IHE Report

Screening Newborns for Hearing

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THE USE OF THE AUTOMATED AUDITORY BRAINSTEM RESPONSE AND OTOACOUSTIC EMISSIONS TESTS FOR NEWBORN HEARING SCREENING

Final STE Report

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EXECUTIVE SUMMARY

Background

Permanent congenital hearing impairment/loss (PCHI) is one of the most common congenital anomalies found at birth which can be expected to lead to delays and deficits in the development of speech, language, cognition and learning, as well as secondary effects on the child and family. Limited scientific evidence suggests that early identification and subsequent appropriate intervention (within the first 6 months) in infants with PCHI can minimize these effects. As a result, there has been a growing interest for universal newborn hearing screening (UNHS) in attempts to diagnose PCHI as early as possible.

Objectives

1. To review the social considerations for the provision of UNHS using Automatic Otoacoustic Emissions (AOAE) and/or Automated Auditory Brainstem Response (AABR) (either alone or in combination) to screen for PCHI in Alberta.
2. To review the published evidence on the efficacy/effectiveness and safety of using AOAE and/or AABR (either alone or in combination) for UNHS.
3. To review the economic literature for the provision of AOAE and/or AABR (either alone or in combination) for UNHS and to determine which screening protocol is cost-effective using an economic model.

Results

Information from the Alberta Health and Wellness administrative databases did not allow for an estimation of PCHI prevalence or an analysis of the current age at which children are diagnosed with PCHI in Alberta.

A pilot UNHS program from 2001 to December 2004 provided the only Alberta specific PCHI prevalence estimates of 4 per 1000 screened infants. Analyses of Alberta Health and Wellness databases identified a 1998 cohort and found that for children with more than five audiological examinations the median age to first audiological examination was 2 years, with fewer than 25% examined at or before 1 year of age. None of the children with cochlear implants were seen by physicians for hearing loss or received an audiological examination before 6 months of age; the median age at first examination was approximately 1 year.

Evidence from two systematic reviews state that:

- There is good evidence to suggest that AOAE and AABR are equally accurate screening tests for moderate to profound PCHI. A 2-stage protocol using AOAE followed by AABR, may achieve better specificity (>97%) and lower overall referral rates (<2%) than 1 stage protocols using either technology. However, loss to follow-up is a limiting factor for overall program sensitivity.
- The long-term efficacy/effectiveness of using AOAE and/or AABR for UNHS in terms of improved developmental outcomes is not definitive. The existing evidence that early detection and start of habilitation promotes improved communication and language development in an infant with PCHI is limited.
- No safety issues or concerns associated with applying the technology AABR and/or AOAE in newborns have been reported. Conclusive evidence regarding the impact of false positives has yet to be established.
- Another concern is the increased number and impact of false negative results that occur with a multi-stage protocol.
- Data to directly compare the short- and long-term benefits and harms of UNHS versus those associated with selective screening are lacking.

According to the economic evaluation conducted for this review:

- The 1-stage AABR protocol is more cost effective compared to the 1-stage AOAE protocol, since it has lower costs and greater effectiveness.
- There is no clear answer on which is the cost effective alternative between the 1-stage AABR protocol and the 2-stage protocol (AOAE followed by AABR). The 2-stage protocol is more effective with higher expected costs when compared to the 1-stage protocol. However, the 2 stage protocol includes a greater number of sequential screens over time, and this increases the number of false negative cases, but decreases the number of false positive cases. The additional cost to correctly identify the hearing status of one additional infant between the two protocols is $7,574.78 (Cdn 2003 $).

Conclusions

This review's findings suggest that:

- UNHS using AOAE and/or AABR technology (either alone in a 2-stage protocol) is effective in terms of increasing early identification of moderate to profound PCHI and may lead to early intervention in diagnosed infants (before 6 months).
- The 1-stage screening protocol using AABR is a cost effective alternative to the 1-stage screening protocol using AOAE, which is less accurate and costs more.

- The 2-stage protocol (using AOAE followed by AABR) is more effective with higher expected costs compared to the 1-stage screening protocol using AABR. It is a value judgment if whether correctly identifying one additional infant is worth the additional cost.

If UNHS is implemented, those considering AOAE and/or AABR technologies (either as a 1-stage protocol or a 2-stage protocol) should be aware that:

- AOAE and/or AABR cannot screen for all types and degrees of PCHI.
- The screening accuracy of AOAE and/or AABR depends on many factors including the cut-off impairment and the screening protocol used.
- The efficacy/effectiveness of AOAE and/or AABR in terms of longer-term outcomes may be difficult to establish because developmental outcomes are related to more factors than just the accuracy of the screening technologies.
- The AOAE and/or AABR technologies are still evolving.

This review also leads to several conclusions that are especially relevant to the implementation of Newborn Hearing Screening programs:

- Alberta data currently collected/reported does not allow for an analysis of prevalence of PCHI or a definitive analysis of the current age of diagnosis of PCHI individuals. The creation of a registry of PCHI individuals would be necessary for the effective evaluation of any form of Newborn Hearing Screening Program.
- The safety and clinical efficacy of UNHS has not been established by well-designed clinical trials and only limited evidence supports the pivotal assumption of a UNHS program which is that early detection of PCHI leads to more effective habilitation.
- The available evidence suggests that a UNHS program's effectiveness is lower than efficacy estimates based upon analysis of the technology's characteristics alone. Specific strategies to minimize failure to screen and loss to follow-up are integral in the implementation of UNHS.
- Although there is limited evidence to suggest that UNHS is superior to selective screening, data that directly compare the short- and long-term benefits and harms of these alternatives is still lacking. Higher false positive rates (and therefore increased audiological assessments) threaten the cost-effectiveness of UNHS over selective screening programs. The weakest link in the evidence chain is the demonstration that earlier detection of individuals not located by a selective screening program will receive more effective habilitation.
- In view of the widespread adoption of UNHS programs in Canadian provinces, the potential to perform a natural experiment in Alberta to contribute to the evidence base around Newborn Hearing Screening is worth consideration.

