (Fromkin & Rodman, 2010). For this imprintation to be successful for oral language, the child must be able to hear speech sounds (Carney, 1999). As language must be imprinted on the brain at the right time of rapid neuronal and synapse development, auditory depravation in the form of hearing loss results in an imperfect, delayed or absent imprintation (Yoshinaga-Itano, 2003). This "Critical Period" of language learning occurs much before an infant speaks, from 0-48 months (Kuhl, 2005).

Hearing loss (at a level that affects language learning) is the most common congenital birth defect (Erenberg, 1999; Low, 2005). The prevalence of severe bilateral permanent hearing loss (>70 dB) is estimated at 1 to 3 per 1000 newborn infants (Bagatto, 2010). If you include infants with a moderate hearing loss (>40dB), the prevalence almost doubles (Eskander, 2014). In the Neonatal Intensive Care Units (NICU) the prevalence is 2-4 per 100 newborn infants (Erenberg, 1999).

Traditional methods of diagnosis can miss children with congenital hearing loss as it is a "silent disorder". An example of this is screening by high risk registry, which involves testing children with a family history of deafness, and can miss 50% of newborns with congenital hearing loss (Erenberg, 1999; Low, 2005). Relying on physician or parental recognition has also not been successful in the past in detection of significant hearing loss in the first year of life (Erenberg, 1999; Yoshinaga-Itano, 2003). Failure to achieve early diagnosis of congenital

hearing loss leads to no or imperfect speech and language abilities, and often a lifetime of educational and vocational challenges (Erenberg, 1999). Yoshinaga-Itano (2003) showed that if a child is identified and treated for hearing loss by 6 months of age then they will have significantly better language scores than children identified and treated after 6 months. The goal of Newborn Hearing Screening (NHS) Programs, also called Early Hearing Detection and Intervention (EHDI) Programs, align with the Healthy People 2010 goals (JCIH, 2007), which are to screen for hearing loss by 1 month of age, undergo audiologic evaluation by 3 months of age, and obtain appropriate intervention services by 6 months of age, therefore providing auditory input to the child before the "critical period" is over (Erenberg, 1999; Low, 2005).

Otitis media with effusion (OME), defined as the presence of fluid in the middle ear without signs or symptoms of acute ear infection (Rosenfeld, 2016), causes a blockage of sound transmission and prevents the effective transmission of sound through the middle ear (Shriberg, 2000). OM is used interchangeably with OME (Otitis Media with Effusion) in this paper. Synonyms for OME are serous, secretory or non-suppurative otitis media (Rosenfeld, 2016). Persistent OM, or chronic otitis media (COM) can block the sound signal for long enough to cause a constant mild to moderate hearing loss that can affect language and learning in the critical period (Friel-Patti, 1986; Gravel, Wallace, & Ruben, 1996; Shriberg, 2000).

First Nations and Metis children have been shown to have a higher prevalence of OM in the early years with bouts that last longer (Ayukawa, Bruneau, Proulx, Macarthur, & Baxter, 2004; Boswell, 1995; CASLPA, 2010). This can lead to an increase in language and learning problems in later years. Despite this, few prevalence studies have been done to look for differences in middle ear conditions in different ethnicities, including First Nations and Metis neonates, at birth.

The focus in Newborn Hearing Screening (NHS) programs is to diagnose permanent hearing loss, most often sensorineural hearing loss, using Otoacoustic Emissions (OAE's) and Automatic Auditory Brainstem Response (AABR) tests to determine the status of the cochlea. OM can delay the diagnosis of a sensorineural hearing loss as the OAE and AABR testing signal does not reach the cochlea or the cochlear response is not able to return to the testing probe due to the effusion blocking the middle ear space (Aithal, 2014b; Prieve, Calandruccio, Fitzgerald, & Mazevski, 2008; Prieve & Dreisback, 2011). This is a false positive referral, as a child receives a fail result even though they may have a well-functioning cochlea. As such, a refer result can either be a true positive result from a sensorineural loss or a false positive result from a permanent or transient conductive loss. This diagnosis does not happen at the time of initial screening and instead further testing occurs at later visits. The inability to determine cause of a refer result at screening delays diagnosis and intervention for both sensorineural and conductive conditions. There is a need in NHS programs for a test that accurately determines why an infant receives a refer result. Such a test would reduce the false positive rate thereby reducing the time to diagnosis and intervention for children with SNHL. Such a test would also reduce the stress of parents at time of screening, and would aid in the identification of children who are likely to develop COM (Allen, 2005; Gorga, 2001; Keefe et al., 2000).

Some NHS programs include a tympanometric measure to investigate the status of the middle ear at the time of initial screening, which can give information as to the cause of a refer result. 226 Hz tympanometry has been shown to be ineffective at determining the status of the newborn middle ear and it is common practice to use 1000 Hz tympanometry (Kei, 2003; Margolis, 2003; Mazlan, 2007; Meyer, 1997; Rhodes, 1999). However, some researchers have

indicated that a more accurate technique is needed to determine the prevalence of conductive conditions (Aithal, 2014b).

The use of Wideband Acoustic Immittance (WAI) in a newborn hearing screening protocol has promise in accurately diagnosing conductive problems as the cause of a "refer" at the time of newborn hearing screening thereby decreasing the time to appropriate intervention for both sensorineural hearing loss and conductive hearing loss (Aithal, 2015, 2017a; Hunter, Feeney, Lapsley-Miller, Jeng, & Bohning, 2010; Sanford, Keefe, & Liu, 2009). The two WAI measures used in the current study are Wideband Absorbance (WBA) and Admittance Phase angle ($Y\varphi$).

In addition to possibly providing a diagnosis of middle ear pathology at the time of screening, WAI measures can be of use in determining if different middle ear measure normative values are needed for neonates of different ethnicities. Currently, the normative values used in hearing screening programs are determined by Caucasian and mixed ethnicity newborns. There are few studies that look at WAI differences in neonates of different ethnicities, but studies in Caucasian and Chinese adults, (Shahnaz & Bork, 2006) and children (Beers, Shahnaz, Westerberg, & Kozak, 2010) show that there are significant differences in Wideband Reflectance (WBR) values between ethnicities and that ethnic differences are related to middle ear characteristics. If the normative middle ear values used to test FNAM children are incorrect, it is possible that a FNAM neonate could pass hearing screening when they should have failed or vice versa. If a neonate passes hearing screening, then sound should have been effectively absorbed into the middle ear system and if a neonate fails hearing screening due to OME then sound should not have been effectively absorbed into the middle ear. WBA in particular, as a measure of sound absorbed by the ear, can identify the need for different normative values if neonates of

different ethnicities have different WBA patterns on the pass and refer of a NHS program

(Aithal, Kei, Driscoll, & Khan, 2014a).

1.1   Otitis Media and Conductive Hearing Loss in Children

1.1.1   Need for detection of Otitis Media

Otitis media (OM) is the most common cause of conductive hearing loss in children and

is the most common infectious disease of childhood (Uhari, 1996). The symptoms of OME are

often undetected, including those of children with conductive hearing loss or school performance

problems. In OM, the fluid and pressure differences in the middle ear cause the auditory signal to

be delayed, reduced and distorted on its way from the outer ear to the cochlea which results in an

inconsistent auditory signal reaching the brain (Shriberg, 2000). The fluid in the middle ear

decreases the movement of the tympanic membrane and the ossicles, which then delays the

sound transmission and translation (Alaerts, 2007). OM is often transient but when it is not

resolved it causes a persistent or fluctuant mild to moderate hearing loss (defined as a PTA >= 25

and <=40 dB HL) which is a form of auditory deprivation (Hanks, 2009). The amount of hearing

loss can be variable with some children experiencing little to no hearing loss at all. The average

hearing threshold for children experiencing OM is 25 dB HL but may range from 0 to 50 dB HL

(Howden, 2007). The inconsistency of the signal experienced in a child with OM results in an

incomplete language transmission and can lead to problems with speech and language

development and the acquisition of oral language (Friel-Patti, 1986; Gravel et al., 1996;

Shriberg, 2000).

1.1.2 Otitis Media and resulting minimal/mild hearing loss and its effects on language learning, auditory processing, and extended high-frequency hearing sensitivity

Minimal and mild hearing loss has been shown to affect child development and school performance (Bess, Dodd-Murhpy, & Parker, 1998; Holstrum, Gaffney, Gravel, Oyler, & Ross, 2008). Children with minimal to mild hearing loss have been found to experience more difficulty than normal hearing children on educational and functional test measures (Bess et al., 1998). Specifically, they have been found to have poorer scores on tests involving reading vocabulary, language mechanics, phonologic short-term memory, phonologic discrimination, word analysis, spelling and science (Bess et al., 1998; Blair, Peterson, & Viehweg, 1985; Davis, Elfenbein, Schum, & Bentler, 1986; McKay, Gravel, & Tharpe, 2008; Yoshinaga-Itano, 2003). Children with minimal to mild hearing loss might also have higher levels of dysfunction in a classroom setting (Bess et al., 1998; Dodd-Murphy & Murphy, 2007).

A study from 1986 (Friel-Patti) on language delay in infants associated with middle ear disease and mild fluctuation hearing impairment found that there was a 71.5% incidence of language delay with 42.9% delayed greater than 6 months in the otitis-prone group (minimum of three episodes in 24 months) compared to a normal group that had 21.4% language delay with one child having a delay greater than 6 months.

In 2000 (Shriberg) researchers looked at the long-term effects of early OME with and without hearing the loss in 70 children. They found that hearing levels at 12-18 months were significantly associated with speech delay and low language outcomes at 3 years of age. They also found that the risk of speech delay at 3 years was 2% for children with less than 20 dB HL average hearing levels at 12-18 months and 33% for children with greater than 20 dB HL average hearing levels at 12-18 months.

A literature review conducted in 2004 (Roberts) looked at research on the link of OME to children's hearing and development. They stated that about half of children with an episode of OME experience a mild hearing loss while 5-10% of children had a moderate hearing loss. They found that for typically developing children, OME may not be a substantial risk factor for later speech and language development or academic achievement, however, they also stated that most of the studies used the presence of OME and not hearing loss as the independent variable. Their conclusions were that hearing and language should be screened after 3 months of bilateral OME, when families or caregivers express concern, and that special population should be screened. They also noted that physician adherence to guidelines has been low and that continuing education is needed.

A study in 2014 (Tomlin) looked at the long-term impact of childhood otitis media (OM) on listening ability in school-aged children. They looked at speech perception in background noise in 2 groups of 35 children aged 6- 12 year with normal middle ear function and hearing at the time of assessment. This study did not look at language outcomes but rather at functional listening ability such as binaural speech perception and special listening. They used the LiSN-S (Listening in Spacialized Noise) binaural speech perception evaluation which simulates a 3D listening environment under headphones by synthesizing the test stimuli using head related transfer function, head shadow, timing and intensity cues. Speech Reception Threshold (SRT) measures were collected under these conditions. A clinical history including the number of ear infections and age of onset and duration was obtained from the parents of the children. The researchers found that the children with a reported history of middle ear dysfunction demonstrated significantly poorer binaural speech perception ability than their healthy peers despite having normal sound detection at the time of hearing assessment. They also found that

binaural speech processing ability was more affected in children with a reported early onset of middle ear pathology. This link of reported age of onset with binaural processing ability concurs with the theory of "Critical Periods" which suggest that the influence of sensory input on the auditory brain is not consistent across development. The limitation of this study was that history of OME was by parental report.

Hogan and Moore (2003) stated that OME can cause lasting effects on binaural hearing and other central auditory deficits and looked at how binaural hearing specifically is affected by COM. They tested how OME affects masking level difference (MLD), a measure of binaural hearing, in 6-year-old children whose lifetime history of OME was known. All children were OME free at the time of MLD testing. They found that only those children with a cumulative OME experience of more than about half the time during the first five years consistently had a lasting impaired binaural hearing. The highest OME prevalence group (7/31) had smaller MLD's than their age-matched peers.

Margolis et al. (1993) studied the effects of COM on extended high frequency (EHF) hearing in children. They found that children with a history of OM had poorer EHF hearing than children without OM and that it appeared to be related to OM severity. These results suggest that OM not only affects the middle ear but can also permanently affect the cochlea and sensorineural hearing. In summary, the risk of long-term side effects in the form of language, speech, high-frequency hearing, and auditory processing outcomes, is increased with earlier onset and longer duration of OME.

1.1.3   Prevalence of Otitis Media and Conductive Hearing Loss

OM is the second most prevalent childhood disease after the common cold and (Hendley, 2002) OME represents about 25 to 35% of OM cases (Stool, 1994). About 90% of children in North America have an episode of OME before they enter school and develop on average 4 episodes of OME every year. In the first year, over 50% of children will experience OME (Rosenfeld, 2016).

In neonates, White et al. (1993) reported that 17 per 1000 well-baby unit neonates and 36 per 1000 neonatal intensive care unit (NICU) infants had CHL. Australian neonates had a prevalence of CHL at 2.97 per 1000 neonates, a rate 1.8 times that of SNHL (1.64 per 1000) (Aithal, 2012). It is likely that neonatal CHL prevalence rates differ due to the lack of a non-invasive gold standard in testing.

Most episodes of OME resolve within 3 months but in 30-40% of children the episodes repeat and in 5-10% of children the episodes last over 1 year (Rosenfeld, 2016). OME that lasts over 3 months is considered COM and can be associated with hearing loss, balance problems, poor school performance, behavioural problems, ear discomfort, recurrent AOM and an overall reduced quality of life (Rosenfeld, 2016). It is these occurrences of COM, where the sound signal is constantly delayed in children, that we want to diagnose and prevent, thereby allowing for proper language learning.

1.2   Otitis Media and First Nations and Metis populations

1.2.1   Otitis Media in First Nations and Metis children

The incidence of OM and COM in FNAM and Aboriginal children in Canada (Ayukawa et al., 2004; Boswell, 1995; CASLPA, 2010; Harris, 1998), the United States (Wiet, 1979),

Greenland (Pedersen, 1988), and Australia (Jeffries-Stokes, 2004; Kelly, 1991), is higher than in the general population with an earlier onset and longer duration.

In Canada, a survey of 1109 First Nations children in 5 communities in B.C. reported that the rate of middle ear disease requiring treatment in preschool and primary school aged children was 12%. Pure tone audiometry showed that 19% of these children had hearing loss and tympanometry was abnormal in 38% (Roberts, 1976).

In the United States, First Nations infants and children have more than three times the rate of outpatient and hospital visits with an OM diagnosis compared to the general population (Hunter, 2007). In a survey of 15,890 school aged children on a Navajo reservation, researchers found that 4% had tympanic membrane perforations and 5.6% had a failure for a combined test of audiometry, tympanometry, and otoscopy (Nelson, 1984). Also, in the United States, Moore (1999) studied the rate of OME and hearing loss in three different ethnic subgroups: Inuit, American Indian, and Non-Aboriginal, and found that there was a significant interaction between OME, ethnic group and hearing loss.

In a publication on "Otitis Media: It's Health, Social and Educational Consequences Particularly for Canadian Inuit, Metis, and First Nations Children and Adolescents" (Bowd, 2002, pp. 34-35), the author concludes that: "Middle ear disease and consequent hearing loss have an impact on Canadian aboriginal children and adolescents that can only be characterized as alarming. In some Inuit communities, the prevalence of chronic otitis media has been estimated at more than sixty times the rate for southern Canadians and among First Nations people it is not unusual for the disease to be as much as ten times more prevalent than amongst non-aboriginal Canadians. The economic, social, health and educational costs are immense and yet research in

this area is fragmented." Chronic ear disease in Aboriginal youth leads to an increased risk for lower academic performance and increased behavioral problems (CASLPA, 2010).

The World Health Organization (WHO), has compiled information from different ethnic groups estimating a prevalence rate among Inuit for COM of 12-46% and for Native Americans of 4-8% (WHO/CIBA 1996). Bowd (2002) notes that prevalence data for COM are limited and sometimes ambiguous, particularly concerning sub-populations (such as aboriginal groups) within countries. He states that different studies use different methods of diagnosis, including a variety of age groups and do not specify what type of OM is being reported. He concludes that "systematically collected prevalence data from a regionally and culturally representative sample of communities would enable more accurate estimates of prevalence than is evident at present."

1.2.2   Otitis Media in First Nations and Metis neonates

The most recent study on hearing screening and middle ear measures on North American First Nations neonates was performed in 2007 (Hunter). The study notes that although "American Indian children have 3 times the rate of OM compared to the general population, that prospective cohort studies of OME and hearing loss have not previously been reported in American Indian infants" (Hunter, 2007, p. 1429). In a longitudinal study, Hunter (2007) found that in the newborn period 23.5% of infants failed hearing screening in at least one ear and that OAE test results were associated with OM diagnosis. Of 366 hearing screening failures, only one infant was identified with SNHL and therefore most of the hearing screening failures reflected a middle ear origin or another temporary problem. She concluded that "The practical use of using just OAE for screening was limited in this population and that efforts to develop public and

medical education as well as screening diagnosis and treatment programs were needed to detect and decrease recurrent OME in American Indian infants and children" (Hunter, 2007, p. 1430).

In Australia, Aithal (2012) found that Australian Aborigines (AA) had nearly twice the prevalence of CHL at initial screening (35.19%) compared to non-AA neonates (17.83%). She also noted that CHL persisted in 75% of AA infants compared to 27.78% of non-AA infants.

Prevalence data on OM in Canadian FNAM neonates versus other ethnicities are needed to address the population health issue of why FNAM have a higher incidence, earlier onset, and longer duration of OM. No robust data currently exists on the incidence of OM in Canadian FNAM neonates as is acknowledged by Speech-Language and Audiology Canada (SAC, formerly known as CASLPA) and Health Canada (CASLPA, 2010).

1.2.3   Diagnosis of the type of hearing loss at the screening to determine which risk factors are important in FNAM children

There is clear evidence that the prevalence of COM is higher in Aboriginal children around the world, however, without prevalence data of OM in Aboriginal children at birth, it is difficult to identify the true risk factors (Bowd, 2002). There are many possible risk factors for COM, and the cause and disease progression of OM are complex. Historically, there was an increased prevalence of OM in FNAM groups after European colonization introduced new viral and bacterial pathogens, as well as dietary and social risk factors (Gregg, 1982; Homoe, 2001), however, it is uncertain as to how that would affect modern FNAM peoples. Hunter (2007) notes that social risk factors such as bottle-feeding, exposure to second-hand smoke, crowded living conditions, limited access to medical care among other environmental factors have been implicated in a higher OM rate among American Indian (AI) groups, but are as yet unproven in

these populations (Daly, 2000). Table 1 highlights some of the risk factors for COM in FNAM children in Canada are as follows:

Table 1: Risk Factors for Chronic Otitis Media in First Nations and Metis children in Canada

Risk Factor	Research
Age	Children are more likely to develop OM in infancy and early childhood compared to later ages (Daly, 1997).
Sex	Males are at a higher risk of AOM and OME than females as is true of most infectious diseases in childhood (Adams & Benson, 1991).
Ethnicity	Ethnicity is associated with susceptibility to OME but there is difficulty in determining the meaning of the association in the context of confounding factors such as socioeconomic and environmental variables (Moore, 1999).
Familial Predisposition	There is a clear trend that OM aggregates in families. The relative contributions of genetic and environment remain entangled. The most likely model for the genetic influence of OME is multifactorial, in which genes and environmental exposures play a role in predisposing a child to OME, recurrent OM and chronic OME (Daly, 1997).
Socioeconomic Status	Studies are ambiguous and varied in methodology and location (Bowd, 2002).
Breastfeeding and Nutrition	A paper on OM among the Inuit (Manning & Avery, 1974) found that when breastfeeding was widely practiced there were much lower prevalence levels of COM. Many other studies have reported that the risks of OME, AOM, and recurrent OM are significantly reduced by breastfeeding (Thomson, 1994). Thomson (1994) reviews 8 studies, 7 of which indicated that the risk of bottle feeding presented for significant OM.
Exposure to smoke	Exposure to tobacco smoke studies link passive cigarette smoking to increased risk of OM, but for some northern aboriginal communities, it is relevant to consider the addition possible risk factor of wood burning for cooking and hearing – for which no studies have been done. (Daly, 1997).
Daycare attendance	Studies on the relation of daycare attendance and OM have shown no significant correlation between daycare attendance and repetitive AOM. This may be because the relevant factors in day care attendance, such as size and type of daycare, the age of enrolment, the degree of crowding and hygiene practices all contribute to the risk of COM (Daly, 1997). Daly (1997) concluded that children attending larger centers are

Risk Factor	Research
	at greater risk of AOM and OME and that duration of OME was greater as the number of children increased.
Season	The incidence of OME tends to be highest in winter and lower in summer (Maw & Counsell, 1997).
Maternal Alcohol Consumption	There were no studies that examined an association between OM and maternal alcohol consumption which Bowd (2002) notes is a serious omission as Fetal Alcohol Syndrome occurs at a higher rate in First Nations populations.
Anatomical	Bowd (2002) notes that it is likely that the most important factors that determine OM in infancy are developmental in nature such as the anatomical structure of the ear (Todd, 1985).
Exposure to organochlorides	One study has linked prenatal exposure to organochlorides and the incidence of AOM (Dewailly et al., 2000).

Gathering prevalence data for OM at initial hearing screening can help in determining whether FNAM children have a higher prevalence of OM due to environmental factors or to genetic, developmental, and prenatal exposure factors. For example, OM due to environmental factors such as the exposure to second-hand smoke and daycare settings will not occur until after a child has left the hospital as a newborn. Prevalence data for OM at birth in FNAM neonates can focus health care policy on areas that are more likely to make a long-term difference in the health of FNAM children.

1.3   Newborn Hearing Screening (NHS) and the need for early diagnosis.

In a study that compared the language abilities of early and late identified hard of hearing children, Yoshinaga-Itano (2003) found that if a child is identified and treated for hearing loss by 6 months of age then they will have significantly better language scores than children identified and treated after 6 months. This highlights the vital need to achieve intervention for all types of

hearing loss by 6 months of age. Screening protocols for newborns must identify infants with hearing loss with reasonable cost, quickly and safely.

In the British Columbia, Early Hearing Program (BCEHP) if a neonate in the well-baby unit refers on initial screening with Transient Evoked Otoacoustic Emissions (TEOAE) and refers on second screening with Automatic Auditory Brainstem Response (AABR) then they are sent for a diagnostic tone Auditory Brainstem Response (ABR) (Figure 1) (BCEHP, 2007). This is a positive series screening protocol in that if the neonate passes TEOAE testing they require no other tests, but if they refer on TEOAE then they move to the next test which is AABR. In the Neonatal Intensive Care Unit (NICU) baby screening path, (Figure 2) if a neonate refers on initial screening with AABR and refer on second screening with AABR then they are sent for a diagnostic tone ABR (BCEHP, 2007). This is a positive series screening protocol as well in that if the baby passes the first AABR testing they require no other tests, but if they refer on AABR then they move to the next test which is a second AABR.

Screening Protocol – Two Stage AOAE & AABR
Well Babies - Standard

FIRST STAGE Screening Using AOAE

- Inpatient or within 1 month as outpatient.

- If refer result during the 1st attempt on AOAE, a 2nd attempt per ear should be made during the same session;

- Check late onset risk factors

PASS

REFER

NONE

Presence of late onset risk factors?

PASS

SECOND STAGE
Re-screen using AABR

- First choice: as inpatient, preferably 4 hours or more later; rescreen refer ear(s) only
- Or no later than 1 month of age as an outpatient at community screening sites; rescreen both ears even if one ear passed First Stage
- Only one attempt per ear on AABR

Exit System
Notify Parents
*pass brochure
Screening Report on Hospital Record

Late onset risk factor present

REFER

Notify Parents
*refer brochure
Screening Report on Hospital Record Refer for diagnostic audiological evaluation

Notify Parents
*pass brochure with follow up marked
Screening Report on Hospital Record
Refer for diagnostic audiological evaluation according to risk factor

Go to diagnostic clinical pathways

Figure 1: BCEHP newborn hearing screening protocol for well babies.
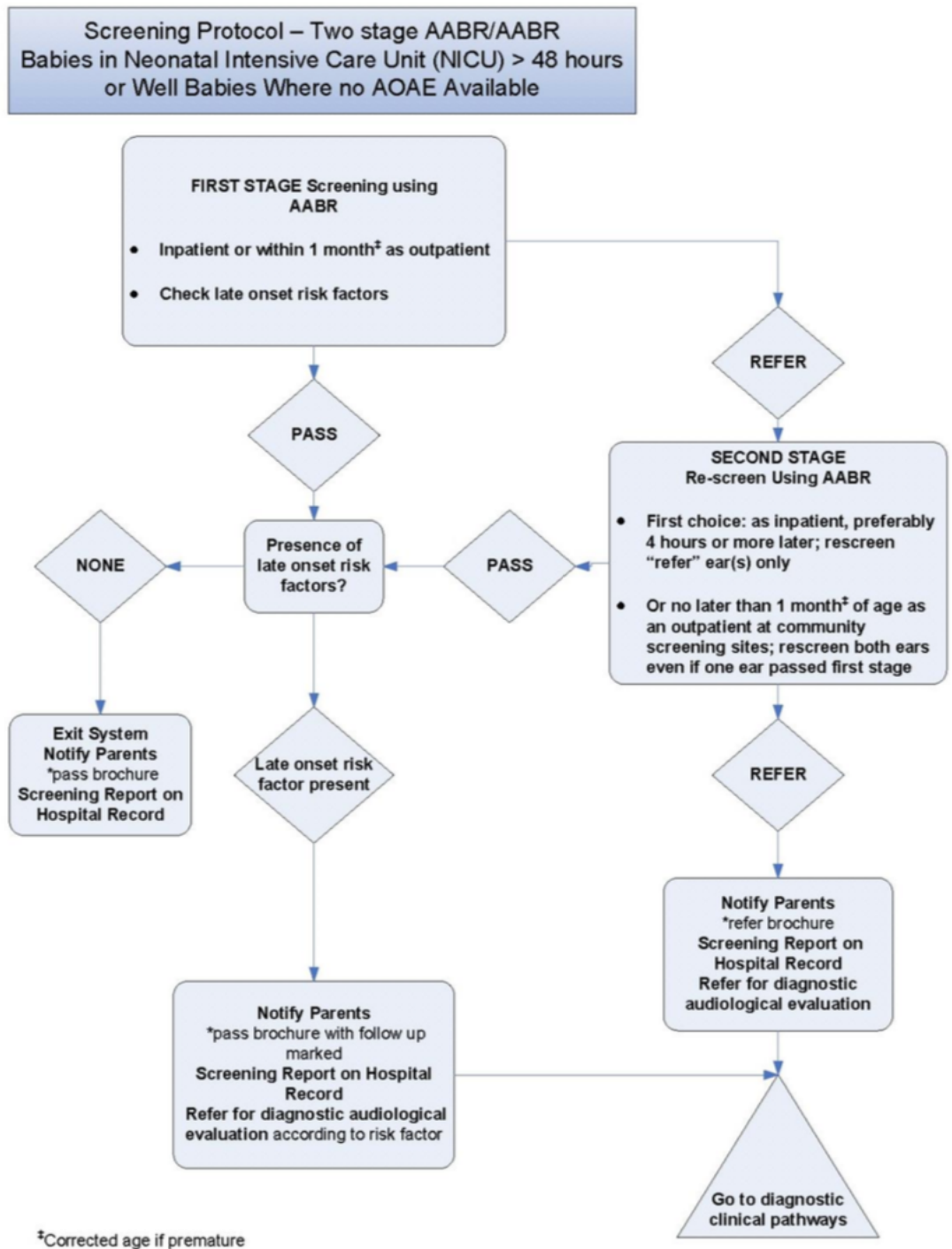
Figure 2: BCEHP newborn hearing screening protocol for NICU babies.

1.3.1 Need for diagnosis to reduce false positive referral rates

Neither of the BCEHP screening paradigms can diagnose the type of hearing loss (conductive versus sensorineural) until the diagnostic tone ABR is conducted. This is because, in hearing screening, a "refer" result can be a true positive result caused by either a sensorineural hearing loss or can be a false positive caused by transient or permanent conductive dysfunction in the outer or middle ear (Boone, 2005; Hunter & Margolis, 1992). Boone et al. (2005) noted that OME may contribute up to 67% of the false positive in newborn hearing screening programs.

To reduce false positive rates in NHS programs and improve identification of infant with a permanent hearing loss it is imperative to be able to discriminate ears with transient conductive problems from ears with SNHL. Diagnosis at screening would streamline screening so that those neonates who have a refer due to middle ear pathology could be rescreened and those who refer due to a sensorineural hearing loss could be immediately sent for diagnostic tests, thereby reducing the time to intervention for both conditions.

1.3.2 Need for an early diagnosis of Chronic Otitis Media

As stated earlier, the prevalence of severe bilateral sensorineural hearing loss in well-baby unit neonates has been estimated to be between 1 to 3 per 1000 newborn infants (Bagatto, 2010). In contrast, it has been reported that conductive hearing losses due to OME or more permanent outer and middle ear conditions occur at a rate thirty times greater than the sensorineural hearing loss in young infants (Gorga, 2001; Orlando, 1998).

In the current BCEHP screening protocol, if a permanent childhood hearing impairment (PCHI) is found on diagnostic tone ABR, then the child is followed and fast-tracked for

diagnosis by 3 months and intervention by 6 months. However, if the hearing loss is found to be transient and conductive, such as in OM, the next step is to seek an ENT intervention and this is the point that the child leaves the BC care path (BCEHP, 2007).

For an ENT, OME can be difficult to diagnose in infants, as 46% of infants that have OME are asymptomatic with no signs of fever, irritability or otorrhea. The use of otoscopy to look for visible fluid behind the eardrum is not recommended in young babies and the use of myringotomy to find fluid is not ethical and not common practice in Canada (Marchant et al., 1986; Marchant et al., 1984). These challenges limit the ability of ENT practitioners to achieve an early diagnosis of OME.

The current British Columbia guidelines for diagnosis and treatment AOM and OME applies only to children over the age of six months and they advise observation at 3-month intervals until the resolution of effusion (Committee, 2010). In 2016 (Rosenfeld) researchers updated American Physician Clinical Practice Guidelines for OME from the previous 2004 guidelines. They include new considerations for early diagnosis and treatment of children aged 2 months to 12 years. The guidelines consider the need to identify OME early and to identify those at risk for speech and language impairment. The recommendations include following up with infants who fail newborn hearing screening to ensure there is no continued hearing loss, documenting diagnosis and resolution of OME, documenting improved hearing as a result of OME, evaluating at-risk children for OME at the time of diagnosis of the at-risk condition, and obtaining a hearing test if OME persists for > 3 months and for OME of any duration in an at-risk child. The guidelines clearly state that new research needs are to "conduct additional validating cohort studies of acoustic reflectometry as a diagnostic method for OME, particularly in children <2 years old" (Rosenfeld, 2016, p. 154). As the new recommendations depend on

initial diagnosis for treatment timelines, an early diagnosis is imperative to catch newborns with OME so that they can be followed and treated in the appropriate timeline for good language outcomes.

There is other evidence that diagnosis of OME at the time of hearing screening is important for identifying children who are at risk of developing COM. Marchant et al. (1984) determined that newborns who have a diagnosis of OME before two months of age may be more prone to developing bilateral chronic OME. Also, infants who have OME 30 to 48 hours after birth are at greater risk of developing chronic OME at a later age than newborns born without OME (Doyle, 2004). The Joint Committee on Infant Hearing 2007 position statement states that OME for at least 3 months is a risk factor for CHL for infants 29 days to three years old (JCIH, 2007).

In summary, currently, a child with OM will likely first get diagnosed closer to 6 months of age and may go without treatment for up to a year or longer. As the first 6 months are crucial for language learning, and as children with chronic OM may not be diagnosed until over 6 months, there is a critical need to develop a screening program that can diagnose a "refer" result as conductive, sensory, or neural at the initial screening. Overall, there is a clear need to develop a gold standard for the diagnosis of Otitis Media in the neonatal period so that early intervention strategies can be implemented and researched in their efficacy in preventing language delay, poor educational outcomes, and poor functional listening ability.