Methodology

Research studies reporting on the epidemiology of PCHI and on the safety, efficacy/effectiveness, and cost-effectiveness of UNHS using AOAE and/or AABR to screen for PCHI were identified through a comprehensive systematic search of the literature published in English, between January 2001 and August 2006. The search included: The Cochrane Library, NHS Centre for Reviews and Dissemination Databases (EED, HTA, DARE), PubMed, EMASE, CINAHL, and the web sites of various health technology assessment (HTA) agencies, evidence-based resources, and clinical practice guidelines sites.

Alberta statistical data was analyzed and presented as a context for considerations of UNHS implementation and program type. The data used to estimate the prevalence of PCHI was obtained from a pilot UNHS program initiated in four Alberta health regions between 2001 and 2004. Data regarding Physician Services provided under a diagnosis of ICD 9 code 389 (Hearing Loss) and Audiometric examinations, audiological assessments, and operations for cochlear implants were extracted from the 1998 Alberta birth cohort consisting of 38,730 individuals followed until March 31, 2005.

For the purpose of this review, only published reports of systematic reviews and HTA studies were selected to formulate the evidence base on the safety and efficacy/effectiveness of using AOAE and/or AABR for UNHS. Individual primary research studies (of any design) published subsequent to the selected systematic reviews and HTA studies were not included.

The economic evaluation involved a literature review (focused on economic evaluations of the technologies) and the construction of an economic model for UNHS using three alternative screening protocols. The model incorporated a societal perspective and included only direct costs (screening and downstream costs of deaf infants).

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Prepared by Don Schopflocher

Social and System Demographics

Introduction

The current review began as an attempt to collate available Alberta statistical information to contextualize the companion Technological Effects and Effectiveness analysis and Economic Evaluation analysis. As it became clearer that much of this information was unavailable, the focus shifted to providing a consideration of Newborn Hearing Screening within the broader framework of the epidemiology of screening programs. This analysis repeats some short sections verbatim from the Technological Effects and Effectiveness analysis with the intent to extend that analysis to a consideration of the implementation of screening programs.

Screening can be defined as "the examination of asymptomatic people in order to classify them as likely or unlikely to have the disease that is the object of screening. The goal of screening is to reduce the morbidity...from the disease screened; this goal is attained by early treatment of the cases discovered."[18]

The criteria for evaluating whether a screening program should be implemented include considerations of the disease or condition, the screening test, and the implementation of the test in a program.[20,23,24] More specifically these criteria include:

Epidemiology of Disease or Condition

- Imposes significant individual and societal burden
- Has a significant detectable preclinical period
- Has improved prognosis with earlier treatment

Screening Test

- Is efficacious
  - adequate sensitivity and specificity for test
- Has minimal risks
- Is safe
- Has low burden for False Positives (e.g. labeling, risks of further testing)
- Has low burden for False Negatives (e.g. potential delay of diagnosis)
- Is acceptable to the population

Health Care system

- Program can be implemented
  - Follow-up of positive screening tests would be provided
  - Intervention would be provided to diagnosed cases
  - Program would reach those at risk

- Program as implemented is effective
  - Minimal inability to screen/loss to follow-up
  - Adequate sensitivity and specificity for protocol and program as implemented
- Program is cost effective
- Program compares favorably to alternative programs.

Specific note should be made of the fact that this framework separates analysis of tests under ideal conditions (test efficacy) from analysis of tests as actually implemented in real world protocols within real world settings (program effectiveness). In general, there will be a decrement in test characteristics in real world programs. Davis et al.[6] make the point that efficacy and effectiveness have not been separately considered in most empirical evaluations of Universal Newborn Hearing Screening (UNHS) programs.

Epidemiology of infant hearing impairment

An understanding of the basic epidemiology of the hearing impairment is essential to addressing:

- questions of its burden;
- questions about test characteristics since the sensitivity and specificity of tests interacts with the size of the population screened and the prevalence to determine the actual number of individuals with positive or negative results which in turn is important in considerations of system capacity;
- ongoing monitoring and evaluation of the program.

Definition of condition

Hearing impairment is a broad term used to describe complete or partial loss of the ability to hear in one or both ears.[2,7] Hearing impairment in childhood may be sensorineural or conductive or a combination of the two (mixed) with additive effects, and may be congenital, acquired, transient, fluctuating, recurrent, progressive, or permanent. Etiologically, sensorineural hearing impairment involves a problem with the inner ear (e.g., cochlear dysfunction) and occasionally with the hearing nerve going from there to the brain. This type of hearing impairment is usually permanent and requires habilitation. Conductive hearing impairment is due to a problem in the outer (external) or middle ears and it is often medically or surgically treatable.

The prevalence of hearing impairment in childhood depends on what is included in the target disorder. Ideally the target disorder is described by impairment severity, frequency range, laterality (one or both ears), and permanence, as well as the site of the disorder in the auditory system and the associated categories of impairment type. The degree of hearing impairment refers to the severity of hearing loss and it is described in decibels (dB),

a unit of intensity or loudness, at various hearing frequencies. Several different classification schemes have been used for degree of hearing impairment and currently there is no universally accepted system. The World Health Organization classifies impairment as slight/mild (26-40 dB, in better ear), moderate (41-60 dB, in better ear), severe (61-80 dB, in better ear), and profound (≥81 dB, in better ear).

For the purposes of this review, the target disorder is hearing impairment in childhood that is congenital and is stable or progressive, which is referred to as permanent childhood hearing impairment/loss or permanent congenital hearing impairment/loss (PCHI). Most PCHI is sensorineural and irreversible.[2] Severity may not be symmetrical for both ears. Structural conductive impairments are usually included because they impose long-standing dysfunction, unless treated. The incidence of PCHI varies with race, gender, birth weight, intra-uterine infection, and other risk factors, including family history of hearing impairment or chromosomal abnormality. This condition has a wide range of severity, which for an individual may fluctuate over time.

Incidence/prevalence

PCHI is one of the most common congenital anomalies found at birth. In Western industrialized societies, the prevalence of bilateral PCHI is about 1 in 1000 live births in infancy, if one uses 40 dB hearing loss (HL) in the better ear as the cut-off audiometric criteria. This rate increases by up 17 to 33% over the first decade of life. Such increases are attributable to acquired, late-onset, and progressive impairment, the prevalence and time course of which are still unclear. If audiometric criteria for PCHI are broadened to include lesser severities (down to > 25 dB HL) and unilateral losses, the prevalence in early infancy increases to 2 to 3 in 1000. Up to 50% of cases are thought to be due to environmental factors and the remainder to genetic causes.[7] These are important to note because individuals with this type of impairment would likely be a false negative on screening at birth. This underscores the need for programs to protect against a false sense of security that might arise.

Alberta data

Alberta maintains a record in the Stakeholder Registry for (almost) every individual. Physicians bill the Alberta Health Care Insurance Plan for each service administered. These services can be connected to particular individuals because a single lifetime identifier is assigned to each member of the population and is used for billing.

While each claim must record a diagnosis as an ICD 9 code, only the first three digits of the code are mandatory. This coding is insufficient to separate conductive hearing losses from sensorineural hearing loss and no definitive prevalences can be calculated.

While individual practitioners or the facilities in which they practice will keep records of the number of individuals examined (e.g. for audiological evaluations), and administrative records may also provide this information, apparently no records are kept of the results of these evaluations. Establishing such records and potentially a registry of children with permanent childhood hearing impairment would be both a requirement for the ongoing evaluation of a newborn hearing program, and also a potential advantage of establishing such a program.

A pilot universal hearing screening program, initiated in four Alberta Health regions between 2001 and 2004 and funded by the Alberta Health Innovation Fund, provides the only Alberta specific prevalence estimates.[26] Ultimately, the program diagnosed 49 infants with hearing loss. There were 14,348 infants born in the catchment area, of which 2170 were lost to follow-up at some stage in the process. Unilateral and Bilateral hearing loss figures were not separated. The estimated prevalence was therefore 4.02/1000 screened infants.

Burden

Severe or profound hearing impairment has traditionally been seen to be severely disabling. In the most comprehensive existing study, Mohr et al.[17] analyzed secondary data sources from the United States in a cohort-survival model to estimate the lifetime costs of severe to profound bilateral deafness. The cost components (expressed in year 2000 US dollars) were estimated to be $504,900 in special education costs, $11,500 in vocational rehabilitation, $70,200 in medical costs and costs for assistive devices and $433,000 in lost productivity, for a total of $1,020,000. These estimates have been widely cited, and have formed the basis of other economic studies.[14]

Early identification

In the absence of systematic infant screening, the detection, confirmation, diagnosis and treatment of hearing impairment may be significantly delayed. All degrees and configurations of PCHI present with great subtlety, and the majority of parents experience great difficulty in identifying their child's hearing loss before speech and language delay make it self-evident. Hearing loss in many children with hearing impairment is not identified until after the age of 1 year or well after the development of speech and language skills. The age at which hearing loss is detected without a screening program depends on the severity of the hearing loss and is found later in those with less severe deficits. With screening, the median age of diagnosis for children with PCHI ranges from 2 to 6 months. There are no significant differences in the ages at diagnosis for children with different degrees of hearing loss.

The reported average age at which hearing impairment is detected in North America ranges between 1 year and 3 years. A study of ages at detection, diagnosis, and intervention in Canada examined the records of 613 children

fitted with hearing aids at the Children's Hospital of Eastern Ontario.[33] The ages at diagnosis ranged from about 2 to 4 years in a referred group with risk indicators and from 2 to 7 years in a group without risk indicators, the lower age limits relating to "profound" impairment and the upper age limits to "mild" impairment. The median age at diagnosis was 6 months or less in a screened group, irrespective of impairment severity. Results reported in other studies are consistent with these findings.[2,21,25]

Alberta data

While diagnoses of PCHI cannot be extracted from Alberta Physician Services data, it is possible to extract Physician Services provided under a diagnosis of ICD 9 code 389 (Hearing Loss). It is also possible to locate adiometric examinations, audiological assessments, and operations for cochlear implants. The statistics which follow are taken from the 1998 Alberta birth cohort consisting of 38,730 individuals followed until March 31, 2005 when all were at least 6 years of age.

Table 1 shows the number of individuals with one or more physicians' services with a diagnosis of hearing loss. Figure 1 shows the number of days until the first such service for individuals with one or more service. It shows the cumulative survival, which means the proportion remaining who had not yet had a service by the number of days on the horizontal axis. Note that only a very small proportion were first seen prior to 1 year of age.

Table 1: Frequency of physician services for hearing loss (ICD-9-Cm 389) in 1998 birth cohort through March 31, 2005

Physician services	Individuals	Cumulative Percent
0	37,358	96.9
1	414	98.0
2	227	98.5
3	101	98.8
4	117	99.1
5	87	99.3
6	52	99.5
7	22	99.5
8	34	99.6
9	19	99.7
10	131	100.0
Total	38,730	