1.3.3 The missing elements of current newborns hearing screening protocols and the need for a new paradigm

Numerous researchers have noted that a barrier to studying OME and hearing loss rates in infants is the lack of validated objective tools since conventional tympanometry is ineffective at detecting OME in young infants (Hunter & Margolis, 1992; Paradise, 1976). Hunter (2007) notes that because the middle ear is the conductive pathway for both the incoming sound stimulus and the reverse propagation of the emission generated by the outer hair cells, OME has an effect on hearing screening with OAE's. Researchers have determined that there is a need for a screening tool that is sensitive, specific and user friendly that can permit better identification of outer and middle ear status and can be used as an adjunct to OAE, AABR and tone ABR screening in neonates (Aithal, 2014b; Gravel, 2005; Hunter, Prieve, Kei, & Sanford, 2013)

The American Academy of Pediatrics Task Force on Newborn and Infant Hearing (Erenberg, 1999), published a series of guidelines for a NHS program. One guideline is for 100% of the target population (newborns) to be tested in both ears, with a minimum of 95% newborns screened for the program to be effective. A second guideline is for 100% follow up of all infants referred for formal Audiologic assessment and 100% follow up for all infants not screened initially in the birthing hospital whose parents did not refuse screening. A third guideline recommends that the program be within an acceptable cost-effective range. A measure, such as WAI, that can possibly diagnose the type of hearing loss at initial screening, would work to both achieve earlier diagnosis and achieve earlier treatment, resulting in reduced cost of the program.

1.4   Audiological diagnosis of Otitis Media with Effusion

This section details information on tests that can provide information about the status of the middle ear.

1.4.1   Otoacoustic Emissions – Transient Evoked Otoacoustic Emissions and Distortion Product Otoacoustic Emissions

Otoacoustic emissions (OAEs) are sounds created by the healthy cochlea, sometimes in response to external sounds and sometimes spontaneously (Prieve & Dreisback, 2011). There are two types of evoked OAE's, Transient Evoked Otoacoustic Emission (TEOAE's) and Distortion Product Otoacoustic Emissions (DPOAE's). TEOAEs are an indicator of normal middle ear function as well as cochlea at the level of the outer hair cells using the frequency range of 1500 to 4000 Hz (Kei, 2003). DPOAE's are an indicator of normal middle ear function and cochlea at the level of the outer hair cells using the frequency range of 2000 to 6000 Hz (Sanford et al., 2009). OAE tests reflect the functioning of the outer hair cells of the cochlea and are typically used to diagnose SNHL. They are reliable, well researched and can be recorded on a calm baby in quiet surroundings (BCEHP, 2007). TEOAE tests can accurately identify infants in a newborn screening program with a hearing loss and are very sensitive to cochlear hearing loss of 30 dB HL or more (Norton et al., 2000).

OAE's require the path of sound conduction to and from the cochlea to be clear and therefore, normal OAE results rule out excessive middle ear fluid (Hunter et al., 2010; Kei, 2003; Sanford et al., 2009; Shahnaz, Miranda, & Polka, 2008). OAE's are affected by even slight changes in the condition of the outer and middle ear (Prieve & Dreisback, 2011). For instance, TEOAE levels are reduced by 4 dB in infants and children with negative tympanometric peak

pressure (TPP) with a mean change of -169 daPa (Prieve et al., 2008). In comparison children with flat tympanograms show dramatically reduced OAE level or no measurable OAE's (Choi, Pafitis, & Zalzal, 1999) Absent TEOAEs are a common finding in children with confirmed OME (Amedee, 1995; Koivunen, Uhari, Laitakari, Alho, & J., 2000).

While OAE measures can give an indication of middle ear status, they are not considered a gold standard for the diagnosis of middle ear effusion as they can still be present in ears with middle ear dysfunction (Sanford et al., 2009). WAI is predicted to be a much better measure of the definitive status of the middle ear.

1.4.2   Broadband Noise Middle Ear Muscle Reflex / Acoustic Stapedial Reflex

The middle ear muscle reflex (MEMR) is a contraction of the stapedius muscle, located in the middle ear, which occurs when an intense sound signal is presented. This contraction results in a change in acoustic admittance due to the stiffening of the ossicular chain (Wiley & Fowler, 1997). The MEMR path involves the inner hair cells, eighth nerve (vestibulocochlear nerve), seventh nerve (facial nerve) and brain stem pathways (Berlin et al., 2005). The MEMR test has been used to differentiate between conductive, cochlear and retrocochlear pathologies (Ferguson et al., 1996), in the estimation of hearing threshold levels (Niemeyer, 1974) and in the evaluation of facial nerve dysfunction (Citron & Adour, 1978).

Broadband Noise (BBN) stimulus is used for the MEMR as lower thresholds can be obtained with a broadband stimulus than those obtained with tones resulting in less of a risk of overstimulation, therefore, creating a safer test for newborns (Keefe, Schairer, Ellison, Fitzpatrick, & Jesteadt, 2009; Mazlan, 2009).

Mazlan et al. (2009) found that ipsilateral BBN MEMR with the use of a 1000 Hz probe tone frequency can be reliably obtained in 100% of healthy newborns who passed AABR and who had single peaked tympanogram at 1kHz probe tone frequency with present TEOAE, making it useful as a screening measure for hearing status in infants. The authors also found that 8.7% of a cohort of 219 infants who passed AABR had absent MEMR and that all of these infants had weak or absent TEOAE and flat tympanogram, providing support for the use of MEMR in the detection of possible middle ear pathology when paired with AABR (Mazlan, 2009). Furthermore, Mazlan (2009) found that a BBN MEMR threshold had good test-retest reliability with the use of a BBN stimulus.

As the MEMR requires the sound signal to reach to cochlea to function, if the MEMR is absent or present at an elevated intensity in a screening battery of tests it can indicate the presence of a conductive or a sensorineural condition (Gelfand, 2009; Plinkert, Sesterhenn, Arold, & Zenner, 1990) MEMR tests are used in a screening protocol as a supportive measure to OAE and ABR measurements. An absence of a reflex lends support to hearing loss found on the ABR measurements and the presence of a reflex indicates a functioning cochlea and brainstem. The absence of a MEMR in conjunction with a flat tympanogram (or lower absorbance on WAI as per above) would indicate a conductive component.

MEMR's will also likely be absent in the presence of Auditory Neuropathy/Auditory Dys-Synchrony (AN/AD) (BCEHP, 2007). In our protocol, the MEMR replaces the AABR as a test that is sensitive to AN/AD. Berlin et al. (2005) found that none of 136 participants with AN/AD showed MEMR at all the frequencies tested. Only 3/136 participants showed any reflexes at 95 dB HL or below but never at both 1 and 2 kHz or in both ears. All other reflex measures in the remaining 133 patients were absent or observed above 100 dB HL, which did not

correlate with the normal otoacoustic emissions testing. He recommends that MEMR be used in any perinatal hearing screening that depends on otoacoustic emissions to rule out AN/AD. If the emissions are present and the reflexes are absent or elevated, then the participant should be referred for ABR testing to confirm AN/AD.

1.4.3   Diagnostic Tone Burst Auditory Brainstem Response

Tone ABR is the gold standard for assessing the auditory function of infants referred from newborn hearing screening (Aithal, 2014b). ABR thresholds can be measured using clicks or tone bursts as stimuli. ABR using click stimuli provide a global measure of physiological thresholds. In contrast, ABR using tone burst stimuli provide frequency-specific threshold information. Normal hearing infants show a mean threshold of about 15-20 dB nHL from 500 to 4000 Hz (Lee, Hsieh, Pan, & Hsu, 2007; Stapells, 2011).

The most common cause of elevated ABR thresholds in young infants, especially those referred from NHS, is a conductive hearing loss (Boone, 2005). Tympanometry and OAE measures are unable to quantify the degree of conductive hearing loss. These measures are typically abnormal irrespective of whether the conductive component is relatively minor or substantial (Stapells, 2011). A combination of air conduction (AC) and bone conduction (BC) tone burst ABR results can be used to determine the presence or degree of conductive hearing loss (Gravel, Kurtzberg, Stapells, Vaughan, & Wallace, 1989; Stapells, 2011).

1.4.4   Tympanometry

1.4.4.1   Low Frequency Tympanometry (220/226 Hz)

The use of low frequency tympanometry is of limited use in infants under 6 months. A study by Paradise et al. (1976) found that about 40% of under aged 6 months infants had a normal single peaked type A tympanogram even though they had confirmed OME. Studies by Pestalozza (1980) and by Schwartz (1980) have shown that 20-94% of infants with confirmed OME show a type A tympanogram. These results have been repeated by other researchers (Balkany, 1978; Hunter & Margolis, 1992; Keefe, 1993; Weatherby, 1980). Therefore, low frequency tympanometry is not an appropriate tool for the diagnosis of OME in infants.

1.4.4.2   High Frequency Tympanometry / 1000 Hz tympanometry

Williams et al. (1995) tested 26 infants under 4 months of age and found that the peak susceptance at 1000 Hz correlated the best with middle ear results from otomicroscopy and pneumatic otoscopy. Meyer et al. (1997) found that in children 2 weeks to 6.5 months old, the 1000 Hz tympanometry was more sensitive to middle ear pathology than 226 Hz tympanometry. The superiority of the use of 1000 Hz tympanometry as opposed to low frequency tympanometry in the diagnosis of OME has since been proven by other researchers (Kei, 2003; Margolis, 2003; Mazlan, 2007; Meyer, 1997; Rhodes, 1999).

In her Ph.D. thesis, Aithal (2014b) noted that 1000 Hz tympanometry adoption as a routine test for neonates has been hindered by difficulties in trace interpretation. Aithal concludes that although 1000 Hz tympanometry is recommended over 226 Hz tympanometry for the assessment of middle ear dysfunction of infants, that: "Further research is needed to develop standardized measures of the 1000 Hz tympanogram that can be universally accepted in the

assessment and interpretation of test findings for this population", and that, "Until such measures are developed, 1000 Hz tympanometry should be used with caution along with other measures of middle ear function."(Aithal, 2014b, p. 20).

1.5   Wideband Acoustic Immittance

Wideband Acoustic Immittance (WAI) encompasses a set of middle ear assessment measures that tests how the middle ear receives, absorbs and transmits sound energy across a wide range of frequencies (from 250 Hz to 8000 Hz) at ambient pressure or at middle ear tympanometric peak pressure (TPP) (Aithal, 2014b; Hunter & Shahnaz, 2014). WAI uses a broadband stimulus and a carefully calibrated probe that allows the calculation of various measures that can include Power Absorption (PA)/Wideband Absorbance (WBA), Wideband Reflectance (WBR), Transmittance, Acoustic Impedance (Z) and Admittance (Y) which includes Admittance Phase (Yφ) (Beers et al., 2010; Hunter & Shahnaz, 2014; Prieve, Feeney, Stenfelt, & Shahnaz, 2013a). These measures evaluate the outer and middle ear function independently of the inner ear and across the frequency range most important for speech perception (Keefe et al., 2009).

1.5.1   Admittance Phase (Yφ)

Most studies that look at the effects of middle ear conditions on WAI have used spectral measures such as Wideband Absorbance (WBA), also called Power Absorbance, or Wideband Reflectance (WBR), also called Energy Reflectance, as the WAI measure of choice. However, these measures only reflect the magnitude of a recording (the proportion of sound absorbed), and do not measure the admittance measures of Phase Angle, or the Admittance Phase (Yφ) (Aithal,

2017b). Although Admittance Phase (Yφ) can be recorded at the same time as WBA and may provide additional information about middle-ear status, it has not received the same attention in research as other WAI measures (Aithal, 2017b, Feeney et al., 2013). As such, Yφ may be useful in the diagnosis of middle ear conditions. An increased Yφ indicates increased stiffness and decreased Yφ indicates increased compliance (Aithal, 2017b). Hunter et al. (2010) claimed that Yφ can be derived from WAI measurements and that using them would "provide better diagnostic accuracy than admittance magnitude alone." Recording Yφ can be advantageous in documenting the increased stiffness that occurs in the ear canal with increasing age in early infancy (Holte, 1991; Sanford, 2008). Holte (1991) showed that the Yφ angle shifted in a positive direction with increasing age at frequencies below 1 kHz in infants indicating increased stiffness with increasing age. Yφ can also give information on the resonance frequency which evaluates the integrity of the outer and middle ear. A lower resonance frequency indicates a middle ear disorder such as ossicular chain discontinuity or otitis media with effusion (Sanford & Feeney, 2008).

1.5.2   Wideband Absorbance

Wideband Absorbance (WBA) represents the sound energy absorbed by the middle ear when a wideband stimulus is presented in the ear canal. WBA values range from 1 where the majority of the sound is absorbed to 0 where the majority of the sound is reflected (Feeney & Sanford, 2012). In this study WBA was measured rather than WBR as was used by Aithal (2014) and as was recommended by Feeney et al. (2013) in the consensus statement produced during the Eriksholm workshop on wideband absorbance measures of the middle ear.

In general WBA in adults is lowest below 1000 Hz and above 4000 Hz and highest between 1000 and 4000 Hz as is shown in Figure 3. This range of frequencies is equivalent to the most effective frequency middle ear transfer function (Hunter, Tubaugh, & Jackson, 2008b; Keefe, 1993; Sanford et al., 2009). In healthy Caucasian neonates, WBA normative data reveals a double-peaked pattern with the 1st peak at 1.25-2 kHz and the 2nd peak at 5-8 kHz (Aithal, 2017b) as is shown in Figure 4.
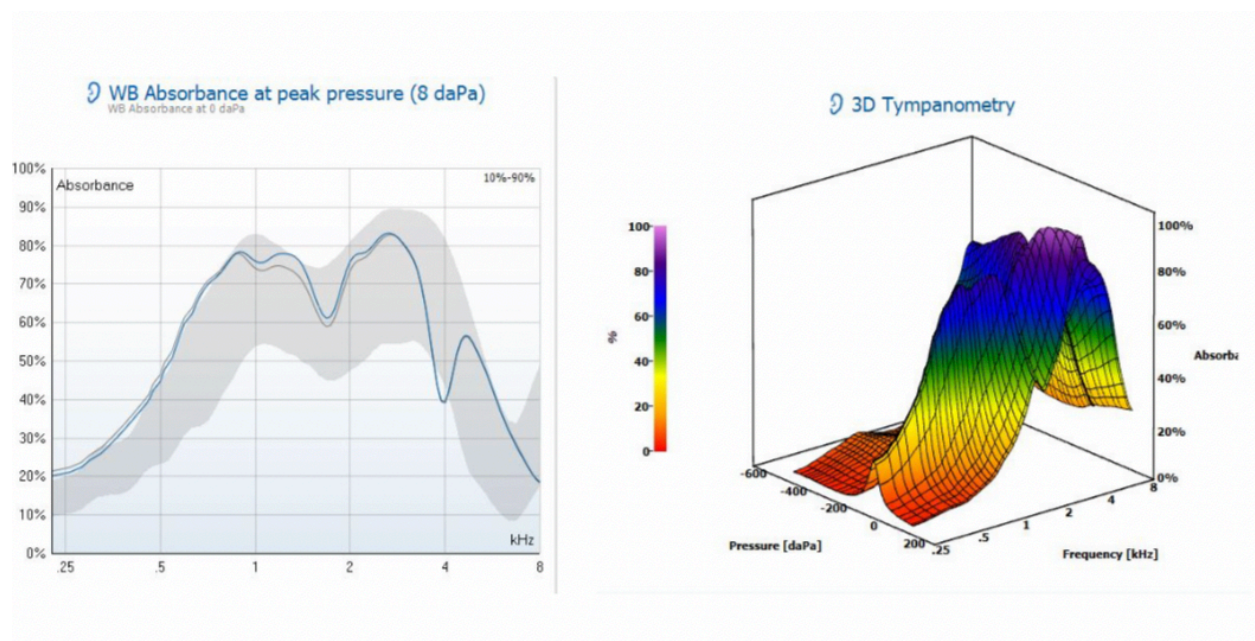
Figure 3: Wideband Absorbance 2D and 3D images indicating a normal adult recording.
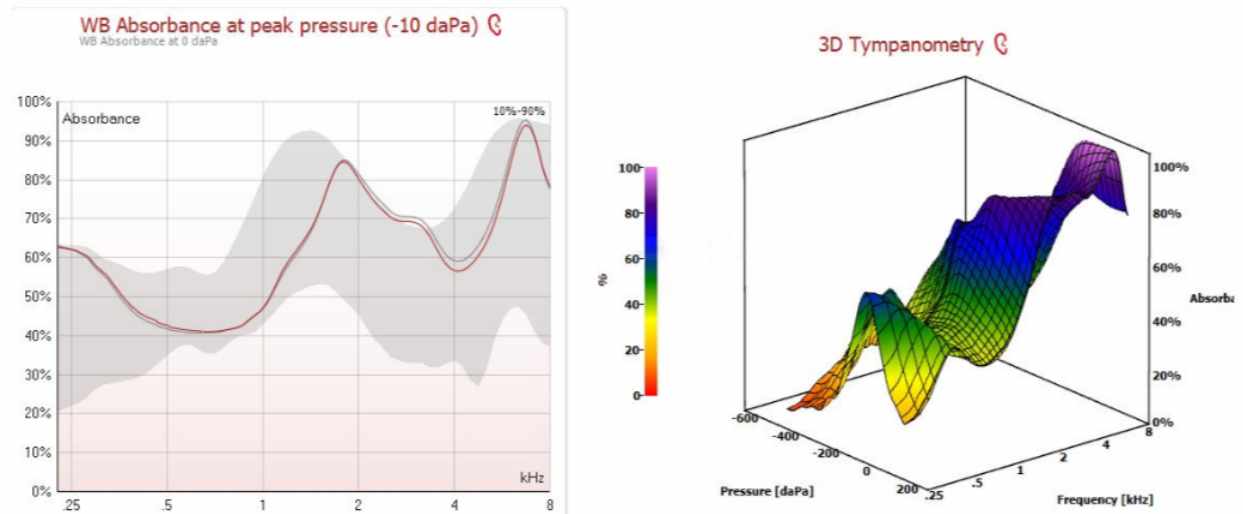
Figure 4: Wideband Absorbance 2D and 3D images indicating a normal neonate recording from the current study.

1.5.3 Ambient Wideband Absorbance in neonates

In (2008) Shahnaz looked at WBA in neonates in a NICU ward and compared them to WBA in normal hearing adults. Shahnaz found a clear separation between NICU babies and adults below 727 Hz, with NICU babies having higher absorbance values than adults. The mean absorbance found for NICU neonate was larger at all frequencies than the corresponding mean for one month's old infants that Keefe and Levi (1996) found in their study of one-month-old infants.

In (2000) Keefe et al. looked at neonates in the NICU and well-baby nursery with and without risk factors. The study included 2081 neonates. Keefe and colleagues found that the median absorbance was about 0.8 across all frequencies from 250 to 8000 Hz and significant ear and gender effects were found on absorption in some frequency bands. They found that 13% of the results showed an inadequate probe seal that resulted in negative ear canal volumes at lower frequencies. One limitation of the study was that the participants were not assessed to exclude

those with a conductive condition. WBA data from normal hearing healthy full-term neonates was reported in other studies (Hunter et al., 2010; Merchant, 2010; Silva, 2013).

The first study to use WBA in a newborn hearing screening program (Sanford et al., 2009) found that the median absorbance of those who passed (375 ears) varied between 0.39 and 0.67 while the median absorbance of those who failed (80 ears) varied between 0.20 and 0.40. Ears that passed screening had higher absorbance compared with those that referred indicating that neonates who passed had a more acoustically efficient conductive pathway (Aithal, 2014b).

Aithal (2014b) presented a summary of the studies that have looked at WBA under ambient pressure conditions in neonates up to the year 2014 that is recreated in Table 2. The studies that have investigated WBA under ambient pressure conditions in neonates post-2014 are listed in Table 3.

Table 2: Summary of studies that have investigated WBA under ambient pressure conditions in neonates up to 2014 (Aithal, 2014b).

Study	Method	Subjects	Summary of Findings
Keefe et al. (2000)	WBA measured in well babies without risk indicators, with at least one risk indicator and NICU graduates	2081 neonates divided into 3 groups	The median absorbance of 0.8 across all frequencies Significant ear and gender effects present Variation of WBA with age present in the first few days of life
Keefe et al. (2003b)	Retrospective analysis of WBA in relation to TEOAE, DPOAE, and AABR	1405 neonate ears	High-frequency absorbance was the most important factor in classifying OAE results that classified OAEs with ROC of 0.79 and ABR of 0.64
Keefe (2003a)	Developed model for middle ear dysfunction The model applied to a different neonate group	2638 ears used to construct the model 1027 normal hearing ears	High-frequency absorbance was the best predictor (Area Under the Receiver Operating Curve (AUROC) 0.87) The inclusion of this model decreased false positive from 5% to 1.1%
Vander Werff et al. (2007)	Infants tested during screening and diagnostic testing	127 infants aged 2 weeks to 24 months	Smaller test-retest differences for the diagnostic group

Study	Method	Subjects	Summary of Findings
		screening group n= 61 Diagnostic group n-66 Control group 10 = normal	Test-retest differences largest for frequencies below 500 Hz and smallest in the mid-frequency range No difference in test-retest performance between infants who passed or failed OAE screening Low WBA from 630 to 2000 Hz in infants who failed OAE screening
Hunter et al. (2008a)	Ears classified as normal or poor using otoscopy, tympanometry, and DPOAE	97 (194) ears infants and children aged 3 days to 47 months 3 days to 2 months n=18 3-5 months n=15 12-23 months n=20 24-47 months n= 19	WBA significantly different between 1000 and 3000 Hz for normal ears
Shahnaz (2008a)	Inclusion criteria-NICU babies with pass in both TEOAE and AABR	54 ears (49 pass 5 fail) from 31 NICU babies 56 adults (age 18-32 years) with normal hearing and pass in TEOAE	Clear separation of absorbance between NICU babies and adults below 727 Hz. Absorbance high in NICU babies Maximum absorption from 1200 to 2700 Hz in normal NICU babies and from 2800 to 4800 Hz in adults
Sanford et al. (2009)	Test performance of WBA and 1000 Hz tympanometry used to predict DPOAE outcomes	455 ears (375 pass and 80 fail DPOAE	AUROC 0.87 for ambient WBA and 0.75 for 1000 Hz tympanometry High absorbance in ears with DPOAE pass Best separation of WBA between pass and fail groups from 1400 to 2500 Hz
Hunter et al. (2010)	Test performance of WBA and 1000 Hz tympanometry used to predict DPOAE outcomes	493 ears from 324 neonates – 353 passed and 141 referred with DPOAE screening	Normative data provided for 1000 to 6000 Hz frequency range and for absorbance area indices 2000 Hz was the best predictor of DPOAE outcome (AUROC) high for WBA (0.90 and 0.82 at 2000 and 1000 Hz respectively) and 0.72 for 1000 Hz tympanometry Absorbance difference significantly as a function of DPOAE status and frequency
Merchant et al. (2010)	Only infants that passed DPOAE screening included	12 ears from 7neonates	Absorbance similar in both groups at most frequencies

Study	Method	Subjects	Summary of Findings
		19 ears from 11 1-month old infants	
Pitaro (2013)	Otoscopy and WBA done on healthy neonates to observe and rate occlusion of the ear canal from 0% (no occlusion) to 100% (fully occluded)	156 neonates	Absorbance significantly different between the 0 to 70% occlusion group and the 80 to 100% occlusion group A significant decrease in absorbance with 70 to 80% occlusion of ear canal diameter.
Silva et al. (2013)	Neonates with TEOAE and tympanogram included	144 ears from 77 infants	Normative WBA data provided Energy absorbance less from 250 to 750 Hz and high from 1000 to 3000 Hz

Table 3: Summary of studies that have investigated WBA under ambient pressure conditions in neonates post-2014 (not including review articles and consensus statements).

Study	Method	Subjects	Summary of Findings
Aithal (2013)	Normative WBR measures in healthy neonates who passed HFT, ASR, TEOAE, and DPOAE	66 ears from 66 neonates	Normative WBA data provided Higher absorbance and more efficient middle ear transfer function compared to other studies that used only OAE's as the reference standard.
Shahnaz (2014)	Tympanograms and WAI on newborns who passed TEOAE at each visit Tested longitudinally at 1-month intervals up to 6 m of age	31 infants	WBR increased at low frequencies (< 400 Hz) and decreased at high frequencies (>2000 Hz) as a function of age. There was little change in WBR from 600 to 1600 Hz across the first 6 months of life.
Aithal (2014a)	WBA in Australian Aboriginal and Caucasian neonates	59 ears from 32 Aboriginal neonates and 281 ears from 158 Caucasian neonates who passed or failed 1000 Hz tympanometry and DPOAE's	Aboriginal and Caucasian neonates had identical pass rates of 61%, however, the mean WBA of Aboriginal neonates who passed the test battery was significantly lower than the Caucasian neonates between 0.4 and 2 kHz. Mean WBA of Aboriginal neonates who failed was significantly lower than Caucasian neonates who failed
Aithal (2015)	WBA and newborns comparison with HFT ABR and TEOAE	298 ears from 192 neonates	Test performance of WBA against the test battery reference was better than that against single test reference standards 1-4 kHz best discriminability to evaluate conductive status.

Pitaro (2016)	WR in newborns and relationships to otoscopic findings	156 neonates	Significant reflectance increases when 70-80% of ear canal diameter is occluded.
Voss (2016)	WR on infants who passed one ear and failed one ear on AABR and DPOAE NHS and bilateral normal hearing at one-month-old	30 neonates	Newborn ears may have a "ME transient state" associated with fluid or debris that can be detected by WAI, that resolves from hours to days and warrants a rescreen. Preliminary criteria for determining when reflectance measures on neonates are corrupted by acoustic leaks, blocks or other problems.

1.5.4   Pressurized Wideband Absorbance

While testing under ambient conditions has provided important information into the nature of sound absorbance of the middle ear, many studies have stated that testing absorption under pressurized conditions would be beneficial (Aithal, 2017b; Margolis, 1999; Pitaro, 2016). Wideband Tympanometry (WBT) is the measurement of WBA under pressurized conditions. The middle ear is likely to be better at absorbing sound at TPP as the eardrum is at maximum mobility (Feeney & Sanford, 2012; Katz, 2015, p. 157). As well, Kei et al. (2013) noted that WBT could provide a better understanding of the variations in acoustic measures that were caused by developmental changes than WBA would and that the use of WBT would be useful as: "It is important to distinguish between variations in WBA caused by maturation compared to those caused by disorders of the conductive system".

The studies that looked at the effect of ear canal pressure on WBA in neonates and infants are summarized in Table 4 below.

Table 4: Summary of studies that have investigated WBA under tympanometric peak pressure conditions in neonates.

Study	Methods	Subjects	Summary of Findings
Sanford 2008	WBR and Yφ obtained under various pressures	4, 12 and 27-week-old infants and young adults	Between 2 and 6 kHz, negative pressures were associated with decreased absorbance and positive pressures were associated with increased absorbance. 0.75 to 2.0 kHz was a developmentally stable frequency range.
Sanford 2009	DPOAE then WBA under ambient and pressurized conditions and 1 kHz tympanograms	375 passed and 80 referred newborns	WBA under pressure performed better than WBA at ambient in predicting the conductive status of 230 neonates who passed or failed a DPOAE test.
Aithal 2017	Effects of ear canal static pressure on the dynamic behaviour of the outer and middle ear in newborns	29 newborns, 9 infants each at 1 and 4 months and 11 infants at 6 months who passed DPOAE tests	Significant changes in WBA were observed as a function of pressure and age. Developmental effects of WBA were evident during the first 6 months.
Hunter 2016	Longitudinal development of wideband reflectance tympanometry in normal and at-risk infants	182 infants	Separate normative references are recommended for clinical application for birth, 1 month and 6-15-month-old children due to significant age effects. Immature absorbance and group delay patterns were apparent in the lower frequencies but changed to an adult like pattern by 6 months.
Aithal 2017	Normative study of WAI measures in newborn infants	326 ears from 203 Caucasian neonates	Normative WBA and Yφ in neonates who passed a test battery Increased absorbance and admittance and reduced phase angle in the 1 to 2.5 kHz range. WBA ambient was similar to WBA TPP for normal hearing Caucasian infants which was similar to that reported by Sanford 2008 and Hunter 2016.

Researchers have noted that pressurized WBA results below 1 kHz should be weighted less strongly in predicting middle ear problems as the ear canal wall of neonates in a pressurized system influences WBA measurements (Keefe et al., 2000; Keefe, 2003b; Piskorski P., 1999).

Many studies have concluded that the range of frequencies of interest in neonates is 0.8 to 2 kHz as this range did not change significantly with age (Aithal, 2017a; Sanford, 2008). Ambient studies in neonates also show that absorbance is highest between 1 and 5 kHz (Aithal et al., 2013; Hunter et al., 2010; Keefe et al., 2000; Sanford et al., 2009; Shahnaz, 2008a; Vander Werff et al., 2007). Aithal (2017b) recommended that future studies focus on changes in WBA between 1 and 4 KHz in neonates. She noted that, as changes in middle ear pressure had a differential effect on WBA in neonates compared to older infants, that future research should compare WBA ambient to WBA pressurized in infants with negative middle ear pressures.

1.5.5 Wideband Absorbance as part of a Newborn Hearing Screening program to assess middle ear status.

WBA has been noted to have several advantages over other types of testing in a newborn hearing screening program. The stimulus tones and pressures used are all within normal hearing range and level and are delivered to the ear of the infant via a single insertion of the soft probe tip of the handheld device. WBA testing is fast and if needed can be measured under ambient or pressurized conditions (Aithal, 2014b; Keefe et al., 2000; Prieve, 2013a). As well, WBA measures the full range of frequencies from 250 Hz to 8000 Hz and can measure the admittance measures across all frequencies more efficiently and quickly than with multifrequency tympanometry (Aithal, 2017). WAI has another advantage over tympanometry in that it measures absorbance at the level of the ear drum which means there is no need to compensate for

the ear canal volume and that therefore the location of the probe in the ear canal is not as important as it is in tympanometry (Voss, 2008). In comparison to OAE or AABR testing, WBA is less affected by environmental noise (Aithal, 2014b; Keefe et al., 2000).

In a study on novel screening protocols for the differentiation of types of hearing loss in neonatal intensive care units, Millman (2011) noted that Wideband Acoustic Immittance (WAI) was an area of future study for newborn hearing screening as it could give additional insight into the middle ear status of newborns and therefore improve newborn hearing screening protocols. Prieve (2013b) looked at the effectiveness of tympanometry and WBR in the identification of CHL in young infants aged 9 to 36 weeks and found that WBR at seven frequencies effectively identified ears with CHL. They also found that tympanometry for 226 Hz and 678 Hz probe tones did not identify CHL in young infants and that a composite measure of WBR across frequencies was superior to 1000 Hz tympanometry in identifying infants who did not pass OAE screening (Hunter et al., 2010; Sanford et al., 2009).

Evaluating the efficacy of WBA in identifying conductive conditions has been challenging as comparing results to the gold standard of myringotomy is often not possible and has ethical challenges. In a 2015 (Aithal) study that compared the test performance of WBA to other measures in classifying neonatal ears with conductive loss, WBA performed better than any single measure, including HFT, and was comparable in performance to a battery of tests (HFT + DPOAE + TEOAE)(AABR + TEOAE + DPOAE). Overall, WAI has been shown to be to have greater accuracy than tympanometry in identifying conductive conditions in neonates (Aithal, 2015; Hunter et al., 2010; Sanford et al., 2009).

WBA has also been shown to decrease the false positive rate in NHS from 5% to 1% (Keefe, 2003b). In light of encouraging results, the use of WBA in NHS programs has been

recommended by various researchers (Aithal, 2014b; Feeney & Sanford, 2012; Hunter et al.,

2010; Merchant, 2010; Sanford et al., 2009; Vander Werff et al., 2007). Overall, WAI is an

effective tool for assessing middle–ear status in newborns and is a better predictor of conductive

hearing loss in newborn screening compared to tympanometry at conventional 226-Hz and 1-

KHz probe tone frequency (Aithal et al., 2013; Hunter et al., 2008b; Prieve et al., 2013a; Sanford

et al., 2009; Vander Werff et al., 2007).

1.5.6   Ethnic differences in Wideband Acoustic Immittance and the need for ethnicity

specific normative values

Few studies exist on the ethnic differences in WAI measures in neonates, however some

researchers have found differences in the WAI normative values of older participants. Shahnaz

and Bork (2006) found a significant difference in WBR between Caucasian and Chinese adults.