Figure 1: Days to first physician service for hearing loss

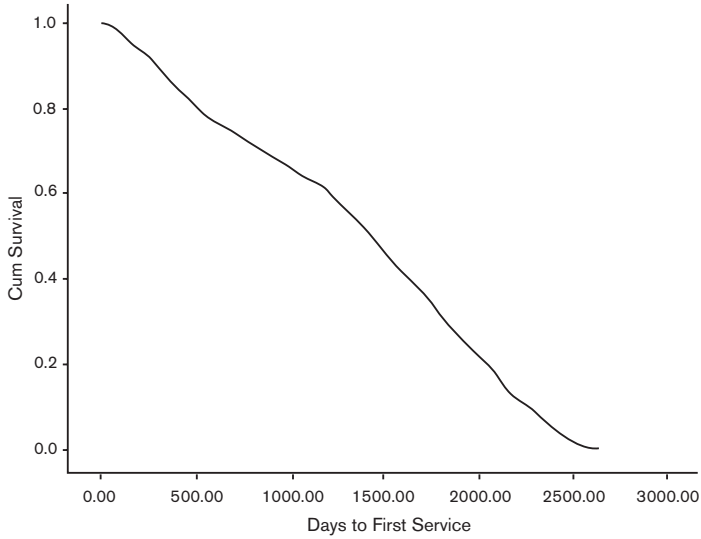


Table 2 and Figure 1 show similar information for individuals with one or more audiometric examination or audiological assessment. Again, only a small proportion had been examined prior to 1 year of age.

Table 2: Frequency of audiometric/audiological examinations in 1998 birth cohort through March 31, 2005

Audiometric or Audiological Examinations	Individuals	Cumulative Percent
0	35,819	92.9
1	290	93.6
2	1074	96.4
3	180	96.9
4	472	98.1
5	56	98.3
6	161	98.7
7	29	98.8
8	118	99.1
9	21	99.1
10+	510	100.0
Total	38,730	

Figure 2: Days to first audiometric/audiological examination

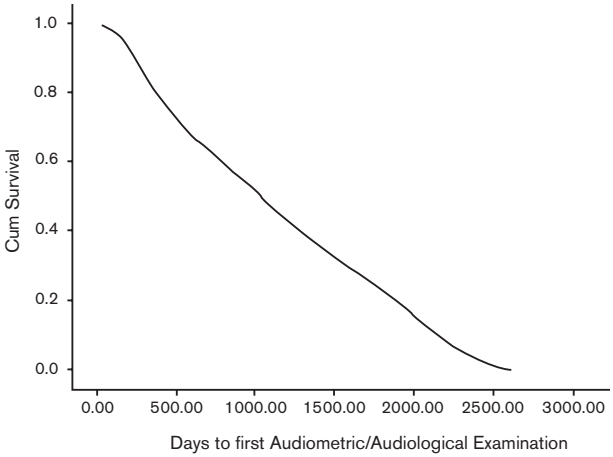


Figure 3 shows the number of days to the first audiometric examination or audiological assessment for the 345 individuals from the cohort who had five more such examinations. The box and "whisker" plot shows the median in the centre of the box, the top and the bottom of the shows the 25 and 75 percentiles and the 95 and 5 percentiles are shown at the end of the "whiskers". The median is approximately at age 2; fewer than 25% were first examined at an age less than 1 year.

Figure 3: Days to first audiological examination for Individuals with 5+ examinations

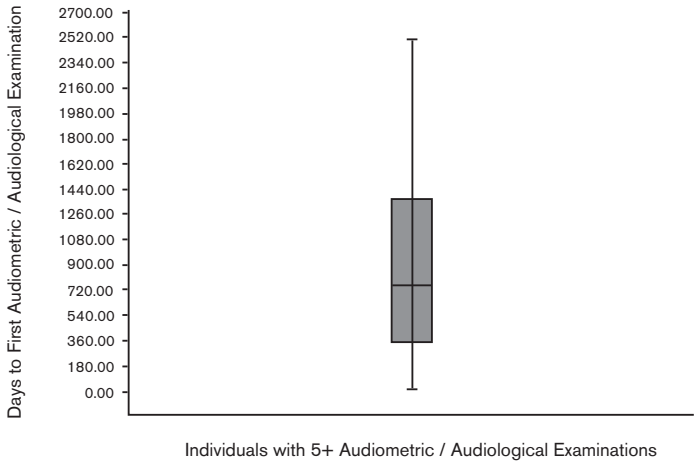
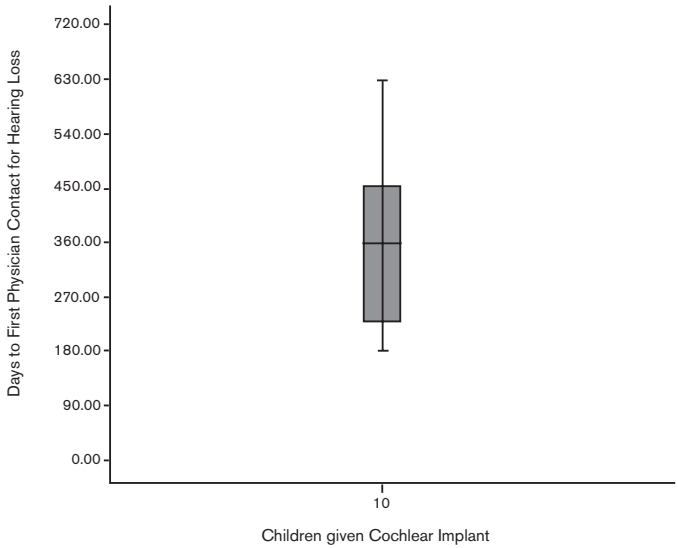


Figure 4 shows similar information for the 10 individuals in the cohort who had cochlear implant surgery before March 31, 2005. None of these were first seen before the age of 6 months, and the median age at first examination was approximately 1 year of age.

Figure 4: Days to first physician service/audiological examination for individuals given a cochlear implant



Finally, Table 3 shows the average age at which cochlear transplant occurred for these children.

Table 3: Mean number of days until cochlear implant

	N	Minimum	Maximum	Mean	Std. Deviation
Days until First Operation	10	791.00	2202.00	1550.20	483.13

Treatment

It is widely believed that early identification (at 3 to 6 months) and administration of appropriate intervention (such as amplification via hearing aids or cochlear implant, sign language, total communication programs, and/or surgery) at or before 6 months of age provides a child with impaired hearing the opportunity to develop normal speech and language. The logic that underlies these beliefs is sketched below:

- PCHI - impairment in language abilities - lifelong burden
- Habilitation - improvement in language ability - decreased burden
- UNHS - earlier diagnosis
- Earlier diagnosis - earlier habilitation
- Earlier habilitation - greater improvement in language ability
  - Specifically habilitation before 6 months of age optimizes improvement in language ability.

As a result of this reasoning, many countries have implemented neonatal hearing screening programs.

However, the evidence to convincingly support the final belief in this chain is apparently lacking in the research literature.

The literature search conducted by Thompson et al.[25] discovered no prospective, controlled study that directly examined whether newborn hearing screening results and early diagnosis and intervention give rise to improved speech, language, and/or educational development. No prospective cohort studies or controlled trials had followed screened and non-screened groups of newborns over time to evaluate language outcomes. (At that time, follow-up of the Wessex 1993-1996 cohort[30] was underway [see below].)

Thompson et al.[25] did review eight retrospective observational studies, which reported results obtained by three intervention programs (studies which investigated speech and language development in children with PCHI identified through UNHS). Although the studies reported improved language and communicative skills in children who were identified and treated before 6 months, these studies were rated fair to poor in methodological quality. Selection bias and baseline differences between compared groups were noted.

Two further studies have been recently reported, one of which did feature a comparison of children discovered while a UNHS program was in place with those discovered when UNHS was not in place.

Wake et al.[28] tested a cohort of hearing impaired children in Victoria, Australia at 7 or 8 years of age. No UHS program was in place at the time of the birth of these children. Age at diagnosis averaged 21.6 months [range 1.2 -53.0] and age of

hearing aid fitting averaged 23.2 months [range 1.2 -53.4]. In regression analyses (in which control covariates included tested IQ, and family socio-economic and social functioning variables), there was no relationship between age at diagnosis and seven separate standardized language assessments. Visual examination also failed to reveal any tendency towards improvement in the small sub-sample diagnosed before age 6 months.

Kennedy et al.[13] showed, in a follow-up of the Wessex 1993-1996 cohort,[30] that there was improvement depending on earlier diagnosis (<9, >9mo) in measures of language. Specifically, the earlier detected individuals had significantly higher scores on two standardized measures of receptive language, and 1 of 2 standardized measures of expressive language. However, both decreased screening characteristics (sensitivity and specificity) and loss to follow-up in a UNHS program will increase the average age at which an individual is identified. Furthermore, some individuals will be diagnosed early even where no UNHS exists and this would be expected to further attenuate a comparison between PCHI individuals who were discovered within UNHS compared to those who were discovered outside UNHS. This may be why the results of Kennedy et al.[13] are not so promising when the abilities of individuals who were discovered under UNHS were compared to those who were discovered outside UNHS. Specifically, the differences were smaller but still statistically significant for receptive language but were not present at all for expressive language. Unfortunately, information that would allow the reader to unravel the relationship between age at diagnosis and presence or absence of a UNHS program is conspicuous by its absence. Given that the age at diagnosis was known definitively, it is also questionable that data was dichotomized in the analysis rather than examined as a continuous variable as in the study by Wake et al.[28]

In a recent editorial Das & Das[5] state that "The fundamental question "does this make a difference to the child's development and life?" remains unanswered in many cases as we still lack a scientific approach to predict the degree of success of early amplification and implantation at an early stage especially during infancy. (p.221)"

It is clear, however, that most communication disorder professionals strongly believe that the age when children begin to have access to language and communication is pivotal to developmental outcomes. It is also widely believed that there are sensitive periods of development for vocabulary development, phonological development, and syntax development and that these periods may not fully overlap. It is recognized that the level of evidence currently available may be sufficient for some purposes (e.g. the initiation of remedial procedures) but not for others (e.g. the justification of medical interventions).[32]

Das & Das[5] note that early diagnosis and amplification has significantly boosted education and communication approaches to remediation.

They believe that there is an ongoing need to continue to concentrate on early diagnosis so that these educational processes can be studied and refined. It is also widely believed that this process will ultimately deliver evidence supporting the efficacy of this early diagnosis and treatment.

Screening Test

The characteristics of various screening technologies are extensively reviewed in the companion Technological Effects and Effectiveness analysis and Economic Evaluation analysis.

Health care system

Considerations in implementing effective UNHS programs

Planning a UNHS program extends considerably beyond choosing an effective screening test. Both decreased test characteristics as a result of protocol or program characteristics and loss to follow up threatens the justification of a screening program by increasing the average age at which an individual child is identified and habilitated. It is important to establish procedures to minimize loss to follow-up at every stage in the procedure from initial registration through diagnostic testing through habilitative intervention.

The literature notes that there is room for improvement in existing systems. For example, Wada et al.[27] report a case series of 49 infants in Japan referred for diagnostic testing as the result of screening by a variety of practitioners in a variety of settings. Some were referred with bilateral hearing loss and some with unilateral hearing loss. Diagnostic testing revealed a 26.5% false positive rate (for ears) and a 7.1% false negative rate (for ears). The authors conclude that better protocols and more experienced examiners would reduce these rates.

Lieu et al.[16] describe a case series of newborns screened in NICU in which 31% of individuals were lost to follow-up before diagnostic testing. Furthermore, only 30% of those who did follow-up did so before the age of 6 months (though there was an increase in this rate through the life of the program). The researchers urge future researchers to determine how to optimize timely follow-up.

Danhauer and Johnson[4] describe both compliance and timing of compliance at each stage of a UNHS program through diagnostic testing and follow-up habilitation. They noted loss to follow-up and a lower proportion complying with suggested timelines at the stage of follow-up habilitation. They also urge an investment in research to improve follow-up rates and timeliness of follow-up.