They also found a significant ethnicity by frequency interaction, with the Chinese group showing

lower WBR at higher frequencies and higher WBR at lower frequencies than the Caucasian

adults. Beers et. al. (2010) found that there was a no significant effect of ethnicity in WBR in

Caucasian and Chinese children aged five to seven years, but found a significant ethnicity by

frequency interaction with Chinese children having lower WBR values over the mid frequency

range.

In a study looking at WBA in Australian Aboriginal and Caucasian newborns, Aithal

(2014a) found that Aboriginal newborns who passed the regular screening test battery had

significantly lower WBA than their Caucasian counterparts between 0.4 and 2 kHz, which are

the frequencies important in the determination of the status of the outer and middle ear. She

suggested that this low energy absorbance in the middle ear of Aboriginal newborns indicated a

greater prevalence of outer and middle ear conditions over Caucasian newborns. This indicates that the Aboriginal newborns may have had outer and middle ear disorders that were not detected by the conventional screening test but were identified by the WBA test. It is likely that a greater proportion of Aboriginal newborns would have referred on the screening, therefore flagging a conductive hearing loss, if a more sensitive test, such as WBA, was included in the screening test battery. Aithal (2014a) recommended further development of age-specific normative WBA data.

1.6   A Novel Screening Protocol – putting it all together

A combination of TEOAE, BBN MEMR and WAI could address the missing screening elements discussed in previous sections. The three measures together give us a cross-check system to determine the type of hearing loss at initial screening. Table 5 outlines some examples of how the 3 measures can be used together to achieve a likely diagnosis. This method of determination of likely diagnosis is similar to that proposed by Hunter et al. (2013) in a study on pediatric applications of wideband acoustic measures.

Table 5: Likely Diagnosis based on outcome of three newborn hearing screening test measures, WAI, BBN MEMR and OAE.

Likely Diagnosis	Wideband Acoustic Immittance	Middle Ear Muscle Reflex	Otoacoustic Emissions
Auditory Neuropathy	Pass	Refer	Pass
Mild Sensorineural Loss	Pass	Pass	Refer
OME	Refer	Refer	Refer or a weak pass depending on amount of fluid

Severe Sensorineural Loss	Pass	Refer	Refer

1.7 The rationale for the study

1.7.1 Synopsis

Otitis Media has a long-term effect on language learning, auditory processing, and high-frequency hearing, however, obtaining an early Otitis Media diagnosis is difficult as there is no gold standard method for diagnosis of Otitis Media in neonates. There is also a need to diagnose middle ear pathology at birth in order to reduce the false positive referrals that delay the diagnosis and intervention for children with the sensorineural hearing loss. Previous research findings (Aithal, 2015; Hunter et al., 2010; Sanford et al., 2009) have indicated that the WAI holds promise as a possible objective, a safe and reliable method of screening or diagnostic evaluation of middle ear pathology in different age groups. WBA testing under ambient pressure has been shown to be a reliable tool to test the middle ear status of neonates, but few studies have looked at WBA under pressurized conditions. As well, few studies have looked at the contribution that the WAI measure of Admittance Phase (Yφ) can make to the evaluation of the middle ear.

In addition to offering a reliable method of diagnosis of OM at birth, WBA can be used to find much-needed prevalence data for OM in neonates. The prevalence of OM is high in FNAM children, however; there is no prevalence data at birth for this population. Prevalence data is needed at birth to understand risk factors and to see if interventions for OM are effective. Studying WBA in neonates of different ethnicities is important as there is a need for ethnic-specific WBA normative values.

1.7.2   The justification for conducting the present study

A review of the literature on the use of WBA in neonates for NHS protocols has

identified some areas that are in need of further study. The present study seeks to address three of

these issues.

First, although there is clear evidence that the prevalence of OM is higher in FNAM

children, (Ayukawa et al., 2004; Boswell, 1995; CASLPA, 2010; Harris, 1998; Hunter, 2007;

Wiet, 1979) there is no prevalence data for middle ear pathology in FNAM neonates, or for

neonates of other ethnicities. The most recent study to look at the results of hearing screening in

North American First Nations neonates was in 2007 (Hunter). They used TEOAE results to

determine the possible diagnosis of OM and found that 23.5% of the Australian Aborigine (A)

neonates failed hearing screening in at least one ear compared to an expected refer rate of 10%

(Hunter 2007). In Australia, Aithal (2012) found that (AA) had twice the prevalence of CHL at

initial screening (35.19%) compared to non-AA neonates (17.83%) and that CHL persisted in

75% of AA infants compared to 27.78 of non-AA infants. Prevalence data for OM and middle

ear pathology is needed at birth in order to determine which risk factors are important in the

pathogenesis of COM. The current study seeks to determine the prevalence of middle ear

pathology in neonates of different ethnicities by using WBA, 1000 Hz tympanometry, MEMR,

and TEOAE data to determine likely diagnosis of hearing at birth.

Second, there is evidence that there is a need for ethnic-specific WBA normative values.

Shahnaz and Bork (2013) found a significant difference in WBR between Caucasian and Chinese

adults. Beers (2010) found a significant ethnicity by frequency interaction for children aged 5-7

years with Chinese children having lower WBR values in the mid frequencies. Aithal (2014a)

found that Australian Aborigine neonates who passed a screening test battery had lower WBA than Caucasian neonates that passed a screening test battery. She also found that the Australian Aborigine neonates had a greater prevalence of outer and middle ear conditions not detected by conventional screening. The present study looks to see if there is a significant difference in the mean WBA of neonates of different ethnicities who pass a screening protocol of 1000 Hz tympanometry, MEMR, and TEOAE.

Third, the most recent (2016) American Physician Clinical Practice Guidelines for OME state that OME should be identified early to identify those at risk for speech and language impairment. The Guideline (2016) recommendations include: following up with infants who fail NHS, documenting diagnosis and resolution of OME, evaluation of at-risk children at the time of diagnosis, and obtaining a hearing test if OME persists for over 3 months or any OME of any duration in an at-risk child. As the new recommendations depend on initial diagnosis for treatment timelines, an early diagnosis is imperative to catch newborns with OME so that can be followed and treated in an appropriate timeline for good language outcomes. However, early diagnosis at the time of NHS is complicated by false positive referrals caused by OME. A review of the literature shows that OME may contribute up to 67% of the false positive referral rates in NHS programs. Diagnosis of OME at screening would streamline screening so that those neonates who have a refer due to middle ear pathology could be rescreened and those who refer due to SNHL could be immediately sent for diagnostic tests, thereby reducing time to intervention. WBA has been recommended as a reliable method of identification of middle ear pathology to use in a NHS protocol (Aithal 2017, Margolis 1999, Pitaro 2016, Keefe 2003a, Sanford et. al. 2009). The current study contributes to the diagnosis of the middle ear (ME) pathology at birth by evaluating the addition of WBA to a NHS protocol. WBA (ambient and

pressurized) and Yφ will be evaluated for the ability to differentiating neonates with a likely diagnosis of CHL from neonates with a likely diagnosis of normal hearing, in differentiating neonates who pass a screening test battery from neonates who fail a screening test battery, and in differentiating between neonates who pass a TEOAE test from neonates who fail a TEOAE test.

1.8   Aims of the current investigation

The current investigation aims to:

(1) Evaluate the ability of WBA (ambient and pressurized) and Yφ in differentiating neonates with likely CHL versus normal hearing neonates.

(2) Evaluate the ability of WBA (ambient and pressurized) and Yφ in differentiating neonates who fail a newborn hearing screening test battery of TEAOE, BBN MEMR and 1000 Hz tympanometry versus neonates who pass the screening test battery.

(3) Evaluate the ability of WBA (ambient and pressurized) and Yφ in differentiating neonates who pass a TEOAE test to those who fail a TEOAE test.

(4) Evaluate prevalence of CHL and ME pathology in neonates of all ethnicities including FNAM neonates.

(5) Compare mean WBA measures obtained from FNAM to non-FNAM neonates who passed a newborn hearing screening test battery of TEAOE, BBN MEMR, and 1000 Hz tympanometry.

1.9   Major hypotheses of the present investigation

There are five null hypotheses to be tested:

Ho1:	There will be no significant difference in WBA (ambient and pressurized) and Yφ in neonates with likely CHL versus normal hearing neonates.

Ho2:	There will be no significant difference in WBA (ambient and pressurized) and Yφ in neonates who fail a newborn hearing screening test battery of TEAOE, BBN MEMR and 1000 Hz tympanometry versus neonates who pass the screening test battery.

Ho3:	There will be no significant difference in WBA (ambient and pressurized) and Yφ in neonates who pass a TEOAE test to those who fail a TEOAE test.

Ho4:	There will be no significant difference in the prevalence of CHL between FNAM neonates and neonates of other ethnicities.

Ho5:	There will be no significant difference in mean WBA results between FNAM neonates and neonates of other ethnicities who pass or fail a newborn hearing screening test battery of TEOAE, BBN MEMR, and 1000 Hz tympanometry.

Chapter 2: Methods

2.1 Participants

A total of 213 neonates (426 ears) were recruited from the well-baby unit of the Royal University Hospital in Saskatoon, Saskatchewan, Canada. Participants for the newborn hearing screening and WAI testing were between 16 and 48 hours old at the time of testing. Gestational Age at time of testing was not available as there was no access to the participant charts.

Participants were recruited through an Invitational Letter (Appendix A) distributed at the beginning of the day to all parents of newborns who were due to have their hearing screening performed that day. A consent form was also distributed at this time for the parents to read over (Appendix B).

The proportion of neonate ears by ethnicity tested is shown in Table 6 in the Results section of this paper.

2.2 Inclusion and Exclusion Criteria

2.2.1 Inclusion Criteria

To be included in the study, infants were required to be in stable medical condition at their initial screening date, as determined by the nursing staff.

2.2.2 Exclusion Criteria

Participants were excluded from the study if their parents did not sign the consent forms, if there was an equipment failure for both ears and if a test was not possible due to contact precautions. The parents of 16 participants (13.3%) did not give consent to be included in the study. Three participants (1.4%) were excluded due to equipment failure for either the Titan

WAI or TEOAE during the screening. When a participant was under contact precautions, a cart was not allowed in the room which presented difficulties in operating the computer run Titan system and therefore these neonates were not tested. Three participants (1.4%) had contact precautions. Therefore, a total of 191 total newborns (382 ears) were included in the study.

All available Accuscreen TEOAE data, and Otoflex tympanometry and MEMR data provided by the hearing screeners were included in the results. Therefore, all data except for 2 participants, for whom there was no access to the information, are included, for a total of 378 ears.

For Wideband Acoustic Immittance data to be included, it was necessary to visually inspect the data and compare to tympanometry and ear canal volume results. Data was discarded when there was a loss of the probe seal (Figure 5), when a test was too noisy (Figure 6), and when the probe was blocked (Figure 7) as determined by visual inspection of the readout by the principal investigator and the graduate student familiar with normal and abnormal patterns. For an example of a normal recording for a neonate please see Figure 4 in the Introduction section of this paper. For Titan WAI data, 171 newborns met the inclusion criteria for one or both ears for a total of 265 ears (70.1%).

All available Titan TEOAE data (351 ears, 92.9%) was included in the results whether or not the data corresponded to the Accuscreen TEOAE data or other tests.
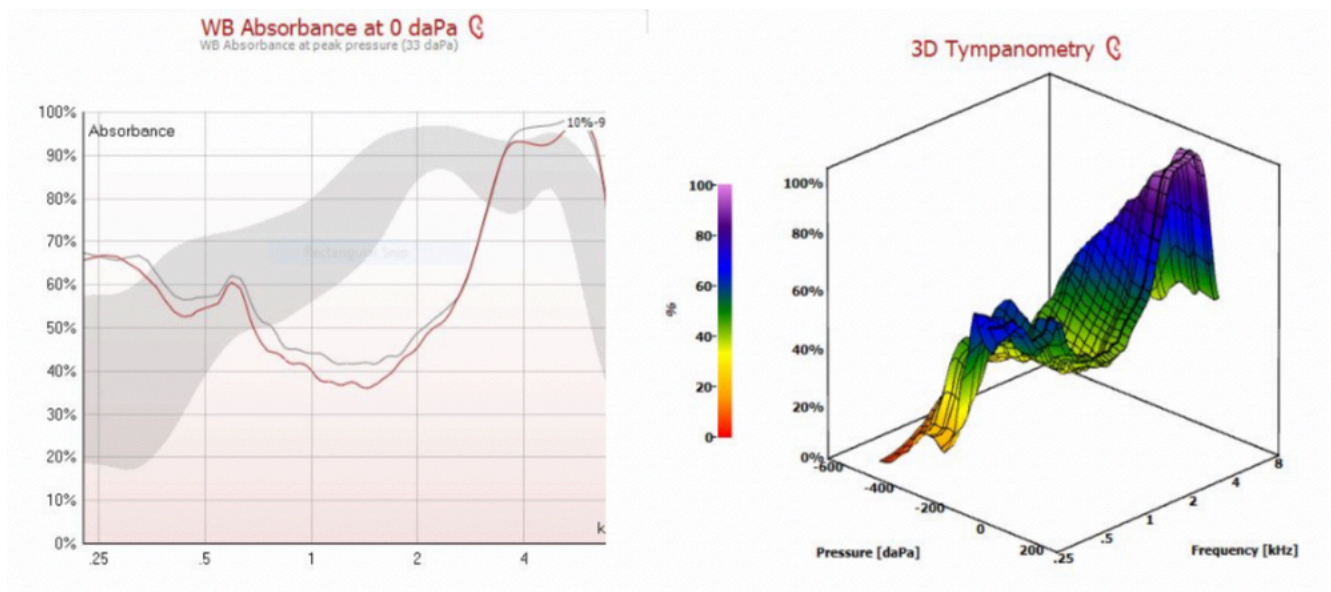
Figure 5: Wideband Absorbance 2D and 3D images with a high absorbance in the frequencies below 1000 Hz indicative of a poor probe seal.
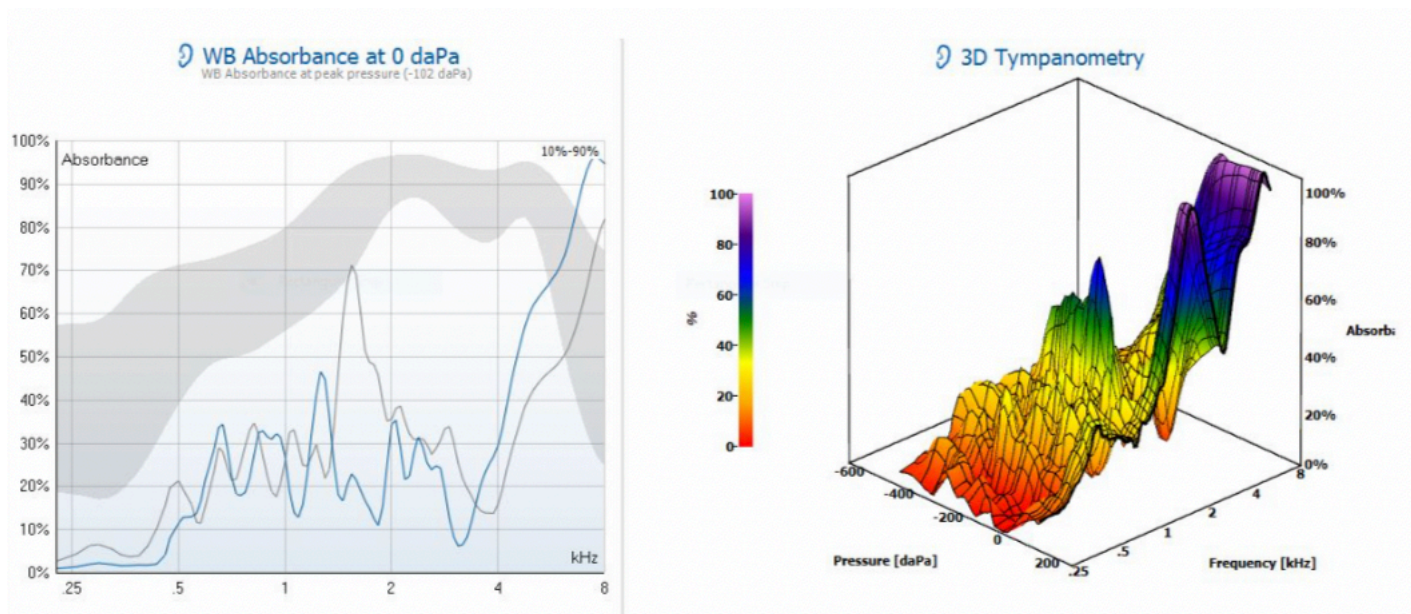
Figure 6: Wideband Absorbance 2D and 3D images indicating a noisy recording.
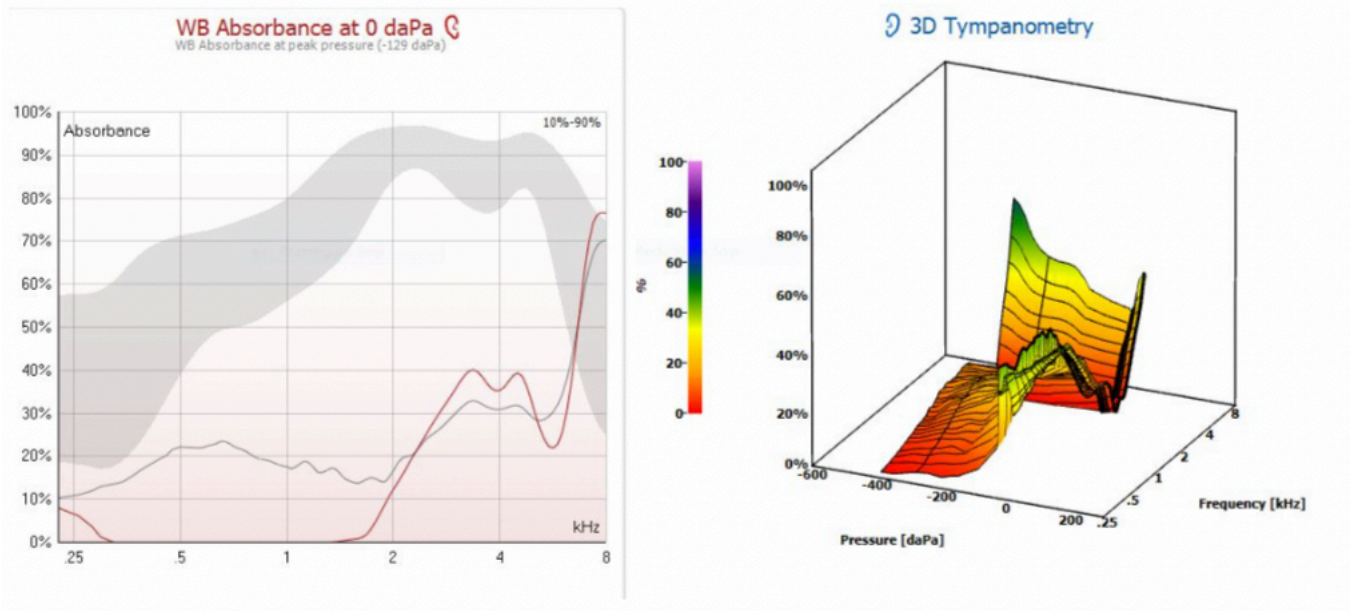
Figure 7: Wideband Absorbance 2D and 3D images indicating a blocked probe.

2.3 Sample Size

In a study on the comparison of Wideband Absorbance to HFT, AABR, TEOAE and DPOAE tests, Aithal (2015) found significance with a sample size of 298 ears. As well, in a study of WBA in Australian Aboriginal neonates versus Caucasian neonates, Aithal (2014a) found significance with a sample size of 59 Aboriginal ears and 281 Caucasian ears. Therefore, the intended sample size for this study was 300 ears of neonates of different ethnicities between the chronological ages of 0 and 120 days from either the NICU or the well-baby units of the Royal University Hospital in Saskatoon. An even distribution of male and female participants was intended.

2.4 Design

This study uses a cross-sectional design. All measurements were performed by hospital newborn hearing screening staff or by the graduate student (myself).

2.5 Instrumentation/Equipment

2.5.1 GN Otometrics Madsen Accuscreen

The GN Otometrics Madsen Accuscreen was used as part of the hospital newborn hearing screening battery to measure TEOAEs. The Accuscreen assesses the presence of TEOAE's through noise-weighted averaging with the counting of significant signal peaks (Otometrics, 2015). A non-linear click sequence stimulus is used at a level of 75dB(A) +/- 5 dB HL, which self-calibrates depending on ear canal volume (Otometrics, 2015). The Accuscreen has a click rate of approximately 67 to 76 clicks per second randomized with a frequency range of 1 to 4 kHz and uses an averaged waveform (Otometrics, 2015). It displays an averaged waveform, the number of TEOAE peaks and overall pass or refer (Otometrics, 2015). Averaging may be stopped after 50 sweeps if reproducibility standards have been obtained. The instrument displays a numerical assessment of the confidence of a true response as well as a numerical assessment of the level of noise in each band. An upper limit to the number of sweeps is averaged. The data collection window is set at 4 to 10 milliseconds and the maximum recording time of 6 minutes is allowed (BCEHP, 2007, p. 56).

2.5.2 GN Otometrics OTOflex Diagnostic Impedance Meter

The GN Otometrics OTOflex diagnostic impedance meter was used as part of the hospital newborn hearing screening battery to measure 1000 Hz tympanometry and BBN MEMR. Tympanometry was performed with the use of a 1000 Hz probe-tone and the pressure was varied from +200 to -400 daPa in a positive to negative sweep direction and was delivered at a pump speed setting of "as fast as possible", or from 500 to 400 daPa per second (Otometrics,

2016). BBN MEMR was tested with a probe-tone of 1000 Hz with pressure compensation from the tympanometric peak pressure (TPP) of the most recently recorded tympanogram at the same probe-tone (Otometrics, 2016). The stimulus was a broadband noise (BBN) in the ipsilateral mode at an intensity of 85 dB HL.

2.5.3   Titan Interacoustics System

The Titan Interacoustics System was used to measure Wideband Acoustic Immittance and TEOAE's. It consists of a handheld screening and diagnostic device and a Windows-based computer with integrated audiologic software modules (Figure 8). The Titan has a pressure pump that can be used to do WAI tympanometry. Depending on which software is installed, the Titan can perform Impedance and Wideband Tympanometry including admittance at a variety of frequencies and pressures, DPOAE's, AABR's, and TEOAE's (Interacoustics, 2015). The Titan software suite version 3.4.0, build version 3.4.6246.26391 was used and accessed through the Interacoustics Otoaccess database software (Otoaccess Version V.121).

The Impedance Measuring System of the Titan uses a wideband click with a broadband range of frequencies between 226 Hz to 8000 Hz at a rate of 21.5 click/second at 96dB peSPL (infant). Responses from a total of 16 clicks were averaged for each measurement. The Titan system recorded 107 data points (1/24th octave frequencies from 226 to 8000 Hz). Pressurized measurements were obtained using an air pressure of -400 to +200 daPa and the pump speed was set at medium. The data acquisition was very quick, and the typical test time was less than 10 seconds per ear once a seal was obtained. WBT was performed at Tympanometric Peak Pressure (TPP), which is defined in terms of the absorbance tympanogram averaged over low frequencies from 0.376 to 2 kHz (Aithal, 2015; Hunter et al., 2010; Sanford et al., 2009).

The Titan TEOAE system uses a frequency range of 500 to 5500 Hz with 1 Hz frequency steps. The stimulus was a non-linear click with a stimulus level of 83 dB peSPL and an acceptable noise level of 55 dB peSPL. The stop criteria was a maximum recording test time of 2 minutes or 1000 sweeps. 3 bands out of 5 were required for a pass but 3K and 4K were mandatory. TEOAE pass criteria was 6 dB S/N for 2000, 3000 and 4000 Hz bands and 3 dB S/N for the 1000 and 1500 Hz bands. The minimum number of sweeps was 150 and minimum TE level was -7 dB SPL. The level used was 30 to 90 dB SPL and the click rate was 43-100 Hz.

Figure 8: Titan Interacoustics Handheld Unit connected to the computer with the probe tip case on the testing cart.

2.5.3.1   Titan Probe Tips

A variety of newborn ear tips were provided for use in this study, however it was found that the flanged blue 4-7 mm and the red 3-5 mm probe tips (Figure 9) were the most effective in obtaining a proper seal to complete testing.
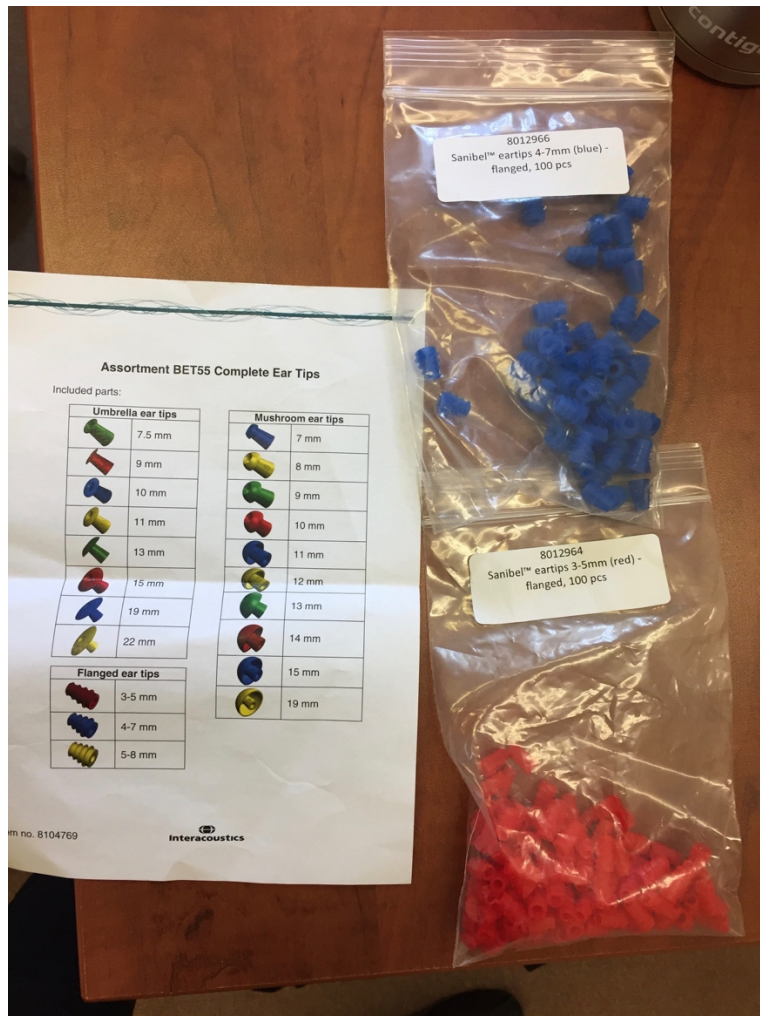
Figure 9: Titan Interacoustics Probe Tips used in the study.

2.5.4   Calibration

As Newborn Hearing Screening is a daily procedure performed by the trained hospital hearing screening staff, the hospital staff performed all daily calibrations of the Madsen Accuscreen and OTOflex devices.

Calibration of the Titan device was performed daily every morning before testing began and involved placing the probe tip into four metal calibration units of 0.2, 0.5, 2 and 5 cc volumes (Figure 10). Calibration determined the source reflectance and incident sound pressure associated with the probe and its transducers based on acoustic measurements in the calibration units. Calibration of the Titan device was based on a new procedure researched by Interacoustics that produces superior results compared to previous methods of calibration (Norgaard, 2016). This procedure does not use an ear tip during calibration which allows for consistent positioning of the probe in the wave-guide input reference and the use of well-defined waveguide dimensions rather than estimating the length from the probe response. The results are that the reference impedances are exactly as seen by the probe and the correct set of source parameters are obtained increasing precision and repeatability of in-ear measurements (Norgaard, 2016).

Figure 10: Four calibration cavities and the probe cord with the light indicator button.

2.6   Procedures

2.6.1   Consent

Upon returning to the room to perform newborn hearing screening, parents were asked if they had any questions about the Invitational Letter and the Consent Letter that were dropped off previously and if they were willing to include the results of the screening in the study. Consent forms for inclusion of the normal hearing screening data and the Titan WAI and TEOAE data were then collected and the hearing screening procedures were performed by the hearing screeners and the graduate student. Parents were also asked if they would participate in a second part of the study, the return visit to collect tone ABR data, and a second consent form (Appendix C) was distributed.

The invitational letter and consent forms 1 and 2 were approved by the Clinical Research Ethics Board of the University of British Columbia and by the Biomedical Research Ethics Board of the University of Saskatchewan.

2.6.2 Ethnicity Data

After the data collection was complete, parents were asked for volunteer ethnicity data and the information was recorded on the data collection sheets (Appendix D) which contained no identifying information. Ethical approval for the study was obtained from the Clinical Research Ethics Board of the University of British Columbia and the Biomedical Research Ethics Board of the University of Saskatchewan.

2.6.3 General Procedures

The current newborn hearing screening protocol at the Royal University Hospital (RUH) in Saskatoon is the following:

1) TEOAE's with the Madsen Accuscreen

2) 1 KHz tympanogram with the OTOflex

3) MEMR in the Ipsilateral Ear at 1 kHz with the OTOflex

This newborn hearing screening protocol is a strict parallel protocol as all tests are performed on all newborns and a pass is required on every measure to receive a pass outcome. As well the test protocol for newborns who refer is a loose parallel protocol in that newborns requires a refer result on any one measure to receive a refer outcome on the protocol.

The procedures for this study followed the newborn hearing screening protocols at the RUH with the addition of a Titan Interacoustics WAI test (WBA and phase). As WAI gives us

absorbance measures across a range of pressures and frequencies, one WAI measurement can tell us the results of tympanometry (absorbance tympanograms) across all frequencies, including the 1 kHz tympanometric measure used in typical hearing screening protocols. The intent was for the Titan device to perform all measures except for the MEMR in the ipsilateral ear as the Titan device is not equipped with a 1 KHz probe tone on the ipsilateral mode which would allow for MEMR measurement.

Following a brief case history (performed by the hearing screening staff) to look for risk factors of hearing loss, the following tests were to be conducted:

1) TEOAE's with the Titan

2) WAI with the Titan

3) MEMR in the Ipsilateral Ear at 1 kHz with the OTOflex

However, during testing it was found that the TEOAE measurement outcomes obtained using the Titan were not comparable to the Accuscreen for screening and therefore the following test protocol was adopted:

1) TEOAE's with the Madsen Accuscreen

2) 1 kHz tympanogram with the OTOflex

3) MEMR in the Ipsilateral Ear at 1 KHz with the OTOflex

4) WAI with the Titan

5) TEOAE's with the Titan

At the beginning of each screening day, the newborns due to be screened were organized according to the time of birth and room. Each newborn was given an identification number on the data collection sheets, consent forms, and invitational letters and then the forms and letters were delivered to the parents. Once all forms were delivered screening began on the earliest born

baby. Newborns were tested in order unless there were doctors, nurses or students in the room, or if a baby was absent from the room or was in an agitated state.

Data Collection Sheets, as shown in Appendix D, included a unique identifier for each participant and were used to collect information on Room Number, Gender, R/L Ear, Consent Obtained, and Results of the 1 kHz tympanogram, TEOAE Accuscreen, TEOAE Titan, MEMR, Ethnicity, and a notes section which was used to write the time of completion of testing.

The Titan system required a separate cart to hold the computer and the handheld Titan unit (Figure 8). The hospital newborn rooms were often small and crowded, and therefore the hearing screener entered the room with the first cart with the Accuscreen and the OTOflex to obtain the first TEOAE, the 1 kHz tympanogram and the MEMR and then the second screener entered with the second cart with the Titan to obtain the WAI and second TEOAE measurements.

Newborns were tested while in a natural sleep, in an awake but quiet state or while feeding. The most accessible ear was tested first. All tests were completed on one ear and then the second ear was tested.

If there was a refer on the TEOAE, 1 kHz tympanogram or MEMR tests, then the usual procedure of the hospital is to schedule a rescreening within 8 weeks. For the purposes of this study, all parents of newborns who passed the screening were asked to return for a Diagnostic Tone Auditory Brainstem Response (ABR) test. Parents were asked to return for an ABR test as ABR is a gold standard test for infant hearing loss that could be used to check the accuracy of the WAI tests. No parents chose to return for the ABR test. Therefore, to get data on the accuracy of our WAI and TEOAE tests, diagnostic ABR tests were offered on children who had returned after 8 weeks for a regular rescreening. Due to the availability of testers, only 3 participants were

recruited for the second part of this study and therefore there were not enough participants to accurately determine the specificity of the WAI tests.

2.6.4   Daily preparation

Every morning before testing the Titan was calibrated and the probe cleaned with floss. Sanitation procedures for the newborn ward required cleaning the cart and equipment and hands before and after every patient contact.

2.6.5   Transient Evoked Otoacoustic Emissions with the GN Otometrics Accuscreen

The Accuscreen TEOAE test was performed first in the most easily accessible ear. The TEOAE test is done first so that the most pertinent information related to hearing status is obtained while a baby is at its most cooperative stage. A new probe tip was placed on the device for each ear.

The Accuscreen uses noise-weighted averaging with the counting of significant signal peaks to look for a TEOAE signal and also uses an artifact rejection system to differentiate external noise and TEOAE signal (GN Otometrics, 2010). A non-linear click sequence stimulus is used at a level of 45-60 dB HL, which self-calibrates depending on ear canal volume (GN Otometrics, 2010). The Accuscreen uses a click rate of about 60 Hz and a frequency range of 1500 to 3500 Hz and uses a binomial statistics algorithm (GN Otometrics, 2010). Criteria for a pass for the Accuscreen TEOAE test involved a good emission-to-noise ratio in three out of five half-octave bands centered at 1, 1.5, 2, 3, and 4 kHz (SNR of 3 dB at 1 and 1.5 kHz and 6 dB at 2, 3, and 4 kHz). If a good SNR was found a "Pass" was displayed on the device. If a good ratio

was not achieved, then a "Refer" was displayed. If a refer result was obtained, the baby was tested again to rule out probe blockage, room noise or baby noise in causing the refer result.

2.6.6   1 kHz tympanogram and Middle Ear Muscle Reflexes with the Otoflex

The OTOflex was used next to obtain both the 1 kHz tympanogram and the MEMR. A new probe tip was placed on the probe and inserted into the ear. Results of both the tympanogram and the reflex were assessed visually to determine if there was a pass.

Criteria for a pass on the 1 kHz tympanogram was a visual confirmation of a type A (single peak) tympanogram on the Otoflex readout.

Criteria for a pass on the measure of MEMR was a reflex obtained ipsilaterally using a 1 kHz probe tone frequency at a fixed intensity of 85 dB HL. Reflex presence is defined by clear, most likely negative deflections that are repeatable at the stimulus level (BCEHP, 2007, p. 52). The use of an 85 dB HL BBN stimulus is supported by Mazlan et al. (2009), who found that more than 95% of babies had reflex thresholds below 85 dB HL using BBN stimulus. The goal is not to establish an accurate reflex threshold but to demonstrate the clear presence or absence of reflexes at a safe stimulus level (BCEHP, 2007, p. 52). The BBN stimulus was used because it can elicit MEMR at a lower stimulus level than those elicited by pure tones (Niemeyer, 1974). This property enables the BBN to be used for screening purposes in newborn hearing screening programs, although it carries no frequency-specific information (Mazlan, 2009). The broadband stimulus also stimulates all areas of the basilar membrane and therefore all of the afferent nerve fibers running from the cochlea to the brain. As a result, the broadband stimulus is more likely to detect diffuse pathology located proximal to the cochlea such as neural degeneration or auditory neuropathy (Mazlan, 2009).

The Accuscreen TEOAE and OTOflex 1kHz tympanogram and MEMR were performed by the hearing screening staff and the results were recorded on RUH hospital forms. These results were copied to the study data collection sheets and were not saved on any device.

2.6.7 Wideband Acoustic Immittance with the Titan

The Titan software must be opened from a database manager for the data to be saved for each participant, therefore, before measurement, each participant was entered into the Otoaccess database with their unique identifier, date of birth and gender and the Titan software opened in preparation for testing. A new probe tip was used for every ear.

Testing for WAI began on the most accessible ear. The probe cord button (Figure 10) showed red for right ear selected but out of the ear, blue for left ear selected but out of the ear, yellow for the probe in the ear but is blocked, leaking or too noisy, and green for the probe in the ear and a seal is present. The WAI test could be started or paused from the probe cord button. The test would not begin unless a seal was detected which would take approximately from 5 seconds to one minute to obtain. If a seal was lost in the middle of testing the test would continue. If a noisy or blocked recording was obtained, then another test was attempted. A noisy recording was indicated by a spiky appearance of the 3D measurement during WAI testing on the computer as shown in Figure 6. A blocked recording was indicated by a low ear canal volume along with a flat 3D picture with a very low absorbance pattern as shown in Figure 7. Newborns that were waking up, crying or moving were soothed either by allowing the mother to feed them, by using a pacifier or by offering a finger for the baby to suck on while testing. Once a seal was obtained testing was very fast, under 10 seconds for each ear.

Titan WAI and TEOAE tests were performed for one ear and then the baby was moved so that the other ear was exposed and a new probe tip was used for testing. Test results were saved and the recorded time was entered into the Data Collection Sheet.

2.6.8   Transient Evoked Otoacoustic Emissions with the Titan

Once the WAI test was completed the probe was kept in the ear and the TEOAE test was toggled by reaching back to the computer with the other hand. The TEOAE test could be started by pushing the probe cord button; however, if too much noise was detected the computer would pause and give a warning message which had to be accepted by touching the computer before the test would continue. Once the testing began, Titan TEOAE tests took from 15 seconds to 5 minutes to obtain. Longer test times were likely due to noise in the room and probe fit. Often, probe tips that worked well for TEOAE did not work well for WAI which would require a change in the probe tip, resulting in 4 probe tips used for each participant.

Criteria for a pass for the Titan TEOAE test involved a good emission-to-noise ratio in three out of five half-octave bands centered at 1, 1.5, 2, 3, and 4 kHz (SNR of 5 dB at 1 and 1.5 kHz and 6 dB at 2, 3, and 4 kHz). If a good SNR was found a "Pass" was displayed on the device. A pass on at least three bands were required. If a good ratio was not achieved, then a "Refer" was displayed. The stimulus was a non-linear click at a level of 83 dB peSPL with an acceptable noise level of 50 dB SPL. Maximum test time was set at 2 minutes or 1000 sweeps. The minimum TE level was -7 dB SPL. A recording window of 4-12.5 ms (Quickscreen) was used with a stimulus rate of 80.0 per second to minimize the effects of noise on the results.

2.6.9   Tone ABR with the Intelligent Hearing Systems (IHS) SmartEP system

Newborns that received a "refer" were asked to return in 8 weeks for a rescreening and participants who received a "pass" result were asked to return in 2 weeks for a rescreening. It was intended to use tone ABR to confirm type of hearing loss in participants who have a "refer" outcome from our new screening protocol and to test 10% of those children who have a "pass" outcome to use as a control group, however no participants returned for the optional 10% tone ABR testing. Three infants that returned for rescreening after a "refer" result or after a missed screening were tested with WAI and then with Tone ABR. Tone ABR procedures were as per the recommendations laid out in the BCEHP protocols (2007). This protocol involves testing infants while in natural sleep. BCEHP recommendations include testing babies for air conduction and bone conduction in a specific order of frequency and intensity to get the most important diagnostic information first. A conversion factor is applied to each hearing level result to get equivalent numbers for HL thresholds. None of these results were used in the final analysis of the study as there were not enough participants.

2.6.10   Data Management

At the end of each day, the raw Titan WAI data was separated into participant files according to the time that they had been tested. The data was then extracted from the raw files using an excel spreadsheet provided by Interacoustics and transferred to an excel database. All other data was added by hand from the Data Collection Sheets.

For the WBA measurements, data from both the ambient and peak pressures were available but for the $Y\varphi$ measurements, only data from the ambient pressure was available.

2.6.11 1 kHz tympanogram quantification

As WAI assesses absorbance across all frequencies and pressures, a 1 kHz tympanogram was available from the WAI data and was quantified for each measurement. 1 kHz tympanograms were measured according to Vanhuyse model on susceptance (B) and conductance (G) tympanograms and labeled according to the number of peaks and troughs on B and G. While this data was available, it was not used in the final study analyses.

2.6.12 Reasons for Invalid Results

WAI measurements were not included if there was a poor seal if the probe was blocked, or if the recording was too noisy. Examples of these measurements are shown in the Exclusion Criteria section of this paper.

2.7 Statistical analysis

Descriptive statistics were used to describe the proportion of neonates of different ethnicities that passed and failed the screening test battery of Accuscreen TEOAE, 1 kHz tympanometry and BBN MEMR and to describe the proportion of neonates of different ethnicities that had a likely diagnosis of CHL, NH , AN or SNHL.

The significance of the difference between the following populations were analyzed using a two-proportion Z-test with a significance level of 0.01:

1 - The proportion of FNAM and Caucasian neonates who passed the NHS test battery.

2 - The proportion of FNAM and Caucasian neonates who failed the NHS test battery.

3 – The proportion of FNAM and Mixed Other ethnicity neonates who passed the NHS test battery.

4 – The proportion of FNAM and Mixed Other ethnicity neonates who failed the NHS test battery.

5 – The proportion of FNAM and Undeclared ethnicity neonates who passed the NHS test battery.

6- The proportion of FNAM and Undeclared ethnicity neonates who failed the NHS test battery.

7 – The proportion of FNAM and Caucasian neonates who had a likely diagnosis of CHL.

8 – The proportion of FNAM and Mixed Other ethnicity neonates who had a likely diagnosis of CHL.

9 – The proportion of FNAM and Undeclared ethnicity neonates who had a likely diagnosis of CHL.

A Z test is used to determine whether two population means are different when the variances are known and the sample size is large (greater than 30). When using a Z test, the distribution of the test statistic under the null hypothesis can be approximated by a normal distribution.

Four analysis of variance (ANOVA) were applied to the WBA data and four ANOVA were applied to the $Y\varphi$ data as shown below:

WBA:

1) For neonates who passed or failed a screening test battery of Accuscreen TEOAE, 1 kHz tympanometry, and BBN MEMR. Pass or fail as a between-group factor and frequency and ambient vs peak pressure as within-group factors.

2) For neonates who had a likely diagnosis of NH, CHL, or SNHL. Likely diagnosis as a between-group factor and frequency and ambient vs peak pressure as within-group factors.

3) For neonates of FNAM, Caucasian, or Mixed Other Ethnicity. Ethnicity as a between-group factor and frequency and ambient vs peak pressure as within-group factors.

4) For neonates who passed or failed Accuscreen TEOAE. Pass or fail as a between-group factor and frequency and ambient vs peak pressure as within-group factors.

Υφ:

1) For neonates who passed or failed a screening test battery of Accuscreen TEOAE, 1 kHz tympanometry, and BBN MEMR. Pass or fail as a between-group factor and frequency as within-group factor.

2) For neonates who had a likely diagnosis of NH, CHL, or SNHL. Likely diagnosis as a between-group factor and frequency as within-group factor.

3) For neonates of FNAM, Caucasian, or Mixed Other Ethnicity. Ethnicity as a between-group factor and frequency as within-group factor.

4) For neonates who passed or failed Accuscreen TEOAE. Pass or fail as a between-group factor and frequency as within-group factor.

ANOVA analysis was used in this paper to look looking at the general trend of differences. Post-hoc analysis was not run on the results as a high number of frequencies were used to get an idea of general trends (107). Future research could collate the data into 1/3 octave frequency bins and run post-hoc analysis.

As all 107 frequencies were used for the ANOVA interactions, each analysis was also reanalyzed using Greenhouse-Geiser (GG) correction. GG correction is used when data violates

the sphericity assumption in statistics (that variance is homogeneous between groups) and it operates by adjusting the degree of freedom in the ANOVA test in order to produce a more accurate significant (p) value (Baguley, 2004). GG correction was used because of the large number of frequencies used for the analysis.

Chapter 3: Results

3.1   Newborn Hearing Screening (NHS) test battery results

3.1.1   NHS test battery pass/fail

Table 6 illustrates the proportion of ears of First Nations, Caucasian, Other (mixed ethnicity) and Undeclared Ethnicity neonates who passed or failed the screening test battery of Accuscreen TEOAE, BBN MEMR, and 1000 Hz tympanometry. A total of 305 ears passed the test battery and 69 ears failed the test battery. 81.55% of neonates in all ethnic groups passed the test battery. 8 ears that did not complete the full test battery were removed from the analysis.

Table 6: Proportion of neonate's ears by ethnicity that passed or failed a NHS test battery of 1000 Hz tympanometry, TEOAE, and BBN MEMR.

	First Nations n (%)	Caucasian n (%)	Mixed Other n (%)	Undeclared n (%)
Pass	28 (68.29%)	179 (86.89%)	38 (80.85%)	60 (75.00%)
Fail	13 (31.71%)	27 (13.10%)	9 (19.15%)	20 (25.00%)

Table 7 illustrates the results of a Z-test analysis (Appendix E.1 and E.2) that showed a significant difference in the proportions of FNAM and Caucasian ears that passed or failed the test battery.

Table 7: Results of a Z test for evaluating the significant difference in proportions of FNAM and Caucasian neonate ears that passed or failed a NHS test battery of Accuscreen TEOAE, 1 kHz tympanometry, and BBN MEMR.

	First Nations n (%)	Caucasian n (%)	Z value	Significance p
Pass	28 (68.29%)	179 (86.89%)	2.952	0.003
Fail	13 (31.71%)	27 (13.10%)	-2.952	0.003

Table 8 illustrates the results of a Z-test analysis (Appendix E.3 and E.4) that did not show a significant difference in the proportions of FNAM and Mixed Other ethnicity ears that passed or failed the test battery.

Table 8: Results of a Z test for evaluating the significant difference in proportions of FNAM and Mixed Other ethnicity neonate ears that passed or failed a NHS test battery of Accuscreen TEOAE, 1 kHz tympanometry, and BBN MEMR.

	First Nations n (%)	Mixed Other n (%)	Z value	Significance p
Pass	28 (68.29%)	38 (80.85%)	1.357	0.175
Fail	13 (31.71%)	9 (19.15%)	-1.357	0.175

Table 9 illustrates the results of a Z-test analysis (Appendix E.5 and E.6) that did not show a significant difference in the proportions of FNAM and Undeclared ethnicity ears that passed or failed the test battery.

Table 9: Results of a Z test for evaluating the significant difference in proportions of FNAM and Undeclared ethnicity neonate ears that passed or failed a NHS test battery of Accuscreen TEOAE, 1 kHz tympanometry, and BBN MEMR.

	First Nations n (%)	Undeclared n (%)	Z value	Significance p
Pass	28 (68.29%)	60 (75.00%)	0.7841	0.433
Fail	13 (31.71%)	20 (25.00%)	-0.7841	0.433

3.1.2 Likely diagnosis based on the pattern of passed and failed NHS tests

Likely diagnosis is based on the pattern of pass or fails of 1000 Hz tympanometry, BBN MEMR, and TEOAE as shown in Table 10.

Table 11 shows the proportion of ears of Caucasian, First Nations, Other (mixed ethnicity) and Undeclared Ethnicity neonates who had a pattern of failure according to the likely diagnosis based on the screening test results. A total of 61 ears showed a conductive hearing loss pattern of failure (88.41% of fails), 7 ears showed a sensorineural hearing loss pattern of failure (10.14% of fails), and 1 ear showed an Auditory Neuropathy pattern of failure (1.45% of fails).

Table 10: Determination of Likely Diagnosis by Screening Outcome.

Madsen Accuscreen TEOAE	1000 Hz Tympanogram	BBN MEMR	Likely Diagnosis
Pass	Pass	Pass	**Normal** Results = 305/374 = 81.55%
Pass	Fail	Pass	**Conductive** Results = 33/374 = 8.82%
Fail	Pass	Pass	**Sensorineural (Cochlear)**

			Likely moderate to severe cochlear origin Results = 7/374 = 1.87%
Pass	Pass	Fail	**Auditory Neuropathy (Neural)** Results = 1/374 = 0.27%
Fail	Fail	Pass	**Conductive** Not a likely result, if 1000 Hz tymp is a fail, then it is illogical for MEMR to be present Results = 7/374 = 1.87%
Pass	Fail	Fail	**Conductive** Results = 4/374 = 1.07%
Fail	Pass	Fail	**Sensorineural (Cochlear)** Likely severe to profound cochlear origin Results = 0/374 = 0%
Fail	Fail	Fail	**Conductive** Cannot rule out sensorineural hearing loss Results = 17/374 = 4.55%

Table 11: Proportion of neonate's ears by ethnicity that is likely to have Conductive Hearing Loss, Sensorineural Hearing Loss, or Auditory Neuropathy based on the pattern of failure of a NHS test battery of 1000 Hz tympanometry, TEOAE, and BBN MEMR screening test.

	First Nations n (%)	Caucasian n (%)	Mixed Other n (%)	Undeclared n (%)
Conductive	12 (92.31)	24 (88.89)	8 (88.89)	17 (85.00)
Sensorineural	1 (7.69)	2 (7.41)	1 (11.11)	3 (15.00)
Auditory Neuropathy	0	1 (3.70)	0	0

Table 12 illustrates the results of Z-test analyses (Appendix E.7) that showed a significant difference in the proportions of FNAM and Caucasian ears that failed the test battery and had a likely diagnosis of CHL.

Table 12: Results of a Z test for evaluating the significant difference in proportions of FNAM and Caucasian neonates that had a likely diagnosis of conductive hearing loss.

	First Nations n (%)	Caucasian n (%)	Z value	Significance p
Conductive	12 (92.31)	24 (88.89)	2.920	0.003

Table 13 illustrates the results of Z-test analyses (Appendix E.8) that did not show a significant difference in the proportions of FNAM and Mixed Other ethnicity ears that failed the test battery and had a likely diagnosis of CHL.

Table 13: Results of a Z test for evaluating the significant difference in proportions of FNAM and Mixed Other ethnicity neonates that had a likely diagnosis of conductive hearing loss.

	First Nations n (%)	Mixed Other n (%)	Z value	Significance p
Conductive	12 (92.31)	8 (88.89)	-1.368	0.171

Table 14 illustrates the results of Z-test analyses (Appendix E.9) that did not show a significant difference in the proportions of FNAM and Undeclared ethnicity ears that failed the test battery and had a likely diagnosis of CHL.

Table 14: Results of a Z test for evaluating the significant difference in proportions of FNAM and Undeclared ethnicity neonates that had a likely diagnosis of conductive hearing loss.

	First Nations n (%)	Undeclared n (%)	Z value	Significance p
Conductive	12 (92.31)	17 (85.00)	-0.978	0.328

3.2 Wideband Absorbance (ambient and peak) and Admittance Phase in neonates who passed or failed a NHS test battery.

3.2.1 Wideband Absorbance in neonates who passed or failed a NHS test battery.

To evaluate the effect of pressurization method (ambient and peak) and frequency on WBA for neonates who passed or failed the screening test battery, a mixed model ANOVA (Appendix E.10) was performed with binary screening outcome (pass/fail) as between-subject factors and absorbance across 107 frequency bins and pressure (ambient vs. peak) as the within-subject factor.

The main effect of screening outcome (pass/fail) was significant [$F_{(1, 263)}$ = 18.745, p = 0.00002] indicating that absorbance was significantly higher in the pass group compared with absorbance in the fail groups when the data collapsed across frequency and pressure.

The interaction between absorbance across 107 frequency bins, screening outcome (pass vs. fail) and pressure (ambient vs. peak) (Figure 11 and Figure 12) was significant [F (106,

27878) = 4.3438, p = 0.0000], and remained significant after GG correction (Appendix E.11), indicating that absorbance varies differently between pass and refer group as well as at ambient and peak pressure across frequencies.

Figure 11: Mean absorbance at ambient and peak pressure from 250 – 8000 Hz for a screening outcome of pass and a screening outcome of fail. Vertical bars denote 95% confidence intervals.
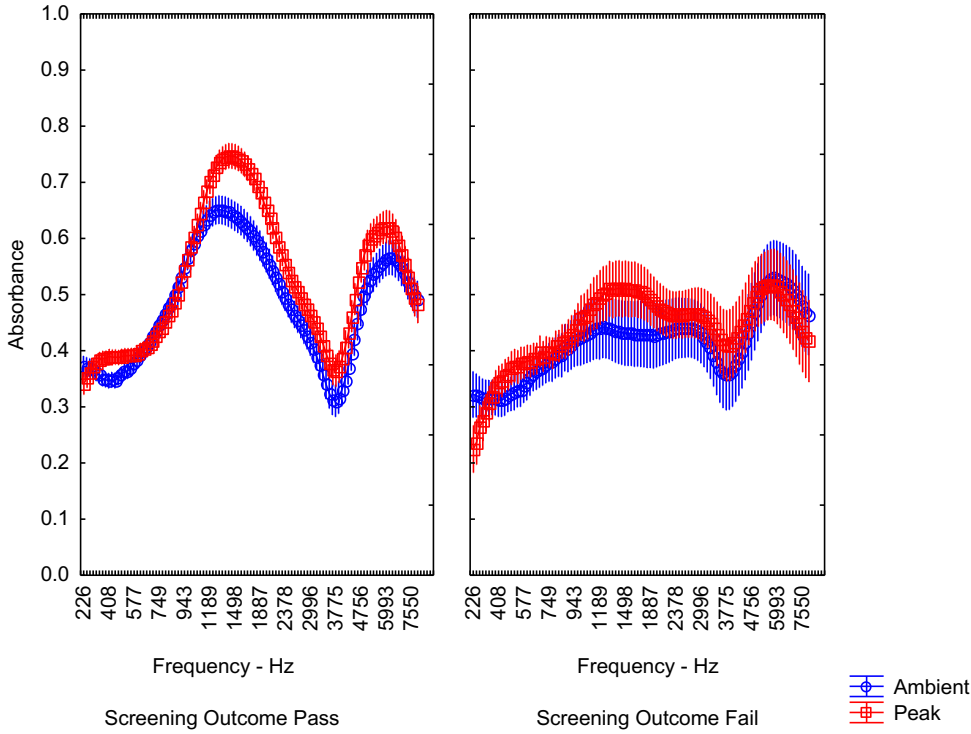
Figure 12: Mean absorbance at ambient and peak pressure from 250 – 8000 Hz for a screening outcome of pass and a screening outcome of fail. Vertical bars denote 95% confidence intervals.

3.2.2   Admittance Phase in neonates who passed or failed a NHS test battery.

To evaluate the effect of frequency on Yφ for neonates who passed or failed the screening test battery, a mixed model ANOVA (Appendix E.12) was performed with binary screening outcome (pass/fail) as the between-subject factor and admittance phase across 107 frequency bins as the within-subject factor.

The main effect of screening outcome (pass/fail) was not significant [$F_{(1, 248)} = 1.5606$, $p = 0.21275$] indicating that admittance phase was not significantly higher in the pass group compared with admittance phase in the fail groups when the data collapsed across frequency and pressure.

The interaction between admittance phase across 107 frequency bins and screening outcome (pass vs. fail) (Figure 13) was significant [F (106, 26288) = 2.6725, p = 0.0000] and remained significant after GG correction (Appendix E.13), indicating that admittance phase varies differently between pass and refer group across frequencies.
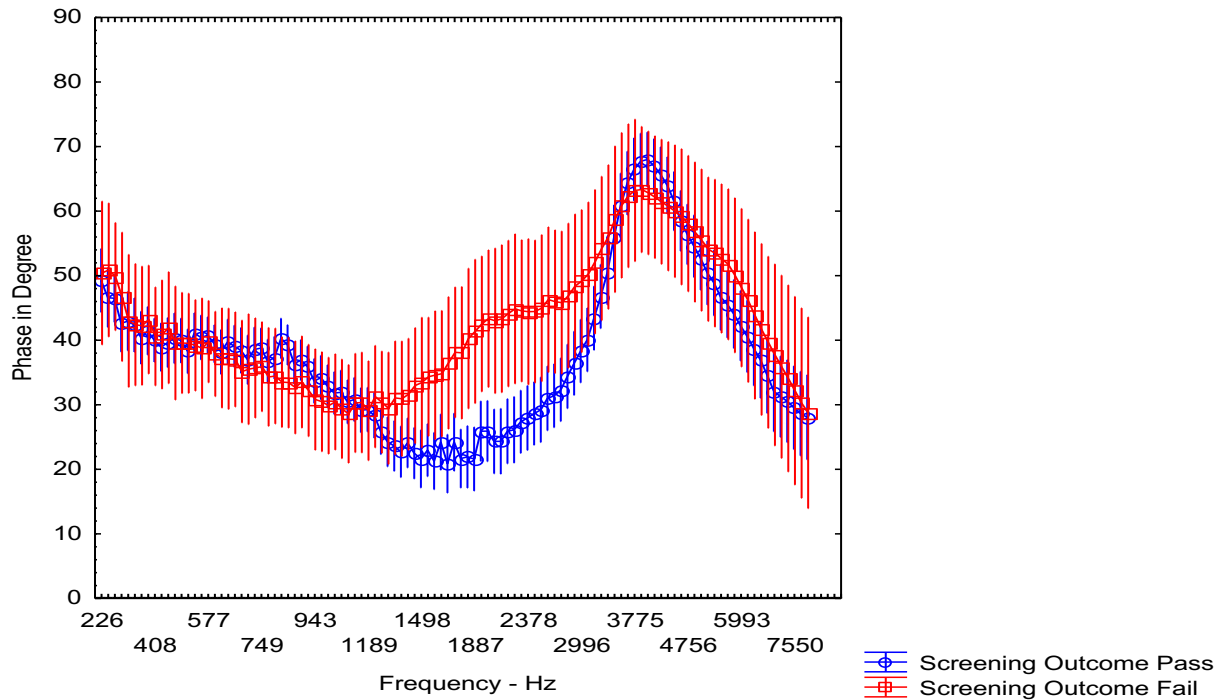
Figure 13: Mean admittance phase at ambient pressure from 250 – 8000 Hz for a screening outcome of pass and a screening outcome of fail. Vertical bars denote 95% confidence intervals.

3.3   Wideband Absorbance (ambient and peak) and Admittance Phase in neonates who have a likely diagnosis of normal or conductive hearing loss.

3.3.1 Wideband Absorbance (ambient and peak) in neonates who have a likely diagnosis of normal or conductive hearing loss.

To evaluate the effect of pressurization method (ambient and peak) and frequency on WBA for neonates who had a likely diagnosis of normal compared to neonates who had a likely diagnosis of conductive hearing loss, a mixed model ANOVA (Appendix E.14) was performed with likely diagnosis (normal vs. conductive) as between-subject factors and absorbance across 107 frequency bins and pressure (ambient vs. peak) as within-subject factors.

The main effect of likely diagnosis (normal vs conductive) was significant [$F_{(1, 257)}$ = 23.712, p = 0.00000] indicating that absorbance was significantly higher in the likely diagnosis of the normal group compared with absorbance in the likely diagnosis of the conductive group when the data collapsed across frequency and pressure.

The interaction between absorbance across 107 frequency bins, likely diagnosis (normal vs. conductive) and pressure (ambient vs. peak) (Figure 14 and Figure 15) was significant [$F_{(106, 27242)}$ = 4.2146, p = 0.0000] and remained significant after GG correction (Appendix E.15), indicating that absorbance varies differently between likely diagnosis of normal and likely diagnosis of conductive group as well as at ambient and peak pressure across frequencies.
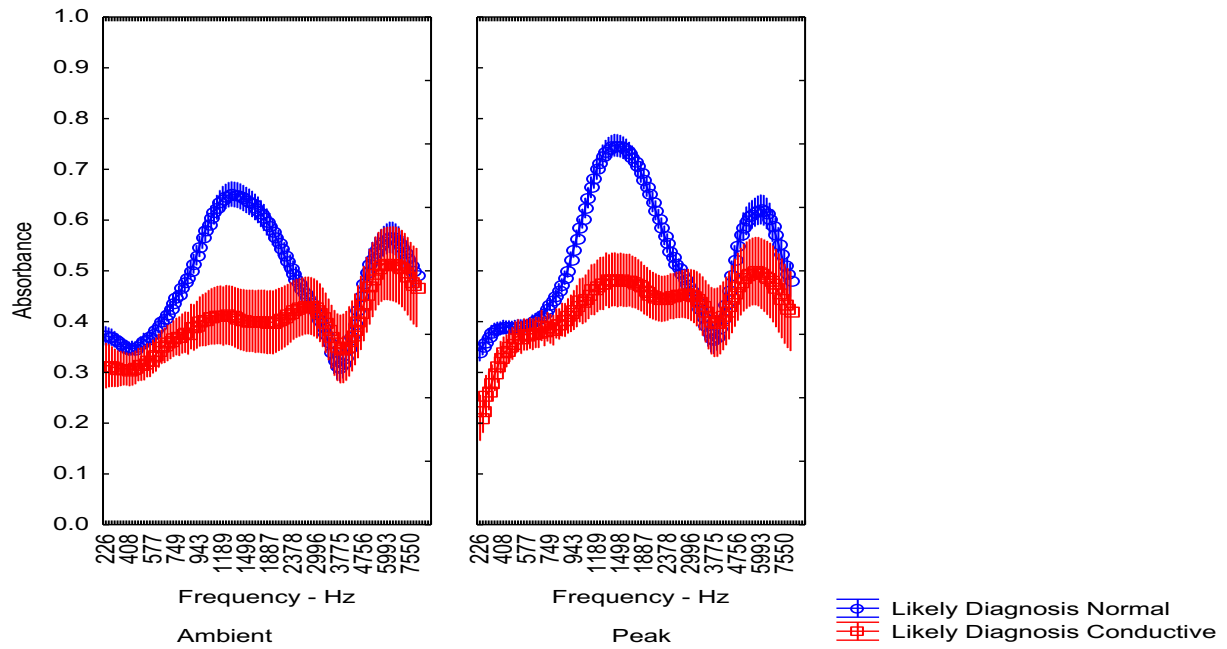
Figure 14: Mean absorbance at ambient and peak pressure from 250 – 8000 Hz for a likely diagnosis of normal hearing and a likely diagnosis of conductive hearing loss based on screening test results. Vertical bars denote 95% confidence intervals.
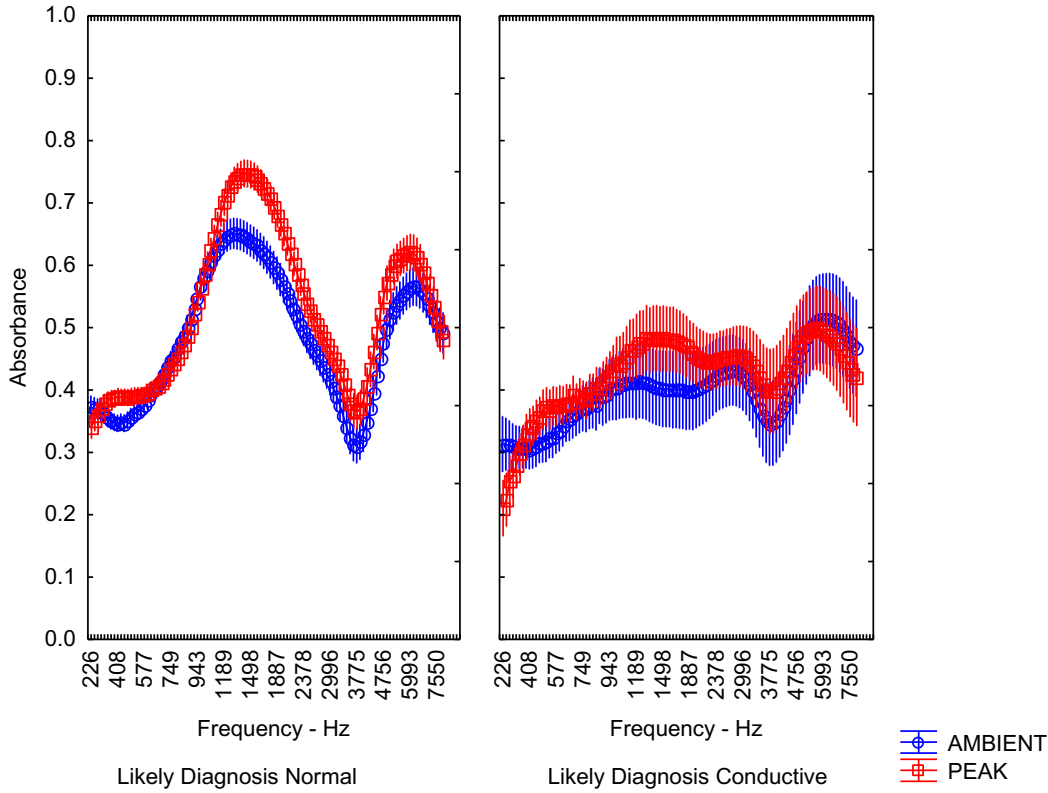
Figure 15: **Mean absorbance at ambient and peak pressure from 250 – 8000 Hz for a likely diagnosis of normal hearing and a likely diagnosis of conductive hearing loss based on screening test results. Vertical bars denote 95% confidence intervals.**

3.3.2 Admittance Phase in neonates who have a likely diagnosis of normal or conductive hearing loss.

To evaluate the effect of frequency on Yφ for neonates who had a likely diagnosis of normal compared to neonates who had a likely diagnosis of conductive hearing loss, a mixed model ANOVA (Appendix E.16), was performed with likely diagnosis (normal vs. conductive) as the between-subject factor and admittance phase across 107 frequency bins as the within-subject factor.