False negatives

The review of incidence and prevalence by Fortnum[7] noted that the incidence of PCHI that had an onset after birth (acquired, late-onset,

or progressive impairment) ranged from 17 to 33 percent. Recent results from follow-ups of cohorts screened in UNHS programs confirm that false negative rates fall in this range.

Kennedy et al.[13] in a follow-up of the Wessex 1993-1996 cohort[30] reported that 9 of 31 cases of PCHI had not been discovered by screening, a program false negative rate of 29%, (though many of these had not actually been initially screened, i.e. falling within the 13% of children not screened under the program).

White et al.[31] report (also reported by Johnson et al.[12]) on a multi site study of UNHS involving 86,634 infants screened at 11 hospitals in seven widely distributed US states. A sample of 973 children enrolled in the study before initial screening was later given a diagnostic assessment. The authors estimate a false negative rate of 23% for PCHI at 8-12 months of age, though this rate includes both unilateral PCHI as well as levels of mild impairment which the screening tests were not designed to detect.

Weichbold et al.[29] report a program false negative rate of 25% for bilateral PCHI (corrected for under-ascertainment) in children who had undergone UNHS testing in Australia between 1995 and 2000. They recommend that additional screening programs such as screening in schools or pre-schools be put in place.

Economic analyses

Most economic analyses have focused on establishing the cost of UNHS programs, usually expressed as costs per diagnosed case.

As previously discussed, there is limited published evidence on the effectiveness of early habilitation on the language abilities of PCHI individuals. Cost effectiveness studies are therefore based on benefit assumptions with very limited support. Thus Gorga and Neely[8] used arbitrary assumptions in a cost effectiveness analysis as had Keren et al.[14] While the companion Economic Evaluation analysis uses benefit assumptions derived from Keren et al.,[14] more conservative estimates of benefit are used, and a sensitivity analysis that varies these benefits across a wide range is reported.

Schroeder et al.[22] recently reported the first economic study of a birth cohort that had been subjected to UNHS (a follow-up of the Wessex 1993-1996 cohort.[30] The researchers calculated the societal costs of the previous year's services (social service, medical, and educational) for 62 PCHI individuals aged 7 to 9 years of age who had been subjected to UNHS, 60 PCHI individuals aged 7 to 9 years of age who had not been subjected to UNHS, and 63 controls of the same age and born in the same areas in the UK. The PCHI children averaged £9885.7 greater total costs than the normal children. In a regression analysis, the UNHS PCHI children were associated with a

greater cost than the non-UNHS PCHI children. However, the best estimate of difference (£2213.2) was associated with wide confidence intervals and was therefore not statistically significant.

Program implementation

Grill et al.[10] examined cost differences between UK UNHS programs that were hospital based and those that were community based (involving home visits at 10 days of age). The costs included staff costs, equipment costs, consumable costs, calibration costs, training costs, and travel costs. Community-based program costs were estimated to be slightly lower but the difference was not statistically significant. Of course, the differences between UK and Alberta need to be carefully considered. For example, travel costs in Alberta might be expected to be larger as distances might be longer on average. It may also be the case that UNHS in Alberta may be combined with other programs administered by Public Health nurses.

Alternative programs

One alternative to a UNHS program is a selective screening program which screens only infants judged to be at high risk for PCHI. These risk factors include family history of hearing impairment, low birth weight, congenital anomaly, perinatal infection, and birth complications such as asphyxia. A full comparison of selective screening programs to UNHS program should include not only an analysis of the difference in program effectiveness, but also an analysis of whether PCHI individuals not identified by a selective screening program would have been diagnosed more rapidly (e.g. before 6 mo.) by UNHS. What follows is a selective review.

On the basis of a Cochrane review, Puig et al.[21] note that there have been no RCTs that compare UNHS against any selective screening protocol and on this basis alone conclude that there is insufficient evidence to establish a long term effectiveness advantage for universal screening over selective screening.

On the basis of a systematic review, Thompson et al.[25] present composite estimates that a selective screening program would test 16% of newborns, would detect 55% of PCHI individuals vs 77% for UNHS by 10 months of age, and result in 81% fewer false positive screenings than would UNHS. The Number Needed to Screen (NNS) to treat one additional infant before the age of 10 months was estimated to be 2401.

Keren et al.[14], as part of a cost-effectiveness analysis, compared UNHS with selective screening programs. Based upon a literature review, they provided estimates that a selective screening program would test 10.4% of newborns, would detect 52% of PCHI individuals vs. 77% for UNHS by 6 months of age, and result in 93% fewer false positive screenings than would UNHS.

The Number Needed to Screen (NNS) to treat one additional infant before the age of 6 months was estimated to be 2172. The authors concluded that UNHS would be cost effective only if a high proportion of PCHI individuals achieved normal language outcomes after early intervention.

Grill et al.[9] developed a Markov Chain Model in Decision-making to compare the effectiveness of UNHS and a selective screening protocol. Model parameters were estimated on the basis of a systematic review and a retrospective cohort of German children. The model outputs included estimates that a selective screening program would test 20% of newborns, would detect 50% of PCHI individuals vs. 75% for UNHS by 6 months of age, and result in 80% fewer false positive screenings than would UNHS.

Kileny and Lesperance[15] noted that asymptomatic congenital human cytomegalovirus infection (HCMV) might account for a significant proportion of PCHI individuals not included in a risk factor screening. They suggest that a newborn screening for HCMV followed by continuing audiological follow-up of positive cases in additional to selective screening might be a viable alternative strategy to UNHS. Barbi et al.[1] reviewed the current feasibility of HCMV screening of newborn blood using existing technologies.

Recent advances in genetics research and the identification of genes responsible for many types of hearing impairment suggest a future where hearing testing may be conducted via genetic probes from a small blood sample.[19] Combining genetic screening for more common forms of genetic hearing loss as well as genetic screening for presence of congenital cytomegalovirus infection with electrophysiologic hearing testing may reduce false positive and false negative rates of current screening methods and improve identification of infants at risk for late-onset hearing loss.