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The main effect of likely diagnosis (normal vs. conductive) was not significant [F (1, 243) = 1.2649, p = 0.26184] indicating that admittance phase was not significantly higher in the conductive group compared with admittance phase in the normal group when the data collapsed across frequency and pressure.

The interaction between admittance phase across 107 frequency bins and likely diagnosis (normal vs. conductive) (Figure 16) was significant [F(106, 25758) = 3.1057, p = 0.0000] and remained significant after GG correction (Appendix E.17), indicating that admittance phase

varies differently between likely diagnosis of normal and likely diagnosis of conductive groups across frequencies.
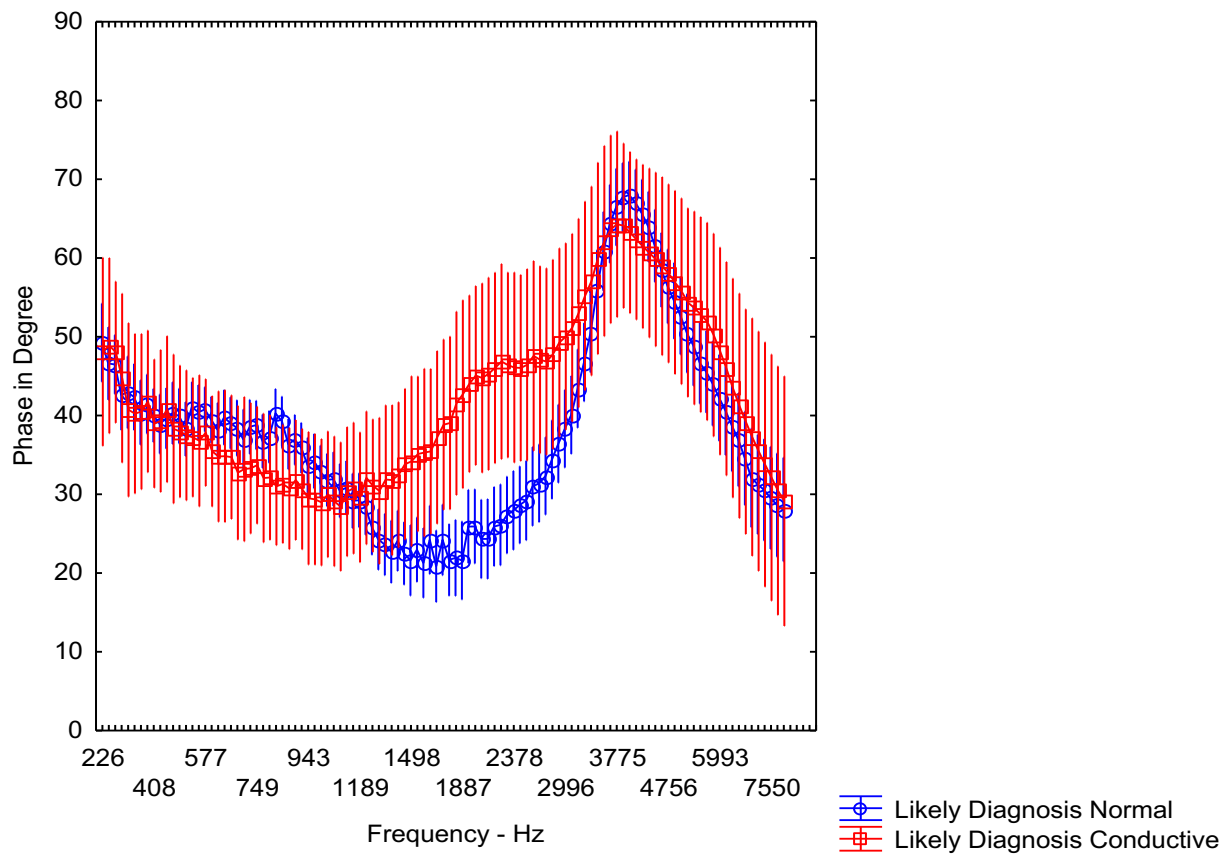
Figure 16: Admittance phase at ambient pressure from 250-8000 Hz for likely diagnosis of normal hearing and a likely diagnosis of conductive hearing loss based on screening test results. Vertical bars denote 95% confidence intervals.

3.4   Wideband Absorbance (ambient and peak) and Admittance Phase in neonates who passed or failed a TEOAE test.

3.4.1   Wideband Absorbance in neonates who passed or failed a TEOAE test.

To evaluate the effect of pressurization method (ambient and peak) and frequency on WBA for neonates who passed or failed the TEOAE test, a mixed model ANOVA (Appendix E.21) was performed with Accuscreen TEOAE results (pass vs. fail) as between subject factors and absorbance across 107 frequency bins and pressure (ambient vs. peak) as within subject factors.

The main effect of Accuscreen TEOAE results (pass vs. fail) was not significant $[F(1, 261) = 3.1956, p = 0.07499]$ indicating that absorbance was not significantly higher in the TEOAE pass group compared with absorbance in the TEOAE fail group when the data collapsed across frequency and pressure.

The interaction between absorbance across 107 frequency bins, Accuscreen TEOAE results (pass vs. fail) and pressure (ambient vs. peak) (Figure 17)(Figure 18) was significant $[F(106, 27666) = 3.2767, p = 0.0000]$ significant and remained significant after GG correction

(Appendix E.22), indicating that absorbance varies differently between Accuscreen TEOAE result of pass and Accuscreen TEOAE result of fail as well as at ambient and peak pressure.
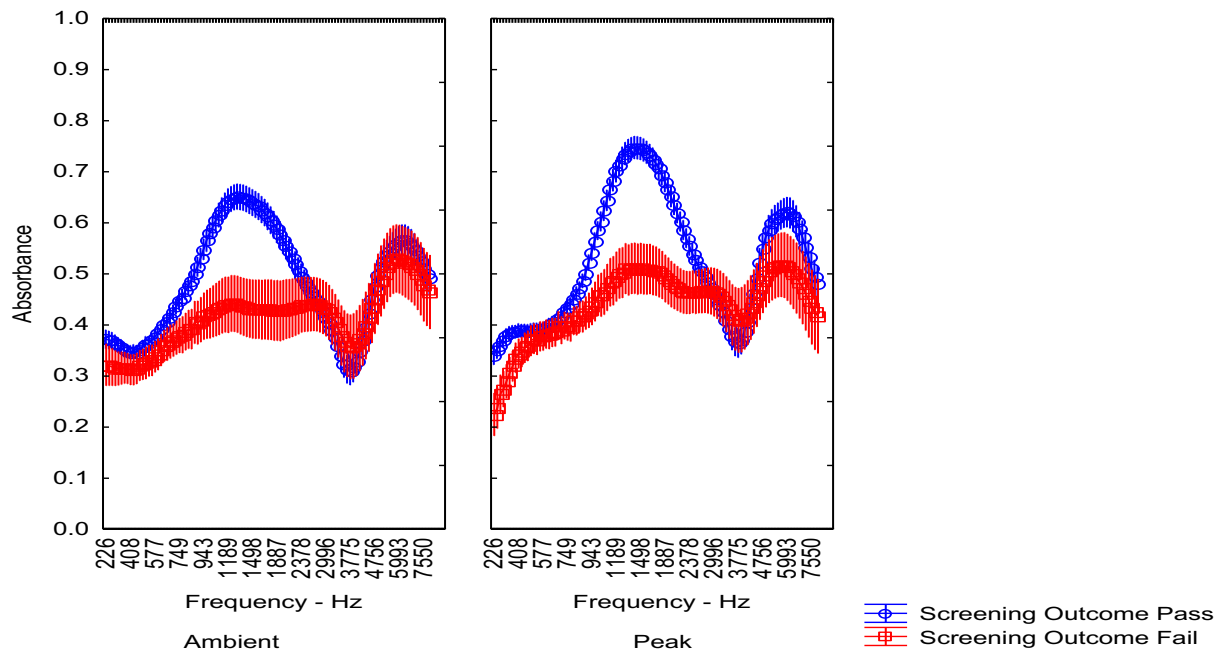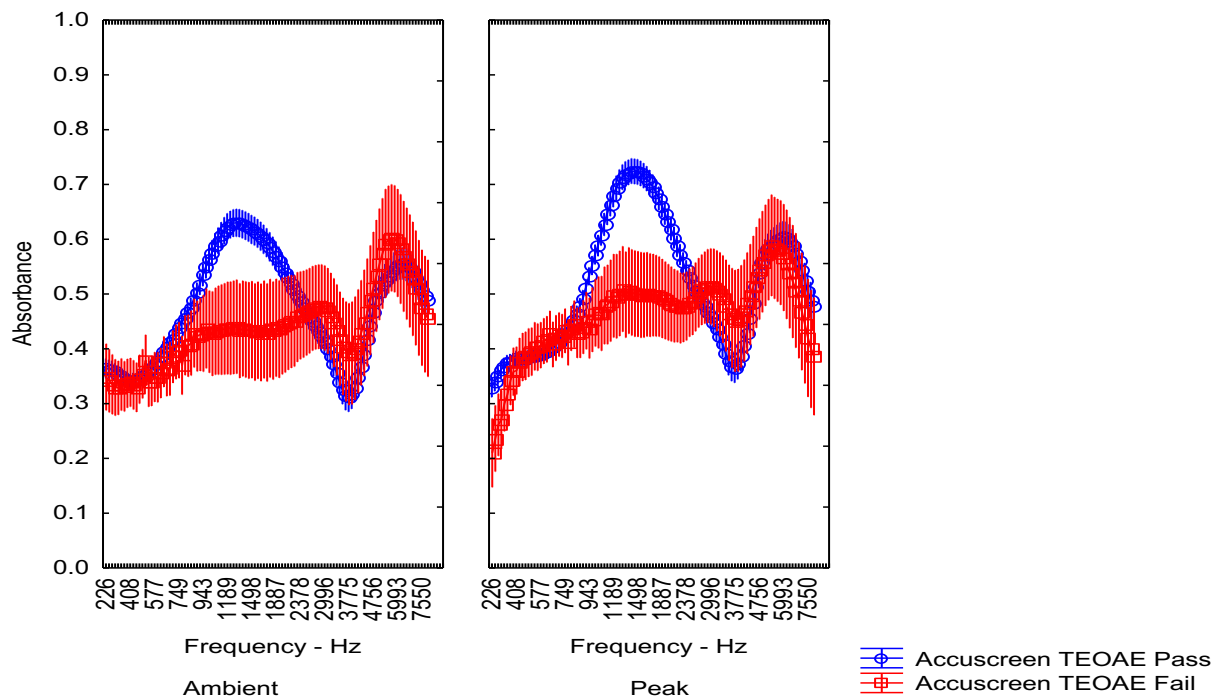

Figure 17: Mean absorbance at ambient and peak pressure from 250 – 8000 Hz for an Accuscreen TEOAE outcome of pass and an Accuscreen TEOAE outcome of fail. Vertical bars denote 95% confidence intervals.
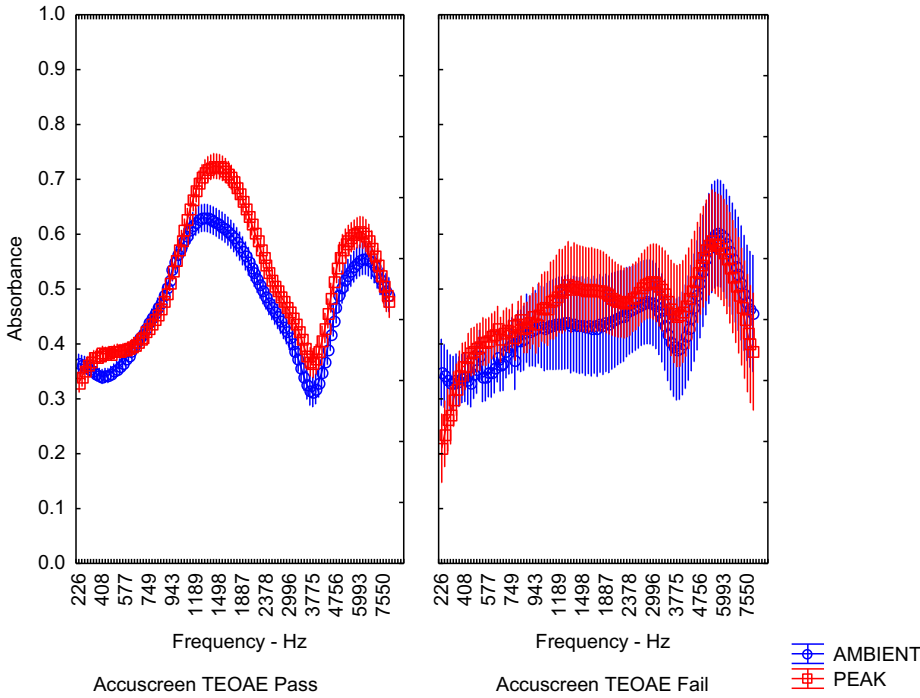
Figure 18: Mean absorbance of TEOAE pass and fail results from 250 – 8000 Hz at ambient and peak pressures. Vertical bars denote 95% confidence intervals.

3.4.2 Admittance Phase in neonates who passed or failed a TEOAE test.

To evaluate the effect of frequency on Yφ for neonates who passed or failed the TEOAE test, a mixed model ANOVA (Appendix E.23) was performed with Accuscreen TEOAE results (pass vs. fail) as the between-subject factor and admittance phase across 107 frequency bins as the within-subject factor.

The main effect of Accuscreen TEOAE results (pass vs. fail) was not significant [F(1, 245) = 0.03147, p = 0.85935] indicating that admittance phase was not significantly higher in the Accuscreen TEOAE pass group compared with admittance phase in the Accuscreen TEOAE fail group when the data collapsed across frequency and pressure.

The interaction between admittance phase across 107 frequency bins and Accuscreen TEOAE results (pass vs. fail) was significant [F(106, 25970) = 2.0812, p = 0.0000] but did not

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remain significant after GG correction (Appendix E.24), indicating that admittance phase does

not varies differently between Accuscreen TEOAE pass and Accuscreen TEOAE fail groups.

3.5   Wideband Absorbance (ambient and peak) and Admittance Phase and Effects of

Ethnicity

3.5.1   Wideband Absorbance and Ethnicity (including only neonates who passed NHS

tests)

To evaluate the effect of pressurization method (ambient and peak) and frequency on

WBA for neonates of different ethnicities, a mixed model ANOVA (Appendix E.18) was

performed with ethnicity (Caucasian, FNAM, and Mixed Other Ethnicity) as between-subject

factors and absorbance across 107 frequency bins and pressure (ambient vs. peak) as within-

subject factors.

The main effect of ethnicity (Caucasian, FNAM, and Mixed Other Ethnicity) was

significant [$F(2, 176) = 3.5990$, $p = 0.02938$] indicating that absorbance was significantly

different between the different ethnicities when the data collapsed across frequency and pressure.

The interaction between absorbance across 107 frequency bins, ethnicity (Caucasian,

FNAM, and Mixed Other Ethnicity) and pressure (ambient vs. peak) was not significant after GG

correction (Appendix E.19) , however the interaction between absorbance across 107 frequency

bins and ethnicity (Caucasian, FNAM, and Mixed Other Ethnicity) (Figure 19) was significant

after GG correction [F(212, 18656) = 1.9813, p = 0.0000] indicating that absorbance varies differently between neonates of different ethnicities across frequencies.
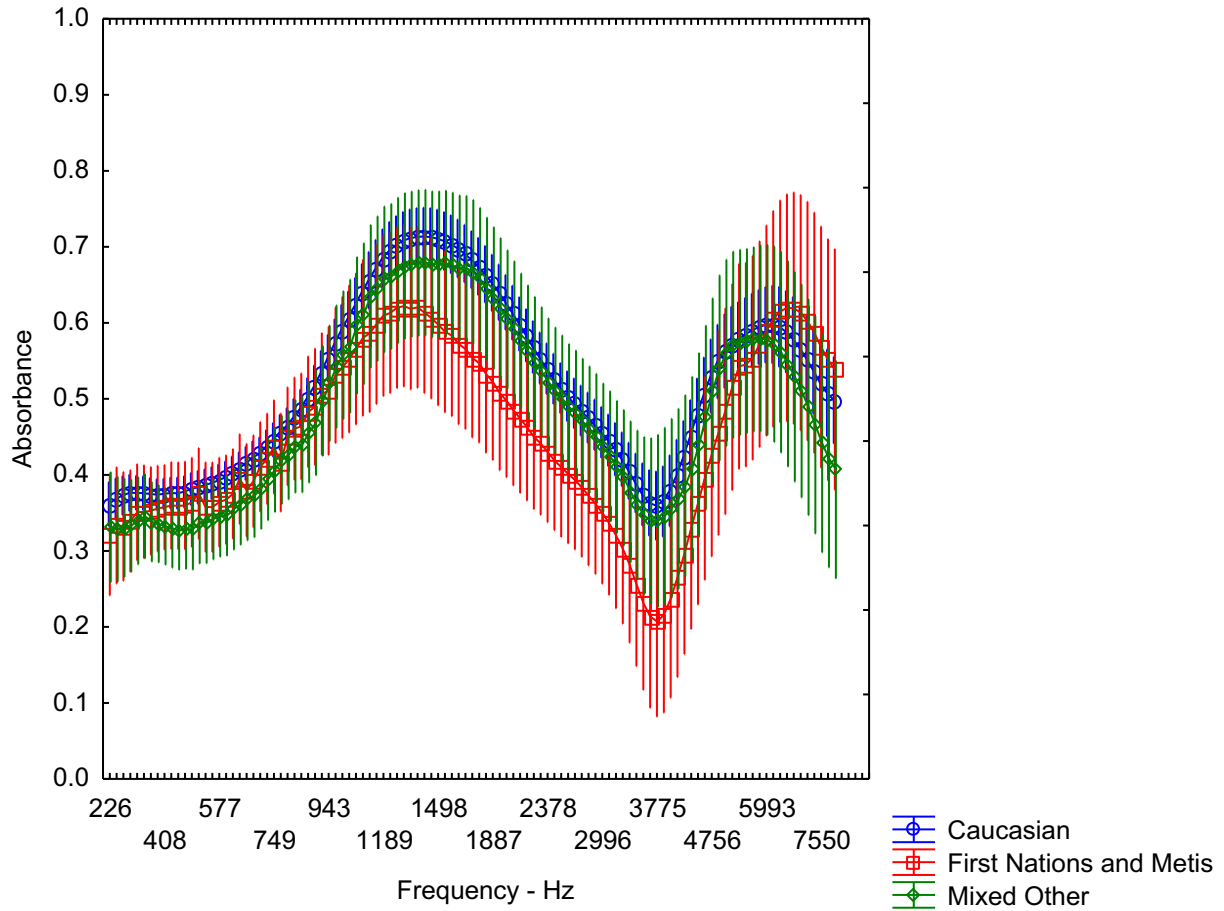
Figure 19: Mean absorbance from 250 – 8000 Hz for neonates of Caucasian, First Nations and Metis, and Other Ethnicities who passed a screening battery. Vertical bars denote 95% confidence intervals.

3.5.2 Admittance Phase and Ethnicity (including only neonates who passed NHS tests)

To evaluate the effect of frequency on Yφ for neonates of different ethnicities, a mixed model ANOVA (Appendix E.20) was performed with ethnicity (Caucasian, First Nations and

Metis, and Mixed Other Ethnicity) as the between-subject factor and admittance phase across 107 frequency bins as the within-subject factor.

The main effect of ethnicity (Caucasian, First Nations and Metis, and Mixed Other Ethnicity) was not significant [$F_{(2, 165)}$ = 0.05137, p = 0.94994] indicating that admittance phase was not significantly higher between ethnicities when the data collapsed across frequency.

The interaction between admittance phase across 107 frequency bins and ethnicity was not significant [$F_{(212, 17490)}$ = 1.0148, p = 0.42780] indicating that admittance phase did not vary differently between neonates of different ethnicities.

Chapter 4: Discussion

The current study sought to examine the addition of Wideband Absorbance (WBA) to a newborn hearing screening protocol of TEOAE's, BBN MEMR and 1000 Hz tympanometry. This addition of WBA at both ambient and TPP were examined in three ways: the ability to differentiate likely conductive hearing loss versus likely normal hearing, the ability to differentiate NHS test pass versus NHS test fail, and the equivalency of WBA results with TEOAE tests. In addition, the study examined the performance of a relatively unstudied measure, Admittance Phase ($Y\varphi$), in the same three tests listed above. Lastly, this study looked at the difference in hearing screening pass and fail rates between neonates of different ethnicities, the prevalence of likely CHL between neonates of different ethnicities, and differences in mean WBA and $Y\varphi$ among neonates of different ethnicities.

4.1 Classification of groups

Four groups of neonates by ethnicity were created based on the ethnicity information obtained consensually at screening. The Caucasian screening group (N = 206 ears), the First Nations and Metis (FNAM) screening group (N = 41 ears), the Mixed Ethnicity Group (N = 47 ears) and the Undeclared Ethnicity Group (N = 80 ears). The Mixed Ethnicity group included neonates whose parents identified as Middle Eastern, Indian, Asian, African, Filipino, Nepalese and Caribbean ethnicities. The undeclared group contained a mix of all ethnicities at unknown ratios. The percentage of FNAM neonates in the Undeclared group may be higher than the percentage of other ethnic groups as the researcher observed that FNAM parents were more likely to decline to offer voluntary ethnic information. This may be because as a group they may be more cautious in divulging ethnicity information for fear of discrimination, or it may be that

this group often had more complicated birthing situations, such as shorter stays in the hospital and complications in birth that required interventions that prevented the researcher from speaking to the parent. These reasons are speculation as no data was collected on this trend and are only the observation of the researcher.

4.2 Newborn hearing screening test pass and fail rates

4.2.1 General trends of NHS pass and fail

In general, our results showed that of all the neonates tested in this study (N = 374 ears), 81.55% passed the screening test battery and 18.45% failed the screening test battery.

The prevalence of permanent childhood hearing impairment is about 1.2 to 5.7 per 1000 births (Aidan, 1999; Bagatto, 2010; Erenberg, 1999; Yoshinaga-Itano, 2003). A very efficient screening program would match this rate and have a theoretical refer rate of about 2% to 6 %. In actuality, fail rates for in-hospital newborn hearing screening range from 5.1% to 30% with an average of 4.8% (NCHAM 2004).

The current study refer rate was 18.45%, much higher than the average of 4.8%. There are many possible reasons for an increased refer rate in this study. First, the screening protocol used in this study is more sensitive to mild hearing losses and transient conductive losses. This extra sensitivity is due to the use of TEOAE which is more sensitive to transient conditions of the external or middle ear (Norton et al., 2000) and to mild hearing loss (Koiyunen et al., 2000, Naeve, 1992; Owens, 1993). Second, A screening test battery that is a loose parallel protocol, such as the one in the current study, will fail/refer a neonate if any of the results are a fail/refer. Resulting in a lower pass rate across all ethnicities as there are more tests to pass. Third, the increased proportion of FNAM neonates, who are more likely to have middle ear pathology,

would have increased the referral rate. Boone et al. (2005) noted that OME may contribute up to 67% of the false positive newborn hearing screenings.

4.2.2 Pass and Fail NHS outcomes by ethnicity

The results of a Z test (Table 7, Appendix E1) showed that the proportion of FNAM neonates who passed the screening test battery (68.29%) was significantly lower than the proportion of Caucasian (86.89%) neonates who passed the screening test battery. As well, the results of a Z test (Table 7, Appendix E2) showed that the proportion of FNAM neonates who failed the screening test battery (31.71%) was significantly higher than the proportion of Caucasian (13.10%) neonates who failed the screening test battery. This is the first study in Canada that has shown that the proportion of FNAM neonates who fail NHS is significantly higher than the proportion of Caucasian neonates who fail NHS.

The number of FNAM neonates who passed the test battery was also lower than the number of Mixed Other Ethnicity (80.85%) and Undeclared Ethnicity (75%) neonates who passed the screening test battery, however, while the pass rate was lower in FNAM neonates in both cases, Z test analysis does not show a significant difference between the FNAM neonates or the Mixed Other ethnicity or Undeclared ethnicity neonates (Table 8-9, Appendices E3-E6).

As the Undeclared Ethnicity group was a mix of neonates of all ethnicities including FNAM neonates, it is expected the screening battery test pass rate of the Undeclared Ethnicity group to be between that of the FNAM and the Caucasian and Mixed Ethnicity group. This proved to be true, although, as stated above, the difference was not significant as per a Z test.

No studies have been undertaken on the pass rates of neonates of different ethnicities in Canada prior to the current study, however Aithal et al. (2014a) found that there was no

significant difference in the number of Australian Aboriginal (AA) (61%) and Caucasian (61%) neonates who passed a test battery of High-Frequency Tympanometry and DPOAE screening tests. Another study from 2008 (Lehmann) found different pass rates for American Aboriginal (90%) and Caucasian (99%) neonates using TEOAE testing.

In the United States, Hunter et al. (2007) screened a cohort of healthy American Indian infants with a median age of 3 weeks old using a DPOAE test. They found that the pass rate was 71.5%, however, their total also included neonates who had incomplete data. They also found that this pass rate was low based on studies in other populations, especially since refer rates decrease after the newborn period due to aeration of the middle ear and decreased vernix in the ear canal (Hunter, 2007).

In the section above, it explains why the overall pass rate across ethnicities is likely to be lower in our study, however, the significantly lower pass rate in FNAM from Caucasian neonates is likely to be due to the increased presence of ME pathology. By looking at the WBA results of neonates of different ethnicities in this study, we can make more conclusions on the status of the middle ear at the time of NHS.

4.3   Likely diagnosis based on the pattern of passed and failed tests

Likely diagnosis was determined by looking at the pattern of the pass and fail for all neonates as per Table 10. Likely diagnosis of conductive pathology was determined if the neonate failed the 1000 Hz Tympanometry test. As conductive pathology masks sensorineural/cochlear pathology and auditory neuropathy pathology in the screening tests, only rates of conductive pathology were analyzed.

The results of a Z test (Table 12, Appendix E7) showed that FNAM neonates had a significantly higher likely diagnosis (92.31% of fail results) of CHL compared to Caucasian neonates (88.89% of fail results). This is the first study in Canada to show that FNAM neonates have a greater likely diagnosis of CHL than Caucasian neonates at birth. This information is essential to understanding the risk factors involved in the pathogenesis of otitis media and conductive hearing loss in FNAM children in Canada.

The proportion of FNAM neonates who had a likely diagnosis of CHL (92.31%) was also higher than the number of Mixed Other Ethnicity (88.89%) and Undeclared Ethnicity (85%) neonates who had a likely diagnosis of CHL. In this case, even though Undeclared Ethnicity neonates were expected to have a rate of likely CHL between that of the Caucasian/Other Ethnicity and the FNAM neonates, the rate of likely CHL in the Undeclared Ethnicity is the lowest at 85%, however the rate of likely sensorineural hearing loss is the highest in the Undeclared Ethnicity neonates at 15%. It is difficult to make conclusions based on the results in the Undeclared Ethnicity group as the distribution of ethnicities in this group is unknown. As well, the Z test analysis (Table 12-14, Appendices E7, E8, E9) does not show a significant difference between the proportion of FNAM neonates with a likely diagnosis of CHL and the proportion of Mixed Other ethnicity or Undeclared ethnicity neonates with a likely diagnosis of CHL.

Although FNAM children have been shown to have greater rates of conductive conditions than children of other ethnicities, as discussed in the introduction, the finding that FNAM neonates have great rates of likely conductive conditions at birth has never before been shown in Canada.

Aithal (2014a) studied pass and fail rates and WBA in neonates in Australia with a screening test battery of DPOAE and HFT and WBA. They did not, however, look at likely diagnosis by the pattern of the pass and fail of the screening test and instead inferred a likely diagnosis of conductive pathology based on lower WBA values. They found that Aboriginal Australian neonates had lower WBA than Caucasian neonates regardless of whether they passed or failed the test battery and concluded that AA had a likely greater prevalence of conductive pathology at birth (Aithal et al., 2014a).

Hunter et al. (2007) tested American Indian (AI) neonates with a DPOAE screening test. If the infants failed the screening they followed up with regular DPOAE, pneumatic otoscopy, and tympanometry tests. Amongst the AI neonates, she found a pass rate of 71.5 % which was higher than in the general population and that there was no significant relationship between OAE pass at birth and risk for recurrent OM diagnosis in the first 2 years of life. However, this study did not compare likely diagnosis at birth as was done in the current study.

4.4   Wideband Absorbance (WBA)

4.4.1   WBA in neonates who passed or failed the Newborn Hearing Screening test battery

When the mean WBA of the neonates (of all ethnicities) who passed the test battery was compared to the mean WBA of the neonates who failed the test battery, it was found that the neonates who failed the screening test battery had a significantly lower WBA than those who passed the test battery. Examining Figure 11, which compares WBA at ambient pressure in neonates who passed the NHS protocols to neonates who failed the NHS test battery, reveals no overlap in the 95th percentile confidence intervals between the 1.0 to 2.0 kHz range. This finding

indicates that this frequency range is likely better at differentiating between neonates who pass and fail the NHS test battery.

These results correlate to results found by Aithal (2014a) where Australian Aboriginal and Caucasian neonates who failed the test battery of HFT and DPOAE had a significantly lower WBA than their counterparts who passed. Aithal (2014a) found that the most significant change was found in the 0.8 to 4 kHz region in the Aboriginal group and across the entire frequency range in the Caucasian group. Both Hunter (2010) and Aithal (2015) have since shown that the best determination of middle ear function is found in the 1.0 to 2.5 kHz range.

The significant difference found in WBA between neonates who failed the test battery and neonates who passed the test battery in the current study shows that neonates who fail the test battery have a significantly lower absorbance in the frequencies important for speech recognition. It is likely that the decreased absorbance in this range is due to the increased mass and resistance of the middle ear caused by OME (Beers et al., 2010; Hunter et al., 2010; Shahnaz, 2010).

4.4.2   Mean WBA in neonates who passed the Newborn Hearing Screening protocol compared to other research.

Figure 20 shows a comparison of the mean WBA at ambient pressure of neonates who passed the NHS protocol in the current study to mean WBA normative values at ambient pressure of neonates who passed a NHS protocol in other studies. The black dashed and solid lines represent the 5th and 95th percentiles for the current study and the red line represents the mean.

The mean WBA pattern for neonates in the current study follows the same pattern as in other studies, with a two-peaked pattern of absorbance. The Sanford and Feeney (2008) study has the highest overall absorbance which is expected as the infants were tested at 4 weeks of age. Longitudinal studies (Hunter, 2016; Shahnaz, 2014) have shown that WBA changes after birth. The Shahnaz (2014) study looked at the how Wideband Reflectance changes in the acoustic properties of the outer and middle ear over the first 6 months of age and found that maturation occurs faster during the first 3 months of life and absorbance decreases at frequencies under 400 Hz and increases at high frequencies over 2000 Hz as a function of age. The 600 to 1600 Hz frequency range showed the least change in absorbance over time. A longitudinal study by Hunter (2016) looked at the change in Wideband Reflectance (WBR) in normal and at-risk infants and also showed that WBR changes as a function of age in the first 6 months; changes over time were most noted in the low frequencies. Due to the significant age effects, Hunter (2016) recommended separate normative references for birth, 1 month, and 6-15 months of age.

The rest of the studies compared in Figure 20 tested neonates who were under 48 hours of age. The Aithal et al. (2017a) studies had a higher WBA in the low frequencies despite being the same age range. A higher WBA in the low frequencies may be due to a poor seal of the probe tip in the ear canal, an example can be seen in Figure 5 of the current paper. The current study used rubber tips with the Titan Interacoustics as did the Aithal (2017a) study. The Shahnaz et al. (2014) study used foam tips (which are cut with scissors to fit the neonate's ear) with the Mimosa Acoustic systems, and the Sanford and Feeney (2008) study used modified (shortened) GSI rubber tips with a Welch Allyn diagnostic middle ear analyzer prototype system. The use of different tips is likely to produce different results in maintaining a proper seal during measurement.

It is also relevant to note that the Titan Interacoustics, Mimosa Acoustic and Welch Allyn systems used different methods of calibration which may result in different results. The Titan calibration method is mentioned in the Methods section of this paper. The Mimosa Acoustic system calibration method involves a four-cavity calibration device and the tolerance region is predetermined by the manufacturer by calculating the tolerance range of the Thevenin (Norton) parameters of the source in four cavities (Shahnaz 2014). The Welch Allyn prototype device was calibrated by calculating the Thevenin source impedance and pressure by modeling the acoustic wave propagation inside two rigid-walled cylindrical calibration tubes and the probe was coupled to the tube using a modified GSI rubber ear tip (Sanford & Feeney, 2008).

Compared to the other studies, the current study has a lower absorbance in the 1-4 kHz range. As the data in the current study included neonates of all ethnicities, and as FNAM neonates who passed the NHS protocol had a lower WBA than neonates of other ethnicities who passed the NHS protocol (Figure 19), the lower overall WBA in the current study may be a reflection of the lower WBA of FNAM neonates found in FNAM neonates who passed the NHS protocol. The lower WBA overall in the current study could also be reflective of the different test NHS protocol used in the different studies. A different NHS test protocol may pass neonates with slightly different levels of middle ear conditions, therefore resulting in different WBA results. The current study and the Shahnaz (2014) study used the same NHS protocol of BBN MEMR, 1 kHz tympanometry, and TEOAE. The Sanford and Feeney (2008) study used a NHS protocol of DPOAE and 1 kHz tympanometry. The Aithal (2017a) study used a NHS protocol of A-ABR, 1 kHz tympanometry and DPOAE.
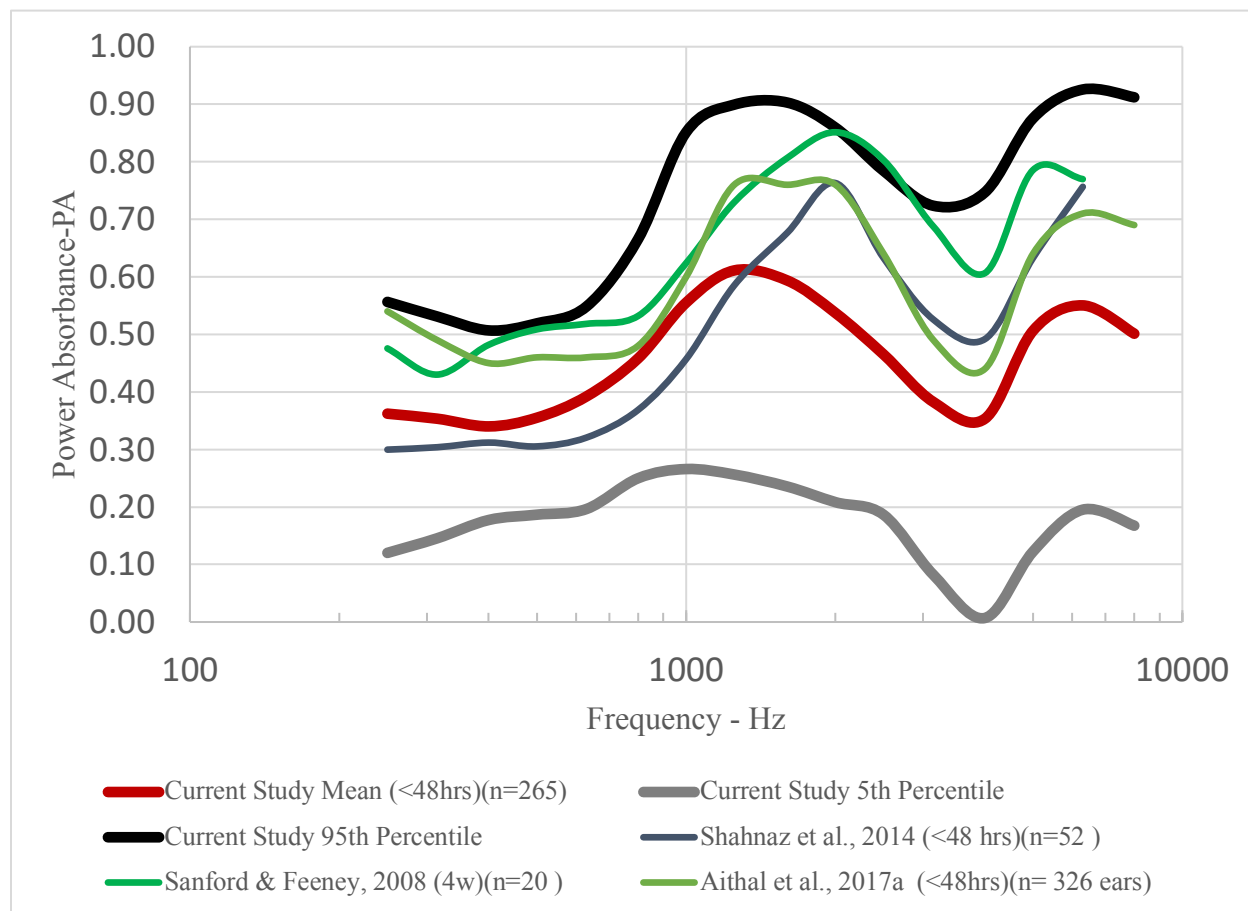
Figure 20: Mean absorbance from 250 – 8000 Hz for all neonates who passed a NHS test battery in the current study compared to mean absorbance values for neonates who passed a NHS test battery determined in other studies.

4.4.3   WBA in neonates with a likely diagnosis of normal hearing versus conductive hearing loss.

WBA was compared between the neonates who had a likely diagnosis (based on NHS test battery results) of conductive hearing loss (CHL) to the mean WBA of the neonates who had a likely diagnosis of normal hearing (NH). ANOVA testing (Appendix E.14) showed that that the neonates who had a likely diagnosis of CHL had a significantly lower WBA. Visual

inspection of the comparison of the WBA means of likely diagnosis of CHL versus likely diagnosis of normal hearing (NH) (Figure 14) shows that the difference is in the 0.8 to 2.0 kHz range as there was no overlap between the 95% confidence intervals. The results show us that WBA is significantly and characteristically different in neonates with a likely diagnosis of CHL versus a likely diagnosis of NH.

4.4.4   Mean WBA in neonates with a likely diagnosis of conductive hearing loss compared to other research.

Figure 21 shows a comparison of the mean WBA at ambient pressure of neonates who had a likely diagnosis of CHL in the current study to mean WBA at ambient pressure of neonates who had a likely diagnosis of CHL in the Aithal et al. (2015) study. The Aithal et al. (2015) study compared Wideband Absorbance measures to DPOAE, TEOAE, AABR and HFT result in neonates. Figure 21 uses the mean WBA from the pass and fail results of the test battery of DPOAE, TEOAE and HFT from the Aithal et al. (2015) study as it is the closest to our own NHS test battery of BBN MEMR, 1000 Hz tympanometry (HFT), and TEOAE in giving us a likely diagnosis of CHL versus NH.

Visual analysis of the graph shows that the results from our study demonstrated the same trends in mean WBA between neonates with a likely diagnosis of CHL versus NH. The mean WBA of neonates with a likely diagnosis of NH in the current study was lower in the1000 to 4000 Hz range than the in the Aithal et al. (2015) study. This trend was commented on in section 4.4.2 where WBA in general in the current study was lower than in other studies. The mean WBA of neonates with a likely diagnosis of CHL from 1000 – 4000 Hz in the current study was higher than in the Aithal et al. (2015) study, however, both show a trend of being lower than the

mean WBA of likely diagnosis of NH in both studies. In general, the mean WBA of likely diagnosis of CHL did not show the characteristic WBA peak pattern found in neonates with a likely diagnosis of NH.
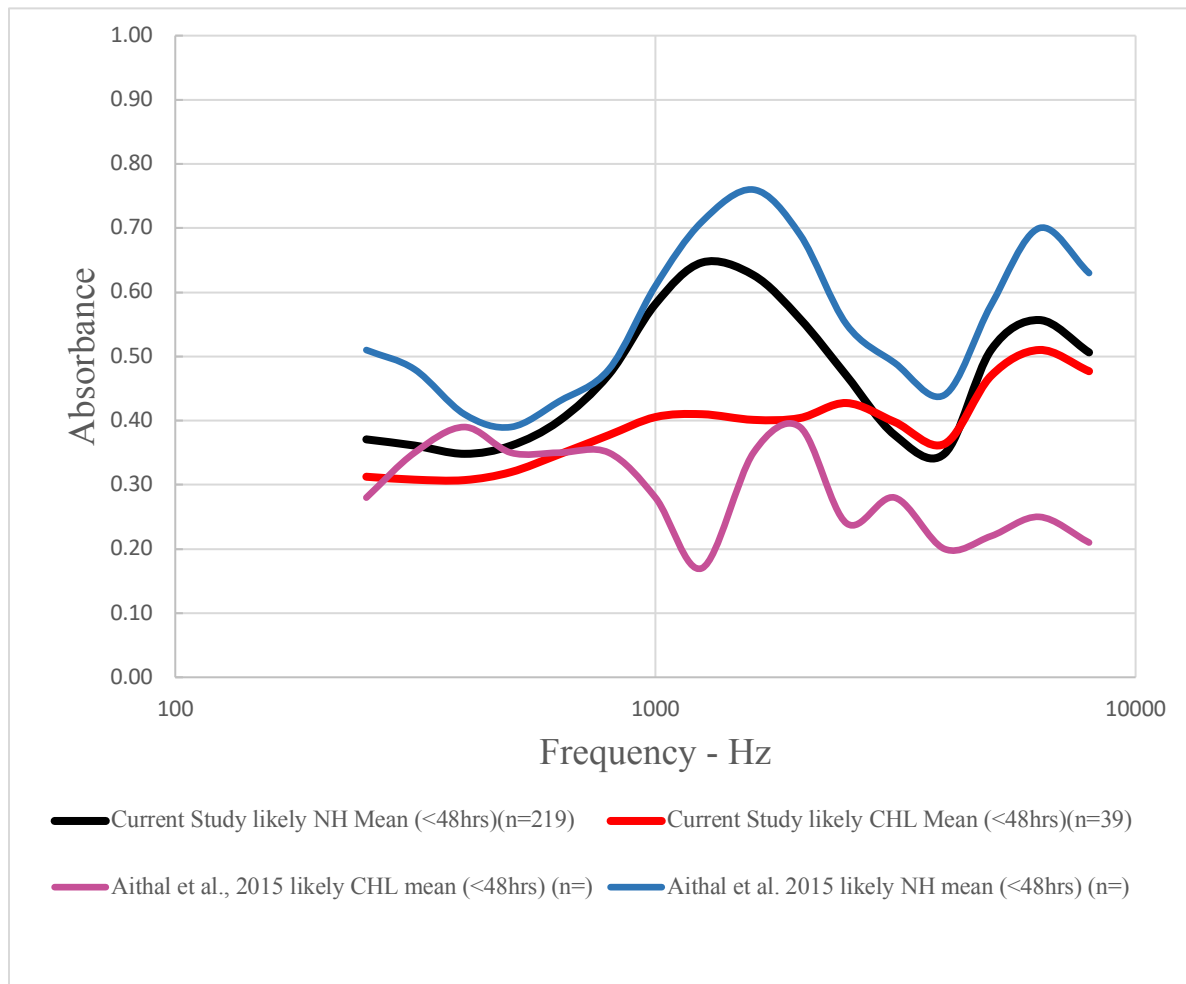
Figure 21: Mean absorbance from 250 – 8000 Hz for all neonates who had a likely diagnosis of CHL and NH in the current study compared to neonates who had a likely diagnosis of CHL and NH in the Aithal et al. 2017b study.

4.4.5 WBA and TEOAE predictability

Many previous studies have compared WBA to single test OAE pass/fail results (DPOAE or TEOAE) to assess the ability of WBA to predict hearing screening failure (Hunter et al., 2010; Keefe & Simmons, 2003; Sanford et al., 2009; Silva, 2013). This analysis was included in the current study to corroborate with previous studies.

When the mean WBA of neonates who received a pass result on the Madsen Accuscreen TEOAE test was compared to the mean WBA of neonates who received a fail/refer result on the Madsen Accuscreen TEOAE test, it was found that neonates who failed the Madsen Accuscreen TEOAE test had a significantly lower WBA than neonates who passed the Madsen Accuscreen TEOAE test. The difference was the highest in the 1.0 to 2.0 kHz region as there was no overlap between the 95% confident interval (Figure 17).

In comparison to previous studies, Sanford et al. (2009) found that the 1-2 kHz region was significant in determining between pass and fail of a DPOAE screen and Hunter et al. (2010) found that the regions involving 2 kHz was significant in determining between a pass and fail of a DPOAE screen which is consistent with the findings of the current study.

4.4.6 Benefits of a screening test battery over a single test

While the difference in the mean WBA was significant between neonates who passed or failed a TEOAE test and was significant in the neonates who passed or failed the screening test battery (which included likely diagnosis of SNHL), the largest significant difference in WBA means was found between neonates who had a likely diagnosis of CHL versus NH. As a likely diagnosis is determined by a screening test battery that can differentiate between NH, CHL,

SNHL, our data shows that a screening test battery may be better at differentiating between neonates with NH and neonates with CHL.

The use of single test for newborn hearing screening has been found to be less than ideal in determining the hearing status (Aithal et al., 2013; Hunter et al., 2010; Kei, 2003; Sanford et al., 2009; Shahnaz, 2008a). A better approach is to use a series of tests that test for different functions. This would include a test for the function of the middle ear, the cochlea, and the auditory nerve (Mazlan, 2012). By using multiple tests the participants can be divided into a group that is to be rescreened for conductive hearing loss and a group that should be sent for immediate diagnostic testing for likely sensorineural hearing loss or auditory neuropathy. The use of multiple tests could streamline the newborn hearing screening testing process thereby decreasing time to diagnosis and intervention. In 2013 Hunter et al. proposed such a diagnostic framework for NHS programs, to determine likely diagnosis.

Aithal et al. (2015) found that when comparing WBA, single screening tests, and combination screening tests against test battery reference standards in the diagnosis of middle ear pathology, that the area under the receiver operating curve (AUROC) was higher for WBA and for a combination of tests than for a single test. This implies that a battery of tests is better for the analysis of middle ear pathology than a single test.

4.4.7   WBA at Tympanometric Peak Pressure (TPP) versus Ambient in all cases

During our data collection, WBA at both ambient and TPP was measured. While ambient WBA has been reported more commonly in the literature, testing at TPP may be beneficial. For example, in 2017 Keefe found that WBR tested at TPP was more accurate (AUROC 5 0.95) than

WBR tested at ambient (AUROC 5 0.88) in classifying adult ears as normal or otosclerotic (Keefe, 2017).

To look at the effect of WBA at TPP versus WBA at ambient, a mean WBA at TPP and ambient pressure was included in the ANOVA analyses for neonates who passed and failed the NHS test battery, for neonates who had a likely diagnosis of CHL and NH, and for neonates who passed or failed a TEOAE test. By looking at the results in Figure 11 for WBA and NHS test battery results, Figure 14 for WBA and likely diagnosis results, and Figure 17 for WBA and TEOAE results, it is seen that in each case a larger difference in WBA was found between the normal condition (pass of screening test battery, pass of TEOAE, and likely NH) and the abnormal condition (fail of screening test battery, fail of TEOAE, and likely CHL) at the TPP pressure than at the ambient pressure. This result implies that testing WBA at TPP may be a better test than WBA at ambient in differentiating between neonates who have likely conductive pathology from neonates who have NH.

Figure 22 compares the difference between the mean WBA from neonates who passed the NHS tests and the mean WBA from neonates who failed the NHS tests at ambient, to the difference between the mean WBA from neonates who passed the NHS tests and the mean WBA from neonates who failed the NHS tests at TPP. From this graph, we can see that in the 1000 – 4000 Hz frequency range the TPP difference is larger, which also indicates that TPP may be better than ambient at differentiating between neonates who have likely conductive pathology from neonates that have normal hearing.
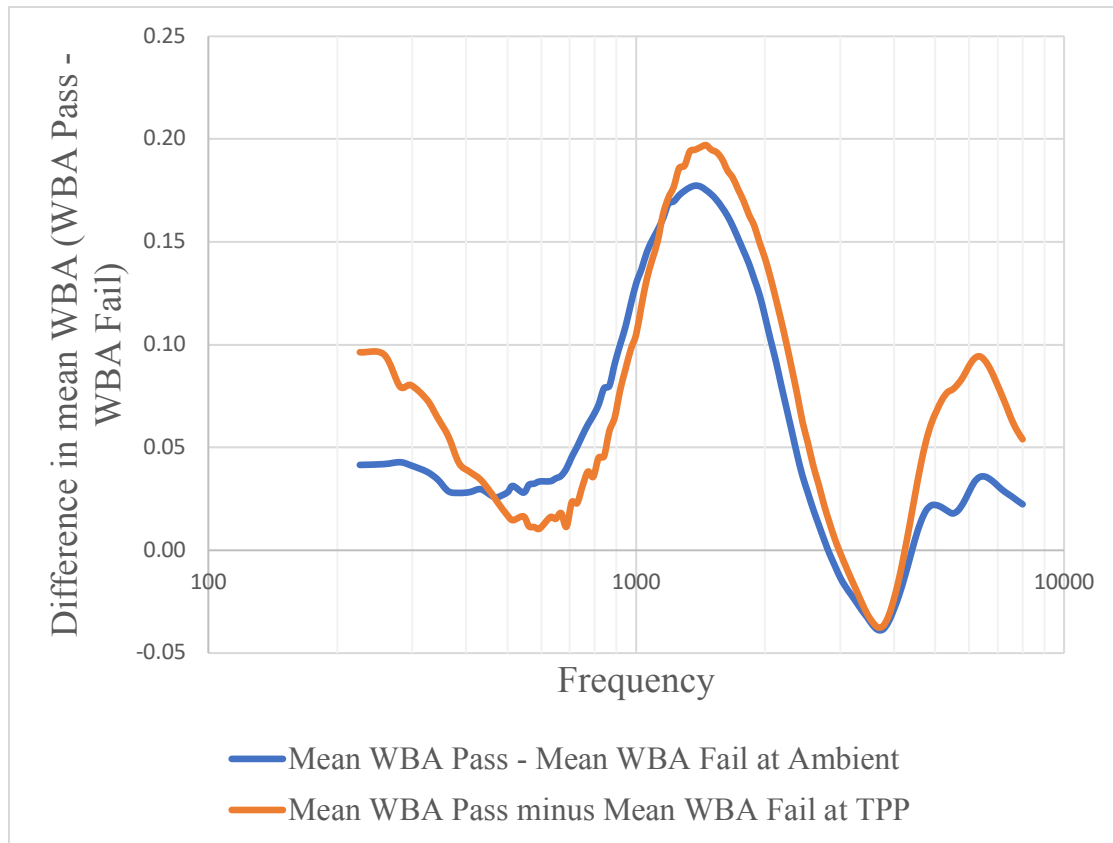
Figure 22: Mean WBA pass minus mean WBA fail at ambient versus mean WBA pass minus mean WBA fail at TPP.

Aithal et al. (2017b) found that the mean WBA ambient was similar to the mean WBA TPP for NH Caucasian infants. Alternatively, Hunter (2016) found that, in NH infants of all ages from birth to 12 months, WBA at ambient pressure was different from WBA at TPP. In the Hunter (2016) study, WBA at ambient was flatter for newborns while WBA at TPP was more rounded with maximal absorbance from 1-4 kHz at TPP and WBA was higher in the low frequencies than at ambient pressure for the neonates. The Hunter (2016) results were similar to those in the current study.

It is expected that, in the case of middle ear pathology, that the middle ear would absorb more sound energy at TPP where the mobility of the eardrum is at its maximum (Feeney &

Sanford, 2012) and that, therefore, testing of WBA at TPP would prove to be better at differentiating between pass/fail and CHL/NH than WBA at ambient. However, there may be complications when testing WBA with pressure. In 2015 Aithal noted that it may be advantageous to use an ambient WBA test because the highly compliant ear canal in newborns could lead to inaccurate results when pressurized for standard immittance testing. Hunter (2016) also noted that the neonatal ear a positive air pressure within the ear canal would tend to open the ear canal wider due to its extremely compliant walls, and a negative air pressure would tend to close the ear canal. Thus, the TPP estimate in the newborn ear may be confounded by ear-canal volume changes or ear-canal wall collapse. Voss (2008) has shown, that even the slightest negative or positive pressure can have a significant impact on WBA, especially in the lower frequencies. Aithal (2017a) found that in healthy young infants, in general, negative ear canal pressures reduced the WBA across the frequency range, while positive ear canal pressures resulted in a reduced WBA from 0.25 to 2 kHz and above 4 kHz with an increase in absorbance between 2-3 kHz at ambient pressure. Therefore, more research is needed to interpret the TPP in newborn ear relative to the task of estimating the air pressure in the middle ear cavity. Aithal (2017a) notes that future research should compare WBA at ambient pressure and WBA at TPP in infants with negative middle ear pressures is to investigate the potential impact of middle ear pressure on WBA patterns.

Data from other studies on ambient versus pressurized WBA results were not available for a graph comparison with the current study.

4.5   Admittance Phase (Yφ)

Yφ is an emerging test of interest in the diagnosis of ME function (Aithal, 2017b) and was recommended as a future area of research in the Eriksholm workshop on wideband absorbance measures of the middle ear (Feeney et al., 2013). Therefore, the Yφ data from our WAI measurement was extracted to see if it would differentiate between normal and abnormal conditions in the previously mentioned three analyses. The Yφ data was only available post data collection for the ambient pressure measure. Manufacturer access to the peak pressure Yφ measurement may provide additional information in the future. The same three measures as used on WBA above were analyzed: the usefulness of mean Yφ in differentiating between neonates who passed a screening battery and those who failed a screening battery, the usefulness of mean Yφ in differentiating between neonates who had a likely diagnosis of NH and neonates who had a likely diagnosis of CHL, and the usefulness of mean Yφ in predicting TEOAE pass/fail results.

Results showed that in two of the analyses, a significant difference in Yφ was found between the normal condition (pass of screening test battery, and likely NH) and the abnormal condition (fail of screening test battery, and likely CHL). Specifically, neonates who had a likely diagnosis of CHL had a significantly higher Yφ measure than neonates who had a likely diagnosis of NH. A visual examination of Figure 16 shows a greater difference in the 2.0 to 2.5 kHz range as seen by a lack of overlap in the 95th confidence interval bars. Neonates who failed the screening test battery had a significantly higher Yφ measure than neonates who passed the screening test battery. A visual examination of Figure 13 shows a greater difference in the 1.8 to 2.3 kHz range as seen by a lack of overlap in the 95th confidence intervals. Neonates who had failed the Accuscreen TEOAE test did not have a significantly higher Yφ measure than neonates who passed the Accuscreen TEOAE test.

In 2017 Aithal conducted a study on normative values for WAI measures in neonates including Yφ measures (Aithal, 2017b). They found that an increased admittance phase (Yφ) indicates increased stiffness and decreased phase indicates increased compliance. Therefore, in the current study the increased Yφ in neonates who had a likely diagnosis of CHL suggests an increased stiffness in the middle ear. The Aithal 2017 study also found that normative admittance Yφ data for healthy Caucasian neonates shows 2 peaks at 0.8 and 4 kHz. This pattern was repeated in our data for normal likely diagnosis and pass screening test battery as is seen in Figure 23 below.
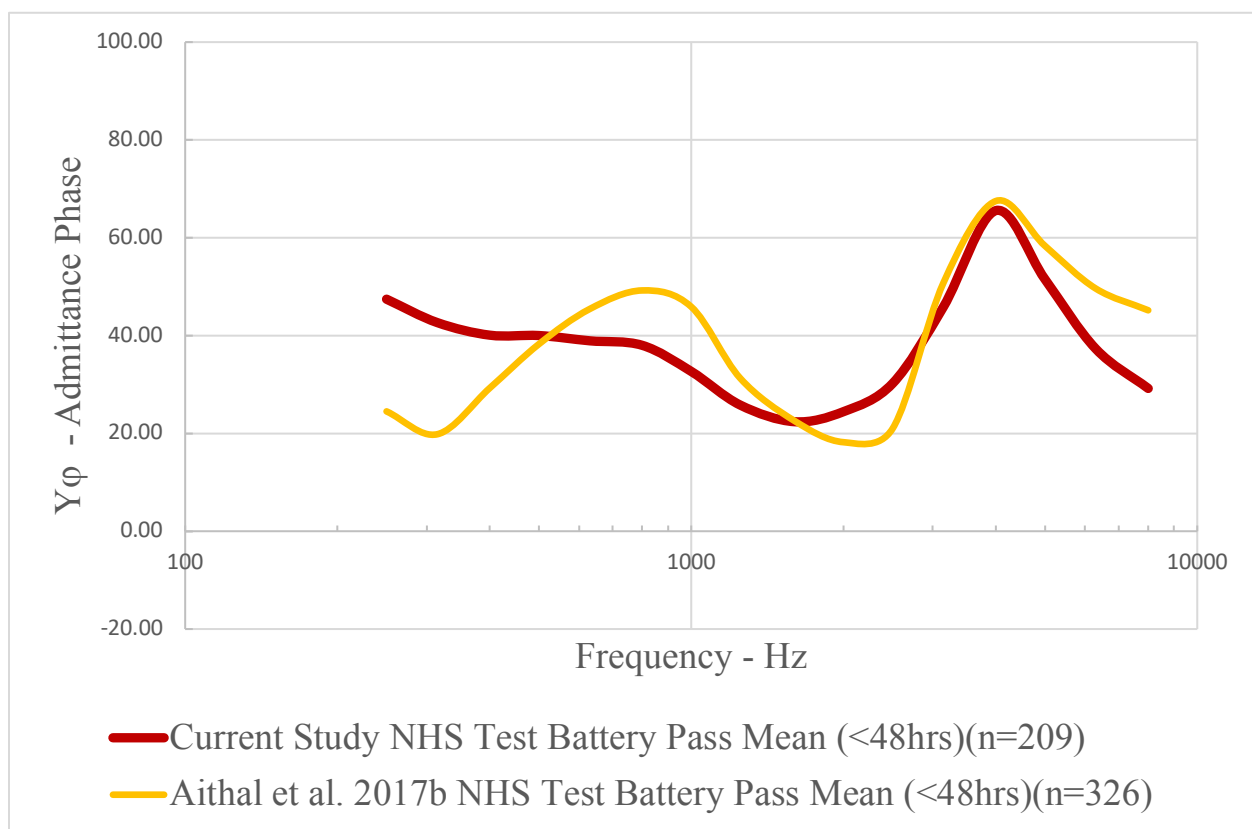
Figure 23: Mean admittance phase from 250 – 8000 Hz for all neonates who passed a NHS test battery in the current study compared to neonates who passed a NHS test battery of A-ABR, DPOAE and HFT in the Aithal et al. (2017b) study.

While there was a difference in the mean Yφ values between the normal conditions and the abnormal conditions, it was not as big of a difference as was found between the mean WBA in each of the three analyses. Therefore, mean WBA may be a better measure in the investigation of middle ear function in neonates. Further statistical AUROC analysis would be needed to compare these measures and to confirm this observation.

As Yφ and WBA can be extracted from the same measurement, it is possible that the combination of the two can provide greater diagnostic accuracy than by using just one without the cost of adding yet another test to the screening test battery. Aithal (2017b) suggested that it may be possible to develop a combination measure incorporating WBA, Yφ to determine middle ear function. Moreover, a study by Ellison et al. (2012) compares WBA, Yφ in 44 children. They found that a predictor combining all the three measures (WBA and Yφ) was the most accurate and most effective in predicting MEE compared with methods currently recommended by clinical guidelines such as pneumatic otoscopy and tympanometry. In light of this, future studies could continue to collect normative data on Yφ and begin to look at the effect of middle ear pathology on Yφ.

4.6   Ethnicity differences

4.6.1   Comparison of WBA across ethnicities who passed, ambient and TPP

In order to look at the differences in absorbance in different ethnicities, the mean WBA between neonates of different ethnicities who passed the screening test battery were compared. It was found that FNAM neonates who passed the screening test battery had a significantly lower mean WBA than both the Caucasian or Other Ethnicity neonates who passed the screening test

battery. Because the Undeclared Ethnicity group was a mixture of all ethnicities and the results would cloud the ability to tell differences between ethnicities, the Undeclared results were removed from the analysis. The current study corroborates Aithal's (2014a) findings in her study of Australian Aboriginal neonates where the mean WBA in Australian Aboriginal neonates who passed a hearing screening test also had a significantly lower mean WBA than the Caucasian neonates.

There was no significant difference in the use of TPP or ambient pressure in the comparison of WBA across ethnicities who passed the screening test battery.

The significantly lower mean WBA found in FNAM neonates who passed the screening test battery compared to neonates of other ethnicities who passed the screening test battery could possibly be explained by two factors. The first explanation is that there may be a difference in the normal anatomy of the middle ear of FNAM neonates compared to neonates of other ethnicities. This anatomical difference could cause a mechano-acoustical difference that lowers the WBA without the presence of middle ear pathology. A study on the differences in WBR in Caucasian and Chinese adults by Shahnaz and Bork (2006) attributed WBA differences between two ethnic groups to the differences in body size. Beers et al. (2010) found that there was a no significant effect of ethnicity in WBR in Caucasian and Chinese children aged five to seven years, but found a significant ethnicity by frequency interaction with Chinese children having lower WBR values over the mid frequency range. A difference in WBA in FNAM neonates due to anatomical differences would be a clear indication that different normative values for WBA testing are essential for neonates of different ethnicities, and specifically for FNAM neonates. Future research is needed to address the question of anatomical differences in the middle ear of neonates of different ethnicities.

The second explanation could be that FNAM neonates may have middle ear pathology that is not found on regular screening tests and does not cause a fail result on the screening test battery, but that is apparent when WBA is used. This failure of the screening test battery could be due to incorrect normative values for FNAM neonates. Aithal (2014a, p. 159) found similar results when using WBA in a newborn hearing screening program with Australian Aborigine neonates and noted that: "It is likely that a greater proportion of FNAM neonates would have failed the screening if a more sensitive test such as WBA was included in the test battery. Further research could consider using a large sample size to evaluate the use of WBA during neonatal hearing screening in FNAM and Caucasian infants."

In the introduction of this paper, the need to determine the prevalence of middle ear conditions at birth in order to understand the risk factors and causal effects of the higher rate of middle ear pathology in FNAM children was discussed. In this study, a greater rate of likely diagnosis of conductive hearing loss at birth was observed in the FNAM children than children of other ethnicities. The low FNAM WBA at birth also suggests that the causal factors may be different than those that occur later in a child's life, such as breastfeeding, daycare attendance, and exposure to smoke. Risk factors that may affect a child's susceptibility to middle ear pathology at birth may include a different anatomy and physiology of the conductive system than other ethnicities, the health of the mother during pregnancy, genetic susceptibility, and birth weight. As none of these metrics were included in this study, it is the hope of the graduate student that further research is conducted into the causal factors of a greater incidence of middle ear pathology in FNAM neonates at birth.