Alberta data

Alberta statistical data is presented below as a context for consideration of program implementation and program type.

Iglesias et al.[11] report that in the calendar years 1999 and 2000, there were 86 hospital catchment areas in Alberta of which 86 were considered rural and 69 offered rural maternal care programs. These delivered 13,684 babies (62.7%) of the 21,840 babies delivered to mothers living in these areas or 18.6 % of the 74,533 babies born in Alberta in those two years.

Using Alberta Health and Wellness Hospital Morbidity records, we determined that in 1998 there were 38,690 births in Alberta. Of these, 3960 were placed into NICU at birth. In 2002, there were 39,983 births in Alberta. Of these, 5579 were placed into NICU at birth.

Summary

The current review leads to the following conclusions:

1. Alberta data does not allow an analysis of prevalence of PCHI or a definitive analysis of the current age of diagnosis of PCHI individuals. The creation of a registry of PCHI individuals would be necessary for the effective evaluation of any form of Newborn Hearing Screening Program.
2. Limited evidence has not yet been published that supports the pivotal assumption of a UNHS program. That is, that early detection leads to more effective habilitation.
3. Evidence has been published to suggest that UNHS program effectiveness is lower than efficacy estimates based upon analysis of technology characteristics alone. Specifically, specific strategies to minimize failure to screen and loss to follow-up should form a focus in the implementation of UNHS.
4. Limited evidence has not yet been published that UNHS is superior to alternative programs such as selective screening. Higher false positive rates (and therefore increased audiological assessments) threaten the cost-effectiveness of UNHS over selective screening programs. However, the weakest link in the evidence chain is the demonstration that earlier detection of individuals not located by a selective screening program will receive more effective habilitation.
5. In view of the widespread adoption of UNHS programs in Canadian provinces, the potential to perform a natural experiment in Alberta to contribute to the evidence base around Newborn Hearing Screening is worth consideration.

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SECTION TWO
TECHNOLOGICAL EFFECTS AND EFFECTIVENESS

Prepared by Paula Corabian

Abbreviations

AABR – Automated Auditory Brainstem Response
ABR - Auditory Brainstem Response
AHRQ – Agency for Healthcare Research and Quality
AN – Auditory Neuropathy
AOAE – Automatic Otoacoustic Emissions
ARC – Auditory Response Cradle
CAA - Canadian Academy of Audiology
CASLPA - Canadian Association of Speech Language Pathologists and Audiologists
CI95 - 95% confidence interval
CWGCH - Canadian Working Group on Childhood Hearing
dB – Decibel(s)
HI – Hearing Impairment
HL – Hearing Loss
Hz – Hertz
mo – Month(s)
NHS – Newborn Hearing Screening
NICU – Neonatal Intensive Care Unit
NNS – Number Needed to Screen
NPV – Negative Predictive Value
OAE – Evoked Otoacoustic Emissions
PCHI – Permanent Congenital Hearing Impairment
PHL – Permanent Hearing Loss
PPV – Positive Predictive Value
RCT – Randomized Controlled Trial
ROC – Receiver Operating Characteristic(s)
Sn – Sensitivity
Sp – Specificity
TEOAE – Transient Evoked Otoacoustic Emissions
THFC - The Hearing Foundation of Canada
UK – United Kingdom
UNHS – Universal Newborn Hearing Screening
USA – United States of America
USPTF – US Preventive Services Task Force
VRA – Visual Reinforcement Audiometry
WBN – Well-Baby Nursery
wk – Week(s)

Introduction

Reduced hearing, whether congenital or acquired during the first year of life, represents a barrier to speech and language acquisition and can interfere with a child's overall development.[1-8 9-16] According to recently published evidence, early identification and subsequent appropriate intervention (within the first 6 months) in children with permanent hearing impairment/loss can minimize these effects. As a result, there has been a growing interest for universal newborn hearing screening (UNHS) in attempts to diagnose permanent hearing impairment in childhood as early as possible. The rapid expansion of UNHS programs during the last decade has brought into focus questions about the most appropriate screening technology for this indication.

Request

This response addresses a request for information by Alberta Health and Wellness. The objective is to inform on and describe the background and the current evidence on the safety and efficacy/effectiveness of automated auditory brainstem response (AABR) and otoacoustic emissions (AOAE) technology when used as screening tools (either alone in a 1 stage screening program or together in a multi-stage screening program) for UNHS.

The specific aim of this review was to answer the following questions:

1. What is the accuracy of AABR and/or AOAE for differentiating newborns with normal hearing from those who need to be referred for diagnostic confirmation of congenital permanent childhood hearing impairment (PCHI) and appropriate intervention within their first six months of life?
2. Does the use of AABR and/or AOAE affect the detection rate for PCHI in infants within their first 6 months of life?
3. Does the use of AABR and/or AOAE affect the age at diagnosis of PCHI in infants?
4. Does the use of AABR and/or AOAE affect the age at start of treatment for PCHI in infants?
5. Does the use of AABR and/or AOAE affect the treatment decisions for PCHI in infants within their first 6 months of life?
6. Does the use of AABR and/or AOAE affect the developmental milestones (such as speech and language development), in infants and children diagnosed with PCHI?
7. Are there any side effects and complications to the newborn/infant and/or the screener due to performing the AABR and/or AOAE testing itself for newborn hearing screening?

Hearing impairment in childhood

Hearing impairment is a broad term used to describe complete or partial loss of the ability to hear in one or both ears (http://www.who.int/mediacentre/factsheets/fs300/en/index.html).[1-5,8,17 12,16] Hearing impairment in childhood may be sensorineural or conductive or a combination of the two (mixed) with additive effects, and may be congenital, acquired, transient, fluctuating, recurrent, progressive, or permanent. Etiologically, sensorineural hearing impairment involves a problem with the inner ear (e.g., cochlear dysfunction) and occasionally with the hearing nerve going from there to the brain. This type of hearing impairment is usually permanent and requires habilitation. Conductive hearing impairment is due to a problem in the outer (external) or middle ears and it is often medically or surgically treatable.