4.6.2 Comparison of Admittance Phase (Yφ) across ethnicities who passed the NHS protocol.

Unlike the difference in Yφ found between the normal and abnormal conditions, there was no significant difference in Yφ for the neonates of different ethnicities who passed the screening test battery. While there are a few studies that have looked at Yφ in slightly older infants (Holte, 1991; Keefe, 1993; Sanford, 2008; Voss, 2016)), there are only a few studies that have looked at Yφ in neonates (Aithal 2017b; Holte, 1991). Neither of these studies looked at the effects of ethnicity on Yφ measurements, therefore there is a lack of research for comparison.

4.7 Clinical Application of WBA and Yφ

The goal of this study was to see if the addition of Wideband Absorbance (WBA) to a newborn hearing screening protocol of TEOAE's, BBN MEMR and 1000 Hz tympanometry could differentiate normal neonate hearing (normal hearing, screening test pass and TEOAE pass) from abnormal states (likely conductive hearing loss, screening test fail, and TEOAE fail).

WBA was significantly lower in neonates with likely CHL who failed the NHS protocol, and in neonates who did not pass the TEOAE protocol than in normal neonates. Moreover, WBA taken at TPP clearly differentiated between normal and abnormal conditions. As no non-invasive gold standard exists for the diagnosis of middle ear pathology in neonates, it is possible that WBA could act as a "surrogate gold standard" for the diagnosis of possible middle ear pathology (Aithal, 2015). WBA can be used as a method to determine likely conductive pathology in a neonate along with the other measures in a screening test protocol, thereby clarifying the cause of a fail in a newborn hearing screening protocol and reducing the time it takes to diagnose neonates with serious sensorineural and conductive pathology. This would reduce the false

positive referrals and could potentially be an excellent choice as an adjunct to a screening protocol. The ease of use and relative speed and accuracy of WBA testing is a clear benefit when testing newborns. With the continued research into developing normative values for WBA (Aithal, 2017b), future WBA equipment could include a standard set of pass/fail criteria that would greater decrease the time and increase the ease of testing.

Admittance phase angle (Yφ) also warrants additional research as a tool in differentiating middle ear pathology from normal hearing neonate ears. While Yφ was not better at differentiating normal ears from ears with middle ear pathology than WBA, a composite measure including Yφ and WBA may be useful and is an area of future interest (Aithal, 2017b).

4.8   Clinical Implications of lower WBA in FNAM neonates

The difference observed in WBA between FNAM neonates and neonates of other ethnicities who passed a screening test battery, could be attributed to anatomical and physiological differences in the FNAM middle ear which may lead to a lowered absorbance, however, this difference has not been researched as of yet. If there is a difference in the normal mechano-acoustic properties of the middle ear of FNAM neonates that causes a difference in WBA, then separate normative values would be required for testing this population

It is also possible that WBA is lower in FNAM neonates due to middle ear pathology that is not identified by a screening test battery. If this is the case then the use of WBA in a screening test protocol could potentially identify FNAM neonates with a likely CHL that was not identified by the original screening test battery. Further research could compare the WBA of FNAM neonates who have been diagnosed with OME using a gold standard test such as tone burst bone and air ABR.

With either of the above scenarios, it is clear that there may be a case for developing normative WBA values for FNAM neonates and that FNAM infants should be monitored more closely for middle ear pathology.

4.9   Challenges encountered during the screening protocol and limitations of the study design

4.9.1   Ward Logistics

Testing in the well-baby newborn ward was conducted while the neonate was settled and with the least interruption of parents and staff as possible. However, the use of a computer to run the Titan Interacoustics handheld device for WBA testing required the researcher to use two separate carts. As only one cart could fit beside a bed or in a room at a time, this required for the first screening tests to be conducted first and then for the second test, the Titan WBA, to be conducted after which required the screeners to enter the room twice. As the newborn ward is a busy place, with doctors, nurse, students, and families competing for time with the new baby, the addition of the second cart likely reduced the number of neonates that were included in the study as sometimes, while the baby was available for the first set of tests, they may not have been available for the second set.

Testing WBA on the second cart also greatly increased the chance that the baby was unsettled during the testing. While every effort was made to test while the baby was sleeping or feeding, often the baby was unsettled after the first set of tests, or the parents or hospital staff needed to perform a duty after the first set of tests and before the second that unsettled the baby. These challenges likely resulted in a smaller number of neonates included in the study.

The requirement of the parents and staff to remain quiet for the length of time during the testing also proved to be a challenge, as the parents were often able to be quiet during the first test but were not able to be quiet during the second due to other children present or due to parental fatigue.

The use of multiple testing machines greatly increased the chance of the neonate not being available for testing, therefore a testing unit that could incorporate all of the screening measures in one unit would be greatly preferable.

4.9.2 Power usage of the computer

The Titan handheld unit was plugged into the computer and the Titan software was run from the computer. As the computer needed to be small to fit on the cart, the battery only allowed for testing approximately 10 participants before the battery of the computer was drained. This meant that either the researcher took a break between participants to charge the battery, or a power outlet was found in each room to plug in the computer from the cart during testing. Power outlets were not available in each room and the time is taken to plug in and unplug the computer added minutes to each visit. As well, plug outlet locations often required moving equipment, such as the bassinet, in the room which increased the demands from the screener and the parents.

4.9.3 Probe Fit for the Titan WBA and the Titan TEOAE

Probe tips for the Titan were supplied by the manufacturer (Interacoustics). The newborn probe tip kit was used and individual probe tips were chosen based on a preliminary external visual check of the size of the neonate's ear. The method of ensuring a tight fit relied on the response of the Titan WBA system. As the WBA test was done first, if the probe did not fit or

was blocked the light indicator on the probe cord would show yellow, and the on-screen indicator would indicate a leak. If the probe did fit the light indicator would show green and the test would go forward. A test that lost a seal after the testing started would be noted later during data analysis as a test with high absorbance in the low frequencies. As well, a visual check of the ear canal volume when testing had finished was used to confirm that a probe seal had taken place.

Many studies have shown that a high absorbance at or below 1 kHz suggests a poor acoustic seal and use a visual check to confirm probe fit (Aithal et al., 2013; Hunter et al., 2010; Merchant, 2010; Shahnaz, 2008a; Vander Werff et al., 2007). In contrast, Keefe (Keefe et al., 2000) used negative equivalent volume to verify the seal only during the recording of results and reported that 13% of neonates had a poor acoustic seal. Voss (2016) proposed a set of criteria for determining when reflectance measures on young babies are corrupted by acoustic leaks, probes against the ear canal or other measurement problems.

Finding a probe tip that worked to get both a good seal for the Titan WBA test and a good seal for the Titan TEOAE test was very difficult, as often a probe tip would work for one but not for the other, which required the changing of the probe tip for each test in each ear, requiring 4 probe tips per infant. The probe tips that worked best for The Titan TEOAE tests were the red rubber (size 3-5 mm) tips and the tips that worked best for the Titan WAI tests were the larger blue rubber (size 4-7 mm) tips. Other studies have mentioned that they experienced problems with probe tips. Merchant (2010) and VanderWerff (2007) compared energy reflectance (ER) measurements between the rubber tip and the foam tips provided for the Titan and found that test-retest differences with the rubber tip were greater than with the foam tip. In our study, only rubber tips were used.

4.9.4   Noise Level on the Ward

Noise levels in individual rooms contributed to the failure and slowing of many of the tests administered by both the hearing screening staff and the researcher. Noise sources included other children in the room, noises from other families in shared rooms, noise from the participant neonate, noise from machines, noise from doctors, nurses and interns, and noise from the ventilation system. It is the researcher's observation that noise from the ventilation was a problem in the failure of the TEOAE tests, especially the Titan TEOAE tests.

In the current study, noise levels were not recorded for the well-baby unit, however, in 2011, Millman recorded noise levels in the RUH NICU ward during her research on a novel hearing screening protocol in neonates (Millman, 2011). C weighting was used to exclude low-frequency rumble and to include frequencies from 100 Hz to 8000 Hz. Millman (2011) found that the mean ambient noise level in the different NICU areas ranged from 55dBC up to 80dBC. While a NICU ward has different noise sources than a well-baby unit, such as the bassinets and monitor alarms, it is important to note that noise is a significant contributing factor to the failure of hearing screening tests.

4.9.5   Titan TEOAE

This study originally intended to use TEAOE from the Titan system as the TEAOE measure in the newborn hearing screening protocol, however, during initial testing, it was evident that the results were not accurate. Many times, the test would not finish, or it would take up to 2 minutes per ear, and it was very difficult to get a seal. As well the Titan TEOAE result often did not agree with the Accuscreen TEOAE result or with the result shown with the other

tests (Figure 24). Therefore, despite having completed Titan TEAOE testing on a large number of subjects, in the end, it was the Accuscreen data that was used in the current study.

The Titan TEOAE may have been more sensitive to noise in the rooms than the WBA was. For the Titan TEOAE test, testing often stopped every few seconds due to noise despite an equivalent amount of noise present in the WBA testing. The Titan TEOAE was also very sensitive to movement of the child, as when the child was moving, even slightly, the test would stop and register as too noisy even if the seal was achieved. The most difficult band to achieve was the 4 kHz band, as often, when the other bands were present, the 4 kHz band was not and the test would result in a refer.

An attempt was made early in testing to change the Titan protocol to reduce the sensitivity to noise, the noise floor was raised and the testing mode switched to 12.5-second method with a maximum testing time of 60 seconds which decreased the number of cases where the TEOAE was not possible on a participant. This change did not, however, cause the TEOAE testing to be successful on enough participants to be considered reliable.

Stimulus

Pa

ms

Probe check

dB SPL   Correlation 99%

kHz

Response waveform

mPa

ms

REFER

TE response

dB SPL

1.3
2.3
-1.0   -5.8   -6.1

kHz

Test summary

Stimulus level	83 dB peSPL
Stimulus type	Non linear click
Stimulus stability	100%
No. of accepted sweeps	798 ✓
No. of rejected sweeps	9
Response reproducibility	2%
Total OAE	-- dB
A & B mean	10.7 dB
A - B diff	13.6 dB
MEP	-1 daPa
No. of detected bands	0 (3)

Band summary

Frequency (kHz)	TE level (dB SPL)	Noise (dB SPL)	SNR	Detected
1.00	3.0	1.7	1.3	
1.50	-0.9	-3.2	2.3	
2.00	-5.2	-4.2	-1.0	( )
3.00	-9.7	-3.9	-5.8	( )
4.00	-9.7	-3.6	-6.1	( )

Figure 24: Typical Titan TEOAE result. This participant had a normal WBA recording as well as a pass on TEOAE Accuscreen.

4.9.6 Access to medical charts

In this study, there was no access to the birth weight, time of birth or gestational age of the infant. Access to this information could greatly increase the results that can be concluded from the study.

4.9.7   Consent

Forms for consent for the first portion of the study were dropped off to the parents before screening began and then were collected when the second cart entered the room. In many instances, the parents did not consent to the data being included in the study due to parental fatigue or disinterest. If testing could have been performed with one machine or on one cart, the burden on the parents would have been less which may have increased the number of parents who participated in the study.

The second portion of the study was intended to be a follow up tone ABR for 10% of the neonates who passed the hearing screening. This was to be conducted one week after the child was born in order to determine the specificity of the screening test. However, despite passing out consent forms and asking every parent if they would return for the test, no parents chose to take part in the second part of the study. It is likely that parents chose not to return because of the difficulty in returning to the hospital for a test that they did not need as their child had already passed the hearing screening. Future research could use additional resources such as recruiting parents who had returned for hearing screening follow ups to take part in a tone ABR once their child had received a pass on hearing screening.

4.9.8   Limitations of the study design

Despite the positive findings of the use of WBA to determine likely CHL in infants in this study, there some limitations on the usefulness of WBA. WBA can determine the amount of sound being absorbed into the middle ear but cannot determine the actual degree of hearing loss caused by the conductive condition. Therefore, while WBA can be a good tool to aid in the

discovery of a middle ear pathology, actual diagnosis of degree of CHL must be performed via tone ABR or by a hearing test in an older infant.

This study made use of research on WBA in Aboriginal populations around the world as a source of research inspiration and to compare with our current findings. While world Aboriginal populations have a similarity in their higher rates of OME and conductive pathology in neonates and children, it is not known how similar in genotype and phenotype these groups would be when compared. The similarity in OME rates in world Aboriginal groups may be due to time since colonization by western cultures, although this is conjecture on the part of the researcher. Therefore, ideal comparisons would be better made in the current study to other Canadian FNAM research which does not exist yet but which will hopefully be present in the future.

The cross-sectional design of this study limited the conclusions that could be inferred from the results. This type of study does not investigate how the results found at birth relate to further development in middle ear pathology. Another limitation in the study design is that there was no easy, noninvasive gold standard method to confirm middle ear pathology in neonates to compare against the WBA results. While the WBA results were compared to both TEAOE tests and to a battery of tests, a gold standard would give us more surety in interpreting the results of the study. Aithal (2015) compared WBA results to a battery of tests and found WBA to be an excellent tool in diagnosing middle ear pathology, however a gold standard test would be preferred.

4.10 Summary and Conclusions

This is the first Canadian study to compare Wideband Absorbance (WBA) at ambient and pressurized conditions and Admittance Phase (Yφ) between neonates of different ethnicities who failed and passed a screening test battery.

1) Wideband Absorbance is an effective test at finding neonates with likely middle ear pathology.

WBA was significantly different between neonates who passed a newborn hearing screening protocol and those who failed a newborn hearing screening protocol, and neonates who have a likely diagnosis of conductive hearing loss versus a likely diagnosis of normal hearing, Therefore, WBA is a feasible measure to identify likely middle ear pathology in neonates.

2) Wideband Absorbance at pressurized conditions is more effective than Wideband Absorbance at ambient in determining middle ear pathology.

The difference in the mean WBA results under pressurization conditions was larger than the difference in the mean WBA results under ambient conditions at determining the difference between pass and fail groups in most tests. This indicates that WBA under pressurized conditions is likely a more effective test to differentiate between neonates with middle ear pathology from those without. The exception was that in looking at mean WBA between ethnicities, the pressurized state reduced the difference between the ethnicities. More research is needed to determine normative values of WBA in neonates under pressurized conditions.

3) Admittance Phase (Yφ) is effective at differentiating pass and fail conditions.

This study found that Yφ is effective at differentiating between pass and fail conditions, although not as effective as WBA. Since Yφ data is measured in the same recording as WBA, an area of future research may be to determine if the combination of Yφ and WBA data may be more effective at determining likely diagnosis in neonates who fail a screening test battery.

4) First Nations and Metis neonates have a higher rate of newborn hearing screening test fail.

Very little data exists on rates of Canadian FNAM newborn hearing screening pass and fail rates. In the current study, a significantly higher proportion of FNAM neonates (32%) failed the screening test battery compared to Caucasian neonates (13%) and neonates of other ethnicities (19%). Screening test fail in these cases was likely to be due to middle ear pathology.

5) Canadian First Nations and Metis neonates have a higher likely diagnosis of middle ear pathology than neonates of other ethnicities.

In looking at the pattern of newborn hearing screening test failure, FNAM neonates had a significantly higher rate (92.3%) of likely conductive pathology compared to Caucasian neonates (88.9%) and neonates of other ethnicities (88.9%).

The lower pass rates and increased likelihood of conductive disease at birth shown in our study further answers the question of risk factors that influence middle ear disorders in FNAM children. As conductive conditions are occurring at a higher rate in FNAM neonates at birth, causal factors can include health in pregnancy, possible C-section rates versus live birth, anatomical differences etc., rather than factors that occur later such as daycare rates and

breastfeeding. More research is needed to compare these children longitudinally and see if the increased rates of OM at birth coincide to increased Chronic OM later.

6) First Nations and Metis neonates have a lower Wideband Absorbance than neonates of other ethnicities.

FNAM neonates who pass the screening test battery had significantly lower WBA than neonates of other ethnicities. Reasons for this lower WBA could include that FNAM neonates have a middle ear pathology at birth that is not recognized by typical newborn hearing screening tests such as TEOAE and 1000 Hz tympanometry. Another explanation could be that there are anatomical and physiological differences in the middle ear that are normal to FNAM children that change the absorbance pattern. More research is needed to develop normative WBA values for FNAM children.

7) FNAM children should be monitored for middle ear pathology

This study shows that FNAM neonates in Canada have a higher rate of newborn hearing screening failure, a higher likely diagnosis of middle ear pathology, and a lower WBA on average than neonates of other ethnicities. These are all clear indices that FNAM children should be monitored more regularly for middle ear pathology in the current early childhood hearing protocols.

4.11 The direction of future research

The amount of data produced by this research exceeded the needs of the study and therefore can be used for future research. Future use of this data could look at gender differences

in WBA and Yφ, could compare OAE outcomes between the Madsen Accuscreen TEOAE results and the Titan TEOAE results, and could compare multifrequency tympanometry results to WBA results. ANOVA analysis was used in this paper as to look at the general trend of differences. Post-hoc analysis was not done on the results as many frequencies were used to get an idea of general trends (107). Future research could collate the data into 1/3 octave frequency bins and run post-hoc analysis.

While comparing WBA to normal and abnormal outcomes gave us an indication of the performance of WBA, it would be preferred to compare the ability of WBA to diagnose middle ear pathology with a true gold standard. Future testing could compare WBA to myringotomy results performed by an ENT physician during procedures that require this intervention such as the insertion of ear tubes for treatment of OM. Future research could also compare WBA tests to tone ABR tests to determine the level of conductive hearing loss.

The current study adds to the general information about the use of pressurized WBA and Yφ measures in testing neonates with and without middle ear pathology, however as most studies have looked at WBA under ambient conditions, more research is needed in developing normative values for this population. Further studies could also look at the combination of WBA and Yφ measures with and without middle ear dysfunction to determine if a combination of WAI tests is better at finding middle ear pathology in neonates.

The cross-sectional design of this study does not allow for the investigation of changes of WBA and Yφ over time. Due to the clearing of fluid from the middle ear in the first few days, it would be beneficial to check referral rates in neonates of different ethnicities a few days after birth. A longitudinal study could look for changes in WBA and Yφ over time and how they related to developmental changes of the middle ear.

Longitudinal studies are needed to determine if lower WBA absorbance in FNAM neonates continues into childhood and if WBA at birth is indicative of future difficulties in speech and learning outcomes. Studies of this sort could then inform educators on the need to develop public education programs and interventions at birth if higher rates of middle ear pathology were found to continue from birth in FNAM children. Socioeconomic status information could be collected to see if the prevalence of OME at birth correlates to SES.

Lastly, it is vital to understand the reasons for the lower WBA in FNAM neonates. Future research could look to see if there are mechano-acoustic differences in the middle ear of FNAM neonates. Studies could also look at FNAM neonates who pass a NHS test and compare a gold standard test to rule our middle ear pathology not found by regular hearing screening protocols. Finally, studies could look at the comparison of BMI or body size in neonates of different ethnicities to WBA results.

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Appendices

Appendix A Invitation Letter

Newborn Hearing Screening Project
A Collaborative Research Project between:
UBC School of Audiology Vancouver Canada,
Royal University Hospital Saskatoon Canada

Invitational Letter for NICU and Well Babies

Project Title:
A Novel Screening Protocol for the Differentiation of Type of Hearing Loss in Neonatal
Intensive Care Unit (NICU) and Well Babies Infants

Principal Investigator:
Dr. Navid Shahnaz
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Dear Parent,

Hearing problems are often invisible to parents because a child with a hearing problem is generally healthy-looking and develops other skills normally during the first year of life. However, listening and language develop very rapidly during the first year of life, therefore, the longer a child has an undetected hearing problem, the more difficult it will be for the child to

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learn to talk normally. This will affect their ability to do well in school and communicate as an adult.

This project is interested in exploring the most efficient method for early identification of the type of hearing the loss in newborns in a timely and cost-effective manner. The School of Audiology & Speech Sciences at the University of British Columbia in Canada, the Royal University Hospital in Saskatoon in Canada, are carrying out a joint research project to improve our ability to distinguish conductive and sensorineural hearing loss in early infancy. Sensorineural hearing loss is a permanent type of hearing loss which is caused by impairment in the inner ear. Conductive hearing loss is a typically a temporary form of hearing loss which, in infants, is most commonly caused by middle ear fluid associated with middle ear infection (otitis media). When present early in life, each of these types of hearing loss can have serious consequences for the health and development of your child. Distinguishing conductive hearing loss from sensorineural hearing loss is vital since the course of medical and hearing intervention is quite different for these two types of hearing problems. The good news is that many of the negative effects of these hearing problems can be prevented or substantially lessened if intervention comes early. Therefore, the hearing loss must be detected and correctly diagnosed as early as possible for an intervention to be most successful. Presently, there is a need to improve our ability to distinguish between types of hearing the loss in newborn infants that are part of the neonatal intensive care unit (NICU) and well-baby nurseries.

It is also within the purpose of this study to determine the prevalence of different types of hearing loss (conductive versus sensorineural hearing loss) in the newborns of different ethnic groups. It has been identified that some ethnic groups have a higher incidence of conductive hearing loss due to middle ear infection which can be attributed to environmental factors (such as breastfeeding, daycare passive smoking) or to genetic, developmental, and prenatal exposure factors.

If you agree to be part of the project, your baby's test results from the routine hearing screening program that is currently being administered to all NICU and well babies and will be collected for this study. All of these tests are part of a routine hearing screening program that is currently being conducted on NICU at Royal University Hospital. The outcome of these tests will be compared to each other to explore the most efficient method for early identification of the type of hearing the loss in neonates in a more timely and cost-effective manner. All the screening is done in natural sleep or when the baby is calm and awake. There are no known risks with these procedures. The screening does not hurt your baby in any way. 10% of newborns who pass initial hearing screening will be asked to return for a diagnostic ABR test. If you consent to this test, it will be beyond the normal time commitment that you would have had if you had not decided to be a part of this research.

By including your baby's screening results in the current study and for later diagnostic follow-up, this will provide more information regarding the efficacy of the screening protocol in terms of its ability for the early identification of the type of hearing the loss in neonates. It will also help us to determine the prevalence of different type of hearing loss among different ethnic groups

Thank you for considering participation in this research project. If you are interested in participating, please inform the NICU or well babies nursing staff or contact, any of the investigators listed above for more information at any time.

_____
Dr. Charlotte Douglas, Local Principal Investigator

Newborn Hearing Screening Project
A Collaborative Research Project between:
UBC School of Audiology Vancouver Canada,
Royal University Hospital Saskatoon Canada

Consent Form for NICU and Well Babies

Project Title:
Investigating the Screening Outcome for a Novel Hearing Screening Protocol in Neonatal
Intensive Care Unit (NICU) and Well Babies Infants

Principal Investigator:
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Associate Professor,
School of Audiology & Speech Sciences
University of British Columbia

Co-investigators:

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University of Saskatchewan
Faculty of Surgery,
Otolaryngology, Saskatoon SK

Introduction:
Your baby is being invited to take part in this study which is investigating hearing and
middle-ear status of babies in the Neonatal Intensive Care Unit (NICU) nurseries and well-baby
units (regular neonatal unit). The procedure explained in this consent form is already a standard

protocol for screening the hearing of the neonatal intensive care unit (NICU) and well babies at Royal University Hospital the Royal University Hospital in Saskatoon in Canada.

Your participation is voluntary. It is up to you to decide whether or not you wish to take part. If you wish to participate, you will be asked to sign this form. If you do decide to take part in this study, you are still free to withdraw at any time and without giving any reasons for your decision.

If you do not wish to participate, you will not lose the benefit of medical care to which you are entitled or are presently receiving. It will not affect your relationship with the researchers or your doctors.

Please take the time to read the following information carefully. You can ask the researcher to explain any words or information that you do not clearly understand. You may ask as many questions as you need. Please feel free to discuss this with your family, friends, or family physician before you decide.

Investigators:

This study is being conducted by Dr. Charlotte Douglas and Dr. Nael Mustafa from the University of Saskatchewan, and Dr. Navid Shahnaz and Lareina Abbott from the University of British Columbia. The researchers are not being paid to conduct this research study.

Eligibility:

Your baby can participate in this study if they are between the chronological ages of 0 to 120 days. To be eligible, you must have undergone the 3 or 4 standard hearing procedures at the Royal University Hospital in Saskatoon that were conducted as per your standard of care. We estimate that we will include 1000 babies in this study.

Purpose:

Your baby has been invited to participate in this research project because we are studying a method of hearing screening in newborn infants that are part of the neonatal intensive care unit (NICU) and well babies. Our objective is to improve our ability to distinguish between conductive and sensorineural hearing loss. Sensorineural hearing loss is a permanent type of hearing loss which is caused by impairment in the inner ear. Conductive hearing loss is typically a temporary form of hearing loss which, in infants, is most commonly caused by middle ear fluid associated with middle ear infection (otitis media). When present early in life, each of these types of hearing loss can have serious consequences for the health and development of your baby.

Current newborn hearing screening protocols are designed to be quick and cost effective and therefore a newborn receives a "pass" if there are no concerns with hearing or a "refer" if there is either a sensorineural (permanent), or a conductive (permanent or transient) hearing loss. If your newborn receives a "refer" result they will be sent for further tests to determine the cause of a "refer". Often a "refer" is the result of normal fluid in the middle ear of the newborn. In our study, we will collect more information than just a "pass" or a "refer" on initial screening. The thorough analysis of the data can give a clearer picture if the "refer" result is due to fluid in the middle ear or a more permanent sensorineural loss, although it takes longer to analyze for the tester later. This increased information can be used in the future to streamline newborn hearing screening so that we can find a quick and easy way to tell the cause of a "refer" result at the time of screening which will lead to faster intervention.

Distinguishing conductive hearing loss from sensorineural hearing loss is vital since the course of medical and hearing intervention is quite different for these two types of hearing problems. The good news is that many of the negative effects of these hearing problems can be prevented or substantially lessened if intervention comes early. Therefore, the hearing loss must be detected and correctly diagnosed as early as possible for an intervention to be most successful.

It is also within the purpose of this study to determine the prevalence of different types of hearing loss (conductive versus sensorineural hearing loss) in different ethnic groups. It has been identified that some ethnic groups have a higher incidence of conductive hearing loss due to middle ear infection (Otitis Media-OM), which can be attributed to environmental factors (such as breastfeeding, daycare passive smoking) or to genetic, developmental, and prenatal exposure factors. By determining which ethnic groups have a higher prevalence of hearing loss, this may assist in the allocation of resources and educational opportunities to address a specific group's unmet needs.

If you agree for your baby to participate in the project, results from his/her routine hearing screening and later follow-up (standard of care re-screening or diagnostic Auditory Brainstem Response test), at Royal University Hospital in Saskatoon Canada will be included in the current study. Each of the tests used in the screening protocol is commonly used in infants and young children for the detection of middle ear problems and assessment of hearing.

Right to Withdraw:

Your baby's participation in this study is voluntary. If you would not like to take part, your care will continue normally and they will still have the routine hearing screening. No reason needs to be given to withdraw from this study or to refuse to consent to this study. If you choose for your baby to be a participant, you may withdraw from the study at any time and no reason needs to be given to withdraw from this study. Withdrawal will not change your baby's care. You may withdraw from the study until the data is published, at which point it will no longer be possible to withdraw. Data from the study will be destroyed 5 years after the last publication using the data. To withdraw from the study please contact the "Investigators" listed in the paragraph above.

<u>Study Procedures</u>:
If you choose to participate in this study, results from your routine hearing screening and later diagnostic follow-up (if any) at Royal University Hospital in Saskatoon Canada will be included in the current study for further data analysis. Pass/Refer information on hearing screening is automatically communicated to your family doctor as part of the newborn hearing screening protocol.

The results of the following standard screening tests will be used for this research study:
    1) Transient-evoked otoacoustic emissions (TEOAE)
    2) Wideband tympanometry (WBT)
    3) Broadband Noise (BBN) acoustic stapedial reflex at 1 kHz probe tone
frequency
    4) Automated auditory brainstem response (AABR) in some babies as it may be deemed necessary by the hearing screening program

We are not asking you to devote any additional time beyond the time that is required to conduct the standard of care tests; however, we would like to ask some participants (approximately 10%), who passed the hearing screening to come back for another diagnostic test. These participants will be selected at random. This would be an additional time commitment beyond your standard of care, however should you pass the hearing screening and be selected for a diagnostic follow-up, a secondary consent form will be provided to you which outlines this portion of the study. If you agree to participate, you will undergo a diagnostic ABR test. This is a standard of care test that is normally conducted when a baby does not pass the screening program. If you choose not to participate in the secondary testing, this will not affect your ability to participate in the main/current portion of the study.

The outcome of these tests will be compared to each other to explore the most efficient method for early identification of the type of hearing the loss in neonates in a more timely and cost-effective manner.

Advantages:

There is a benefit of having useful findings shared with your family doctor. It is hoped that the information obtained will help refine our ability to distinguish between conductive and sensorineural hearing loss, and hence provide early detection and treatment. In the long run, the results may improve the accuracy and earlier detection and treatment of specific types of hearing loss in newborns.

Disadvantages:

We are not asking your baby to have any additional tests beyond the tests that are required to conduct standard hearing screening test protocol that is currently being conducted on NICU babies at Royal University Hospital in Canada. We are simply comparing the outcome of these tests against each other to explore the most efficient method.

10% of participants who receive a "pass" result will be selected to have secondary testing beyond standard of care which involves an extra time commitment.

The main risk of study participation is the inadvertent release of your personal health information. The researchers have taken measures to protect the privacy of your information and this risk is considered very small.

How your baby's information will be used:

Your baby's test results from the four screening measures will be compared to each other. We will use this information to find out which of these measures are better for distinguishing between conductive and sensorineural hearing loss at the time of hearing screening.

Results of the hearing screening will be shared with you at the time of screening, and results of any subsequent tests will be shared with you at the time of the test. Results of the study will be shared upon request in the form of publication.

Confidentiality:

In Saskatchewan, the Health Information Protection Act (HIPA) defines how the privacy of your personal health information must be maintained so that your privacy will be respected. Your baby's identity will be coded using a code known only to the researchers, and all information that is collected from your baby will remain confidential. Only group results or coded individual results will be given in any reports about the study. Coded results only (no personal information) will be kept in computer files on a password-protected hard drive. Your baby's confidentiality will be respected. No information that discloses your baby's identity will be released or published without your specific consent to the disclosure. However, research records and medical records identifying your baby may be inspected in the presence of the Investigator or his designate by the University of Saskatchewan Research Ethics Board and the University of British Columbia Research Ethics Board for the purpose of monitoring the research. However, no records which identify your child by name or initials will be allowed to leave the Investigators' offices.

At the end of each screening day, the data (the result of screening outcome on OAE, WBT, and BBASR along with the age of the baby-gestational age) will be taken from the screening devices, and transferred to a password-protected computer into an encrypted database via a password protected USB device.   The data will be transferred to the middle ear lab at UBC by physically transporting the password protected and encrypted USB device to UBC. For the duration of the retention period the data will be stored at UBC.

Compensation for Injury:
Signing this consent form in no way limits or restricts your or your child's legal rights against the investigators, or anyone else.

Consent:
By signing this document, I am confirming that:
- I have read the information in this consent form.
- I understand the purpose and procedures and the possible risks and benefits of the study.
- I was given sufficient time to think about it.
- I had the opportunity to ask questions and have received satisfactory answers.
- I am free to withdraw from this study at any time for any reason and the decision to stop taking part will not affect my future medical care.
- I give permission for the use and disclosure of my de-identifiable personal health information collected for the research purposes described in this form.
- I give permission for the access of my identifiable personal health information for the research purposes described in this form.
- I understand that by signing this document I do not waive any of my legal rights.
- I understand I will be given a signed and dated copy of this consent form.

If I have any questions or desire further information with respect to this study, I may contact Navid Shahnaz at 604-822-5953 or Charlotte Douglas at 306-655-1327. If I have any concerns about my baby's treatment or rights as a research subject, I may contact the Research Participant Complaint Line at the Office of Research Ethics at the University of British

Columbia, at 604-822-8598 or contact the Chair of the University of Saskatchewan Research Ethics Board, at 306-966-2975 (out of town calls 1-888-966-2975).
I will receive a signed and dated copy of this consent form for my records.

_____   _____
Parent signature   Date

_____
Parent name (please print)

_____   _____
Signature of Principal Investigator/ co-investigator   Date

_____   _____
Name of principal/co-investigator (print)   Date

Appendix C Consent Form #2

Newborn Hearing Screening Project
A Collaborative Research Project between:
UBC School of Audiology Vancouver Canada,
Royal University Hospital Saskatoon Canada

<u>**Consent Form for NICU and Well Babies –Secondary Consent Form**</u>

Project Title:
Investigating the Screening Outcome for a Novel Hearing Screening Protocol in Neonatal Intensive Care
Unit (NICU) and Well Babies Infants

Principal Investigator:
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Reg SK
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Royal University Hospital
Saskatoon, SK

Shoman, Nael Mustafa, MD.
Clinical Assistant Professor
University of Saskatchewan Faculty
of Surgery, Otolaryngology,
Saskatoon SK

The words "you" and "your" used throughout this document will refer to your baby.

<u>Introduction</u>:
You are being invited to take part in this study which is investigating hearing and middle-ear
status of babies in the Neonatal Intensive Care Unit (NICU) nurseries and well babies. You are being
invited to participate in this research study because you passed the hearing screening that was conducted
as part of your standard of care. The procedure explained in this consent form is already a standard
protocol for screening the hearing of the neonatal intensive care unit (NICU) and well babies at Royal
University Hospital the Royal University Hospital in Saskatoon in Canada.

Your participation is voluntary. It is up to you to decide whether or not you wish to take part. If you wish to participate, you will be asked to sign this form. If you do decide to take part in this study, you are still free to withdraw at any time and without giving any reasons for your decision.

If you do not wish to participate, you will not lose the benefit of medical care to which you are entitled or are presently receiving. It will not affect your relationship with the researchers or your doctors.

Please take time to read the following information carefully. You can ask the researcher to explain any words or information that you do not clearly understand. You may ask as many questions as you need. Please feel free to discuss this with your family, friends or family physician before you decide.

Purpose:

You have been invited to participate in this research project because we are studying the accuracy of the hearing screening program. The sensitivity of the current protocol (ability of the screening protocol to identify the hearing loss correctly) is currently embedded in the screening program as a diagnostic ABR. However, there are no measures to assess the accuracy of the screening program in terms of identifying the normal hearing babies (specificity) of the screening program. In order to address this shortcoming, 10% of the babies who pass the screening program will be asked to come back to undergo the diagnostic ABR to determine the specificity of the screening program.

If you agree to participate in the project, results from your routine hearing screening and diagnostic follow-up at Royal University Hospital in Saskatoon Canada will be included in the current study.

Your participation in this study is voluntary. If you do not take part, your care will continue normally. No reason needs to be given to withdraw from this study or to refuse to consent to this study. If you choose to be a subject, you may withdraw from the study at any time and no reason needs to be given to withdraw from this study. Withdrawal will not change your care.

Study Procedures:

You have already passed his/her routine hearing screening at Royal University Hospital in Saskatoon Canada. You have been randomly selected to undergo a diagnostic hearing test (ABR) that is currently being done only for those babies who are referred on the hearing screening program. This is done to determine how well the hearing screening program can accurately identify normal hearing babies. The diagnostic hearing test (ABR) does not pose any risk or danger to your babies hearing and is being done to further corroborate the result of the hearing screening test. This would be an additional time commitment beyond your child standard of care. Diagnostic ABR is the gold standard diagnostic procedure to determine newborn hearing loss. It is performed while an infant is sleeping and measures brain responses to sound using non-invasive electrodes. It requires 30 to 90 minutes of time depending on the how long the baby sleeps and on the status of hearing.

As the diagnostic ABR test gives us an indication of level and type of hearing loss, this test will be compared to your initial screening results to look at the accuracy of the initial screening.

Advantages:

Diagnostic ABR gives specific information as to the type and level of hearing loss. Therefore this test can either serve as a second, more detailed confirmation that hearing is normal, or can catch a hearing loss that was missed (however unlikely) at initial hearing screening. This test can also catch a hearing loss that develops after the initial hearing screening occurs.

It is hoped that the information obtained will help refine and improve the accuracy of early detection and treatment of specific types of hearing the loss in newborns.

You may or may not benefit from this additional testing.

Disadvantages:

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An additional time commitment beyond the standard of care is required. We are simply verifying the outcome of your hearing screening test. The main risk of study participation is the inadvertent release of your personal health information. The researchers have taken measures to protect the privacy of your information and this risk is considered very small.

How your information will be used:

The results from the ABR test will be compared with the screening measures to further corroborate the result of the initial screening test.   The results will be shared with you at the end of the test and with your doctor as per standard of care hearing screening protocols. If the ABR test results differ with the initial screening results you will treated according to hearing loss standard of care and be referred to an ENT physician (Dr. Nael Shoman), for follow up and further diagnosis.

Right to Withdraw:

Your participation in this study is voluntary. If you would not like to take part, your care will continue normally and they will still have the routine hearing screening. No reason needs to be given to withdraw from this study or to refuse to consent to this study. If you choose not to be a participant, you may withdraw from the study at any time and no reason needs to be given to withdraw from this study. Withdrawal will not change your care. You may withdraw from the study until the data is published, at which point it will no longer be possible to withdraw. Data from the study will be destroyed 5 years after the last publication using the data. To withdraw from the study please contact the "Investigators" listed at the beginning of this document.

Confidentiality:

In Saskatchewan, the Health Information Protection Act (HIPA) defines how the privacy of your personal health information must be maintained so that your privacy will be respected. Your identity will be coded using a code known only to the researchers, and all information that is collected from you will remain confidential. Only group results or coded individual results will be given in any reports about the study. Coded results only (no personal information) will be kept in computer files on a password-protected hard drive. Your confidentiality will be respected. No information that discloses your identity will be released or published without your specific consent to the disclosure. However, research records and medical records identifying you may be inspected in the presence of the Investigator or his designate by the UBC Research Ethics Board and the University of Saskatchewan Research Ethics Board for the purpose of monitoring the research. However, no records which identify you by name or initials will be allowed to leave the Investigators' offices.

Compensation for Injury:
Signing this consent form in no way limits or restricts your or your child's legal rights against the investigators, or anyone else.

Consent:

By signing this document, I am confirming that:

- I have read the information in this consent form.
- I understand the purpose and procedures and the possible risks and benefits of the study.
- I was given sufficient time to think about it.
- I had the opportunity to ask questions and have received satisfactory answers.
- I am free to withdraw from this study at any time for any reason and the decision to stop taking part will not affect my future medical care.
- I give permission for the use and disclosure of my de-identified personal health information collected for the research purposes described in this form.
- I give permission for the access of my identifiable personal health information for the research purposes described in this form.
- I understand that by signing this document I do not waive any of my legal rights.
- I understand I will be given a signed and dated copy of this consent form.

If I have any questions or desire further information with respect to this study, I may contact Navid Shahnaz at 604-822-5953 or Charlotte Douglas at 306-655-1327. If I have any concerns about my baby's treatment or rights as a research subject, I may contact the Research Participant Complaint Line at the Office of Research Ethics at the University of British Columbia, at 604-822-8598 or the Chair of the University of Saskatchewan Research Ethics Board, at 306-966-2975 (out of town calls 1-888-966-2975). I will receive a signed and dated copy of this consent form for my records.

_____   _____
Parent signature   Date

_____
Parent name (please print)

_____   _____
Signature of Principal Investigator/ co-investigator   Date

_____   _____
Name of principal/co-investigator (print)   Date

Appendix D Data Collection Sheets

Newborn Hearing Screening Project

A Collaborative Research Project between UBC School of Audiology, Vancouver, Canada

and Royal University Hospital, Saskatoon, Canada

Room	Patient #	Gender	R/L	Consent	Tympp	TE Screen	TE Titan	BBR P/A	Ethnicity	Notes
	NSP-									
	NSP-									
	NSP-										
	NSP-									
	NSP-									
	NSP-									
	NSP-									
	NSP-									
	NSP-									
	NSP-									
	NSP-									
	NSP-									
	NSP-									
	NSP-									

Appendix E Statistical Analysis

E.1   Z test for evaluating the significant difference in proportions between FNAM and Caucasian neonate ears that passed

in a test battery of Accuscreen TEOAE, 1 kHz tympanometry, and BBN MEMR.

Z Test for Two Proportions

Successes in Group 1	179
Sample Size Group 1	206
Proportion Group 1	0.868932039
Successes in Group 2	28
Sample Size Group 2	41
Proportion Group 2	0.682926829
Average Proportion	0.83805668
Difference in Two Proportions	0.18600521
Hypothesized Difference	0
α	0.01
Z	2.952459539
Two-Tailed Test	
Lower Critical Value	-2.575829304
Upper Critical value	2.575829304
p-value	0.003152534
Decision	Reject
One-tailed Test (Lower)	
Lower Critical Value	-2.326347874
p-value	0.998423733
Decision	Do not reject
One-Tailed test (Upper)	
Upper Critical Value	2.326347874
p-value	0.001576267
Decision	Reject

E.2   Z test for evaluating the significant difference in proportions between FNAM and Caucasian neonate ears that failed in a test battery of Accuscreen TEOAE, 1 kHz tympanometry, and BBN MEMR.

Z Test for Two Proportions

Successes in Group 1	27
Sample Size Group 1	206
Proportion Group 1	0.131067961
Successes in Group 2	13
Sample Size Group 2	41
Proportion Group 2	0.317073171
Average Proportion	0.16194332
Difference in Two Proportions	-0.18600521
Hypothesized Difference	0
α	0.01
Z	-2.952459539
Two-Tailed Test	
Lower Critical Value	-2.575829304
Upper Critical value	2.575829304
p-value	0.003152534
Decision	Reject
One-tailed Test (Lower)	
Lower Critical Value	-2.326347874
p-value	0.001576267
Decision	Reject
One-Tailed test (Upper)	
Upper Critical Value	2.326347874
p-value	0.998423733
Decision	Do not reject

E.3   Z test for evaluating the significant difference in proportions between FNAM and Mixed Other ethnicity neonate ears that passed in a test battery of Accuscreen TEOAE, 1 kHz tympanometry, and BBN MEMR.

Z Test for Two Proportions+C22CA1:C23

Successes in Group 1	38
Sample Size Group 1	47
Proportion Group 1	0.808510638
Successes in Group 2	28
Sample Size Group 2	41
Proportion Group 2	0.682926829
Average Proportion	0.75
Difference in Two Proportions	0.125583809
Hypothesized Difference	0
α	0.01
Z	1.357164642
Two-Tailed Test	
Lower Critical Value	-2.575829304
Upper Critical value	2.575829304
p-value	0.174728903
Decision	Do not reject
One-tailed Test (Lower)	
Lower Critical Value	-2.326347874
p-value	0.912635549
Decision	Do not reject
One-Tailed test (Upper)	
Upper Critical Value	2.326347874
p-value	0.087364451
Decision	Do not reject

E.4 Z test for evaluating the significant difference in proportions between FNAM and Mixed Other ethnicity neonate ears that failed in a test battery of Accuscreen TEOAE, 1 kHz tympanometry, and BBN MEMR.

Z Test for Two Proportions

Successes in Group 1	9
Sample Size Group 1	47
Proportion Group 1	0.191489362
Successes in Group 2	13
Sample Size Group 2	41
Proportion Group 2	0.317073171
Average Proportion	0.25
Difference in Two Proportions	-0.125583809
Hypothesized Difference	0
α	0.01
Z	-1.357164642
Two-Tailed Test	
Lower Critical Value	-2.575829304
Upper Critical value	2.575829304
p-value	0.174728903
Decision	Do not reject
One-tailed Test (Lower)	
Lower Critical Value	-2.326347874
p-value	0.087364451
Decision	Do not reject
One-Tailed test (Upper)	
Upper Critical Value	2.326347874
p-value	0.912635549
Decision	Do not reject

E.5   Z test for evaluating the significant difference in proportions between FNAM and Undeclared ethnicity neonate ears that passed in a test battery of Accuscreen TEOAE, 1 kHz tympanometry, and BBN MEMR.

Z Test for Two Proportions

Successes in Group 1	60
Sample Size Group 1	80
Proportion Group 1	0.75
Successes in Group 2	28
Sample Size Group 2	41
Proportion Group 2	0.682926829
Average Proportion	0.727272727
Difference in Two Proportions	0.067073171
Hypothesized Difference	0
α	0.01
Z	0.784115679
Two-Tailed Test	
Lower Critical Value	-2.575829304
Upper Critical value	2.575829304
p-value	0.432972236
Decision	Do not reject
One-tailed Test (Lower)	
Lower Critical Value	-2.326347874
p-value	0.783513882
Decision	Do not reject
One-Tailed test (Upper)	
Upper Critical Value	2.326347874
p-value	0.216486118
Decision	Do not reject

E.6 Z test for evaluating the significant difference in proportions between FNAM and Undeclared ethnicity neonate ears that failed in a test battery of Accuscreen TEOAE, 1 kHz tympanometry, and BBN MEMR.

Z Test for Two Proportions

Successes in Group 1	20
Sample Size Group 1	80
Proportion Group 1	0.25
Successes in Group 2	13
Sample Size Group 2	41
Proportion Group 2	0.317073171
Average Proportion	0.272727273
Difference in Two Proportions	-0.067073171
Hypothesized Difference	0
α	0.01
Z	-0.784115679
Two-Tailed Test	
Lower Critical Value	-2.575829304
Upper Critical value	2.575829304
p-value	0.432972236
Decision	Do not reject
One-tailed Test (Lower)	
Lower Critical Value	-2.326347874
p-value	0.216486118
Decision	Do not reject
One-Tailed test (Upper)	
Upper Critical Value	2.326347874
p-value	0.783513882
Decision	Do not reject

E.7 **Z test for evaluating the significant difference in proportions between FNAM and Caucasian neonate ears that had a likely diagnosis of conductive hearing loss.**

Z Test for Two Proportions

Successes in Group 1	24
Sample Size Group 1	206
Proportion Group 1	0.116504854
Successes in Group 2	12
Sample Size Group 2	41
Proportion Group 2	0.292682927
Average Proportion	0.145748988
Difference in Two Proportions	-0.176178072
Hypothesized Difference	0
α	0.01
Z	-2.919667471
Two-Tailed Test	
Lower Critical Value	-2.575829304
Upper Critical value	2.575829304
p-value	0.003504051
Decision	Reject
One-tailed Test (Lower)	
Lower Critical Value	-2.326347874
p-value	0.001752025
Decision	Reject
One-Tailed test (Upper)	
Upper Critical Value	2.326347874
p-value	0.998247975
Decision	Do not reject

E.8   Z test for evaluating the significant difference in proportions between FNAM and Mixed Other ethnicity neonate ears that had a likely diagnosis of conductive hearing loss.

Z Test for Two Proportions

Successes in Group 1	8
Sample Size Group 1	47
Proportion Group 1	0.170212766
Successes in Group 2	12
Sample Size Group 2	41
Proportion Group 2	0.292682927
Average Proportion	0.227272727
Difference in Two Proportions	-0.122470161
Hypothesized Difference	0
α	0.01
Z	-1.367549413
Two-Tailed Test	
Lower Critical Value	-2.575829304
Upper Critical value	2.575829304
p-value	0.17145316
Decision	Do not reject
One-tailed Test (Lower)	
Lower Critical Value	-2.326347874
p-value	0.08572658
Decision	Do not reject
One-Tailed test (Upper)	
Upper Critical Value	2.326347874
p-value	0.91427342
Decision	Do not reject

E.9   Z test for evaluating the significant difference in proportions between FNAM and Undeclared ethnicity neonate ears that had a likely diagnosis of conductive hearing loss

Z Test for Two Proportions

Successes in Group 1	17
Sample Size Group 1	80
Proportion Group 1	0.2125
Successes in Group 2	12
Sample Size Group 2	41
Proportion Group 2	0.292682927
Average Proportion	0.239669421
Difference in Two Proportions	-0.080182927
Hypothesized Difference	0
	0.01
Z	-0.977954387
Two-Tailed Test	
Lower Critical Value	-2.575829304
Upper Critical value	2.575829304
p-value	0.328096884
Decision	Do not reject
One-tailed Test (Lower)	
Lower Critical Value	-2.326347874
p-value	0.164048442
Decision	Do not reject
One-Tailed test (Upper)	
Upper Critical Value	2.326347874
p-value	0.835951558
Decision	Do not reject

E.10   ANOVA - WBA (ambient and peak) and binary screening outcome (pass/fail)

Results of mixed model ANOVA investigating the effect of binary screening outcome on WBA (ambient and peak) (all participants).

Effect	SS	Degr. of Freedom	MS	F	p
Intercept	6960.913	1	6960.913	2599.503	0.000000
Screening Outcome binary	50.196	1	50.196	18.745	0.000021
Error	704.258	263	2.678		
AMBVSP	9.873	1	9.873	37.699	0.000000
AMBVSP*Screening Outcome binary	0.593	1	0.593	2.266	0.133470
Error	68.879	263	0.262		
FREQUENC	211.073	106	1.991	65.592	0.000000
FREQUENC*Screening Outcome binary	45.188	106	0.426	14.042	0.000000
Error	846.329	27878	0.030		
AMBVSP*FREQUENC	8.406	106	0.079	19.167	0.000000
AMBVSP*FREQUENC*Screening Outcome binary	1.905	106	0.018	4.344	0.000000
Error	115.344	27878	0.004		

E.11 GG correction - WBA (ambient and peak) and binary screening outcome (pass/fail)

Effect	Degr. of Freedom	F	p	G-G Epsilon	G-G Adj. df1	G-G Adj. df2	G-G Adj. p	H-F Epsilon	H-F Adj. df1	H-F Adj. df2	H-F Adj. p	Lowr.Bnd Epsilon	Lowr.Bnd Adj. df1	Lowr.Bnd Adj. df2	Lowr.Bnd Adj. p
AMBVSP	1	37.69925	0.000000	1.000000	1.000000	263.000	0.000000	1.000000	1.000000	263.000	0.000000	1.000000	1.000000	263.0000	0.000000
AMBVSP*Screening Outcome binary	1	2.26566	0.133470	1.000000	1.000000	263.000	0.133470	1.000000	1.000000	263.000	0.133470	1.000000	1.000000	263.0000	0.133470
Error	263														
R2FREQUE	106	65.59175	0.000000	0.042532	4.508406	1185.711	0.000000	0.043530	4.614183	1213.530	0.000000	0.009434	1.000000	263.0000	0.000000
R2FREQUE*Screening Outcome binary	106	14.04248	0.000000	0.042532	4.508406	1185.711	0.000000	0.043530	4.614183	1213.530	0.000000	0.009434	1.000000	263.0000	0.000220
Error	27878														
AMBVSP*R2FREQUE	106	19.16675	0.000000	0.043033	4.561549	1199.687	0.000000	0.044053	4.669625	1228.111	0.000000	0.009434	1.000000	263.0000	0.000017
AMBVSP*R2FREQUE*Screening Outcome binary	106	4.34376	0.000000	0.043033	4.561549	1199.687	0.000982	0.044053	4.669625	1228.111	0.000881	0.009434	1.000000	263.0000	0.038110
Error	27878														

E.12 ANOVA – Yφ and binary screening outcome (pass/fail) (all participants).

Results of mixed model ANOVA investigating the effect of binary screening outcome on Yφ (all participants).

Effect	SS	Degr. of Freedom	MS	F	p
Intercept	23671379	1	23671379	519.8656	0.000000
Screening Outcome Binary	71061	1	71061	1.5606	0.212751
Error	11292344	248	45534		
FREQUENC	1553082	106	14652	22.3944	0.000000
FREQUENC*Screening Outcome Binary	185338	106	1748	2.6725	0.000000
Error	17199129	26288	654		

E.13 GG correction - Yφ and binary screening outcome (pass/fail) (all participants).

Effect	Degr. of Freedom	F	p	G-G Epsilon	G-G Adj. df1	G-G Adj. df2	G-G Adj. p	H-F Epsilon	H-F Adj. df1	H-F Adj. df2	H-F Adj. p	Lowr.Bnd Epsilon	Lowr.Bnd Adj. df1	Lowr.Bnd Adj. df2	Lowr.Bnd Adj. p
FREQUENC	106	22.39442	0.00	0.048931	5.186695	1286.300	0.000000	0.050302	5.331972	1322.329	0.000000	0.009434	1.000000	248.0000	0.00000
FREQUENC*Screening Outcome Binary	106	2.67246	0.00	0.048931	5.186695	1286.300	0.019187	0.050302	5.331972	1322.329	0.018112	0.009434	1.000000	248.0000	0.10336
Error	26288														

E.14   ANOVA - WBA (ambient and peak) and likely diagnosis/dx re screening (normal and conductive participants only).

Results of mixed model ANOVA investigating the effect of likely diagnosis (diagnosis re: screening) according to screening results on WBA (ambient and peak) (normal and conductive participants only).

Effect	SS	Degr. of Freedom	MS	F	p
Intercept	5981.167	1	5981.167	2272.927	0.000000
Dx re screening	62.397	1	62.397	23.712	0.000002
Error	676.291	257	2.631		
AMBVSP	8.798	1	8.798	32.942	0.000000
AMBVSP*Dx re screening	0.516	1	0.516	1.931	0.165857
Error	68.638	257	0.267		
FREQUENC	173.299	106	1.635	54.527	0.000000
FREQUENC*Dx re screening	47.729	106	0.450	15.018	0.000000
Error	816.804	27242	0.030		
AMBVSP*FREQUENC	7.694	106	0.073	17.521	0.000000
AMBVSP*FREQUENC*Dx re screening	1.851	106	0.017	4.215	0.000000
Error	112.863	27242	0.004		

E.15 GG correction - WBA (ambient and peak) and likely diagnosis/dx re screening (normal and conductive participants only).

Effect	Degr. of Freedom	F	p	G-G Epsilon	G-G Adj. df1	G-G Adj. df2	G-G Adj. p	H-F Epsilon	H-F Adj. df1	H-F Adj. df2	H-F Adj. p	Lowr.Bnd Epsilon	Lowr.Bnd Adj. df1	Lowr.Bnd Adj. df2	Lowr.Bnd Adj. p
AMBVSP	1	32.94240	0.000000	1.000000	1.000000	257.000	0.000000	1.000000	1.000000	257.000	0.000000	1.000000	1.000000	257.0000	0.000000
AMBVSP*Dx re screening	1	1.93095	0.165857	1.000000	1.000000	257.000	0.165857	1.000000	1.000000	257.000	0.165857	1.000000	1.000000	257.0000	0.165857
Error	257														
FREQUENC	106	54.52680	0.000000	0.042507	4.505770	1157.983	0.000000	0.043528	4.613945	1185.784	0.000000	0.009434	1.000000	257.0000	0.000000
FREQUENC*Dx re screening	106	15.01762	0.000000	0.042507	4.505770	1157.983	0.000000	0.043528	4.613945	1185.784	0.000000	0.009434	1.000000	257.0000	0.000135
Error	27242														
AMBVSP*FREQUENC	106	17.52058	0.000000	0.042845	4.541561	1167.181	0.000000	0.043880	4.651317	1195.389	0.000000	0.009434	1.000000	257.0000	0.000039
AMBVSP*FREQUENC*Dx re screening	106	4.21460	0.000000	0.042845	4.541561	1167.181	0.001294	0.043880	4.651317	1195.389	0.001165	0.009434	1.000000	257.0000	0.041090
Error	27242														

E.16   ANOVA – Yφ and likely diagnosis/dx re: screening (normal and conductive participants).

Results of mixed model ANOVA investigating the effect of likely diagnosis (diagnosis re: screening) according to screening results on

Yφ (normal and conductive participants only).

Effect	SS	Degr. of Freedom	MS	F	p
Intercept	21105314	1	21105314	459.3340	0.000000
Dx re screening	58118	1	58118	1.2649	0.261840
Error	11165277	243	45948		
FREQUENC	1397963	106	13188	19.9762	0.000000
FREQUENC*Dx re screening	217338	106	2050	3.1057	0.000000
Error	17005446	25758	660		

E.17 GG correction - Yφ and likely diagnosis/dx re screening (normal and conductive participants only)

Effect	Degr. of Freedom	F	p	G-G Epsilon	G-G Adj. df1	G-G Adj. df2	G-G Adj. p	H-F Epsilon	H-F Adj. df1	H-F Adj. df2	H-F Adj. p	Lowr.Bnd Epsilon	Lowr.Bnd Adj. df1	Lowr.Bnd Adj. df2	Lowr.Bnd Adj. p
FREQUENC	106	19.97624	0.00	0.049052	5.199541	1263.488	0.000000	0.050458	5.348550	1299.698	0.000000	0.009434	1.000000	243.0000	0.000012
FREQUENC*Dx re screening	106	3.10566	0.00	0.049052	5.199541	1263.488	0.007723	0.050458	5.348550	1299.698	0.007123	0.009434	1.000000	243.0000	0.079278
Error	25758														

E.18 ANOVA - WBA (ambient and peak) and Caucasian, First Nations and Metis, and Mixed Other Ethnicity neonates (normal and declared ethnicity participants).

Results of mixed model ANOVA investigating the effect of ethnicity on WBA (ambient and peak) (normal and declared ethnicity participants).

Effect	SS	Degr. of Freedom	MS	F	p
Intercept	4209.097	1	4209.097	1797.611	0.000000
Ethnicity	16.854	2	8.427	3.599	0.029383
Error	412.103	176	2.341		
AMBVSP	7.514	1	7.514	26.372	0.000001
AMBVSP*Ethnicity	1.657	2	0.828	2.907	0.057260
Error	50.145	176	0.285		
FREQUENC	222.503	106	2.099	74.287	0.000000
FREQUENC*Ethnicity	11.869	212	0.056	1.981	0.000000
Error	527.151	18656	0.028		
AMBVSP*FREQUENC	6.378	106	0.060	15.099	0.000000
AMBVSP*FREQUENC*Ethnicity	1.163	212	0.005	1.377	0.000246
Error	74.339	18656	0.004		

E.19   GG correction – WBA (ambient and peak) and Caucasian, First Nations and Metis, and Mixed Other Ethnicity neonates (normal and declared ethnicity participants).

Effect	Degr. of Freedom	F	p	G-G Epsilon	G-G Adj. df1	G-G Adj. df2	G-G Adj. p	H-F Epsilon	H-F Adj. df1	H-F Adj. df2	H-F Adj. p	Lowr.Bnd Epsilon	Lowr.Bnd Adj. df1	Lowr.Bnd Adj. df2	Lowr.Bnd Adj. p
AMBVSP	1	26.37239	0.000001	1.000000	1.000000	176.0000	0.000001	1.000000	1.000000	176.0000	0.000001	1.000000	1.000000	176.0000	0.000001
AMBVSP*Ethnicity	2	2.90713	0.057260	1.000000	2.000000	176.0000	0.057260	1.000000	2.000000	176.0000	0.057260	1.000000	2.000000	176.0000	0.057260
Error	176														
FREQUENC	106	74.28720	0.000000	0.043110	4.569692	804.2659	0.000000	0.044904	4.759806	837.7258	0.000000	0.009434	1.000000	176.0000	0.000000
FREQUENC*Ethnicity	212	1.98131	0.000000	0.043110	9.139385	804.2659	0.037724	0.044904	9.519611	837.7258	0.035269	0.009434	2.000000	176.0000	0.140952
Error	18656														
AMBVSP*FREQUENC	106	15.09920	0.000000	0.043380	4.598243	809.2907	0.000000	0.045193	4.790414	843.1129	0.000000	0.009434	1.000000	176.0000	0.000144
AMBVSP*FREQUENC*Ethnicity	212	1.37690	0.000246	0.043380	9.196485	809.2907	0.192597	0.045193	9.580828	843.1129	0.189377	0.009434	2.000000	176.0000	0.255063
Error	18656														

E.20   ANOVA – Yφ and Caucasian, First Nations and Metis, and Other Ethnicity neonates (normal and declared participants, not significant).

Results of mixed model ANOVA investigating the effect of ethnicity on Yφ (normal and declared ethnicity participants).

Effect	SS	Degr. of Freedom	MS	F	p
Intercept	11575995	1	11575995	222.5455	0.000000
Ethnicity	5345	2	2672	0.0514	0.949939
Error	8582689	165	52016		
FREQUENC	1409383	106	13296	18.4129	0.000000
FREQUENC*Ethnicity	155345	212	733	1.0148	0.427797
Error	12629622	17490	722		

E.21   ANOVA - WBA (ambient and peak) and Accuscreen TEOAE results (all participants).

Results of mixed model ANOVA investigating the effect of Accuscreen TEOAE results on WBA (ambient and peak) (all participants).

Effect	SS	Degr. of Freedom	MS	F	p
Intercept	3694.095	1	3694.095	1296.491	0.000000
TEAccuscreen	9.105	1	9.105	3.196	0.074995
Error	743.668	261	2.849		
AMBVSP	4.817	1	4.817	18.208	0.000028
AMBVSP*TEAccuscreen	0.276	1	0.276	1.044	0.307877
Error	69.048	261	0.265		
FREQUENC	98.849	106	0.933	30.102	0.000000
FREQUENC*TEAccuscreen	30.074	106	0.284	9.159	0.000000
Error	857.061	27666	0.031		
AMBVSP*FREQUENC	4.608	106	0.043	10.408	0.000000
AMBVSP*FREQUENC*TEAccuscreen	1.451	106	0.014	3.277	0.000000
Error	115.555	27666	0.004		

E.22   GG correction - WBA (ambient and peak) and Accuscreen TEOAE results (all participants).

Effect	Degr. of Freedom	F	p	G-G Epsilon	G-G Adj. df1	G-G Adj. df2	G-G Adj. p	H-F Epsilon	H-F Adj. df1	H-F Adj. df2	H-F Adj. p	Lowr.Bnd Epsilon	Lowr.Bnd Adj. df1	Lowr.Bnd Adj. df2	Lowr.Bnd Adj. p
AMBVSP	1	18.20773	0.000028	1.000000	1.000000	261.000	0.000028	1.000000	1.000000	261.000	0.000028	1.000000	1.000000	261.0000	0.000028
AMBVSP*TEAccuscreen	1	1.04383	0.307877	1.000000	1.000000	261.000	0.307877	1.000000	1.000000	261.000	0.307877	1.000000	1.000000	261.0000	0.307877
Error	261														
FREQUENC	106	30.10236	0.000000	0.042510	4.506088	1176.089	0.000000	0.043515	4.612590	1203.886	0.000000	0.009434	1.000000	261.0000	0.000000
FREQUENC*TEAccuscreen	106	9.15851	0.000000	0.042510	4.506088	1176.089	0.000000	0.043515	4.612590	1203.886	0.000000	0.009434	1.000000	261.0000	0.002723
Error	27666														
AMBVSP*FREQUENC	106	10.40764	0.000000	0.042842	4.541247	1185.265	0.000000	0.043861	4.649278	1213.462	0.000000	0.009434	1.000000	261.0000	0.001415
AMBVSP*FREQUENC*TEAccuscreen	106	3.27670	0.000000	0.042842	4.541247	1185.265	0.007972	0.043861	4.649278	1213.462	0.007466	0.009434	1.000000	261.0000	0.071420
Error	27666														

E.23   ANOVA – Yφ and Accuscreen TEOAE results (all participants).

Results of mixed model ANOVA investigating the effect of Accuscreen TEOAE results on Yφ (all participants).

Effect	SS	Degr. of Freedom	MS	F	p
Intercept	10665189	1	10665189	235.9224	0.000000
TEAccuscreen	1423	1	1423	0.0315	0.859346
Error	11075556	245	45206		
FREQUENC	585586	106	5524	8.4949	0.000000
FREQUENC*TEAccuscreen	143461	106	1353	2.0812	0.000000
Error	16888722	25970	650		

E.24 GG correction – Yφ and Accuscreen TEOAE results (all participants).

Effect	Degr. of Freedom	F	p	G-G Epsilon	G-G Adj. df1	G-G Adj. df2	G-G Adj. p	H-F Epsilon	H-F Adj. df1	H-F Adj. df2	H-F Adj. p	Lowr.Bnd Epsilon	Lowr.Bnd Adj. df1	Lowr.Bnd Adj. df2	Lowr.Bnd Adj. p
FREQUENC	106	8.494934	0.000000	0.049120	5.206670	1275.634	0.000000	0.050517	5.354809	1311.928	0.000000	0.009434	1.000000	245.0000	0.003891
FREQUENC*TEAccuscreen	106	2.081156	0.000000	0.049120	5.206670	1275.634	0.062431	0.050517	5.354809	1311.928	0.060463	0.009434	1.000000	245.0000	0.150404
Error	25970														