The prevalence of hearing impairment in childhood depends on what is included in the target disorder (http://www.who.int/mediacentre/factsheets/fs300/en/index.html).[1-5,8,17-21,10,12,22] Usually the target disorder is described by impairment severity, frequency range, laterality (one or both ears), and permanence, as well as the site of the disorder in the auditory system and the associated categories of impairment type.

The degree of hearing impairment refers to the severity of hearing loss and it is described in decibels (dB), a unit of intensity or loudness, at various hearing frequencies. Several different classification schemes have been used for degree of hearing impairment, and currently there is no universally accepted system (http://www.asha.org/public/hearing/disorders/types.htm), (http://www.who.int/pbd/deafness/hearing_impairment_grades/en/index.html), (http://www.canadianaudiology.ca/consumers/children/degree.html).[16,23] The World Health Organization classifies impairment as slight/mild (26-40 dB, in better ear), moderate (41-60 dB, in better ear), severe (61-80 dB, in better ear), and profound (≥81 dB, in better ear) (http://www.who.int/pbd/deafness/hearing_impairment_grades/en/index.html).

Definition of target disorder

For the purposes of this document, the target disorder is hearing impairment in childhood that is congenital and is stable or progressive, which is referred to as permanent childhood hearing impairment/loss or permanent congenital hearing impairment/loss (PCHI). Most PCHI is sensorineural and irreversible.[1-5,8,17-21,10,12,22] Structural conductive impairments are usually included because they impose long-standing dysfunction, unless treated. The incidence of PCHI varies with race, gender, birthweight, intra-uterine infection, and other risk factors, including family history of hearing impairment or chromosomal abnormality. This condition has a wide range of severity, which for an individual may fluctuate over the time. Severity may not be symmetrical for both ears.

PCHI can be expected to lead to delays and deficits in the development of speech, language, cognition and learning, as well as secondary effects on the child and the family.[1-5,8,17,18,20,21, 24 26,10,12,15,16,22] The principal factors, which may decide how PCHI affects a child's overall development, are the degree of hearing impairment and the age at which it is diagnosed.

Epidemiology

PCHI is one of the most common congenital anomalies found at birth.[1-5,8,17,18,20,24,25,27,10,12,16,22] In Western, industrialized societies, the prevalence of PCHI is about 1 in 1000 live births in infancy, if one uses 40dB hearing loss (HL) in the better ear as the cut-off audiometric criteria. This rate increases to about 2 in 1000 live births over the first decade of life. Such increases are attributable to acquired, late-onset, and progressive impairment, the prevalence and time course of which are still unclear. If audiometric criteria for PCHI are broadened to include lesser severities (down to $>$ 25 dB HL) and unilateral losses, the prevalence in early infancy increases to 2 to 3 in 1000. Up to 50% of cases are thought to be due to environmental factors and the reminder to genetic causes.[20,25,12,28]

Early identification of PCHI

There is limited scientific evidence to suggest that early identification (at 3 to 6 months) and administration of appropriate intervention (such as amplification via hearing aids or cochlear implant, sign language, total communication programs, and/or surgery) at or before 6 months of age provides a child with impaired hearing the opportunity to develop normal speech and language.[1-4,8,17,18,20,21,24,25,27,12-15,29] As a result, many countries have implemented neonatal hearing screening programs.

In the absence of systematic infant screening, the detection, confirmation, diagnosis and treatment of hearing impairment may be significantly delayed.[1-3,8,17,18,20,21,24,9-11,16,29] All degrees and configurations of PCHI present with great subtlety, and the majority of parents experience great difficulty in identifying their child's hearing loss before speech and language delay make it self-evident. Hearing loss in many children with hearing impairment is not identified until after the age of 1 year or well after the development of speech and language skills. The age at which hearing loss is detected without a screening program depends on the severity of the hearing loss and is found later in those with less severe deficits. With screening, the median age of diagnosis for children with PCHI ranges from 2 to 6 months and there are no significant differences in the ages at diagnosis for children with different degrees of hearing loss.

The reported average age at which hearing impairment is detected in North America ranges between 1 year and 3 years.[8,24,9,11,14] A study of ages at detection, diagnosis, and intervention in Canada examined the records of 613 children fitted with hearing aids at the Children's Hospital of Eastern Ontario.[8,24] The ages at diagnosis ranged from about 2 to 4 years in a referred group with risk indicators and from 2 to 7 years in a group without risk indicators, the lower age limits relating to "profound" impairment and the upper age limits to "mild" impairment. The median age at diagnosis was 6 months or less in a screened group, irrespective of impairment severity. Results reported in other studies are consistent with these findings.[1-3]

Newborn Hearing Screening

Newborn hearing screening identifies those infants most likely to have hearing impairment (auditory disorders) that may interfere with their health, development, communication, or education.[1,3-5,8,17,18,20,21,30] It may result in recommendations for re-screening, standard or complex audiological assessment, or in referral for other examinations or services.

The target population for newborn hearing screening may include only the 8-15% of newborns from the general population who are likely to be at specific risk of PCHI (selective screening) or all newborns (universal, population-based, screening).[1-5,8,17,18,21,31] Prior to the implementation of UNHS, only newborns identified as being at high-risk for hearing loss such as those in a neonatal intensive care unit (NICU) were routinely screened using a risk assessment tool (high risk registry).

Substantially fewer resources are required to screen only the high-risk group, relative to those required for UNHS. Populations at risk for hearing impairment differ from the general population, particularly in the prevalence of PCHI.[1-5,8,17,18,21,31,32 12] The prevalence of hearing impairment in high-risk groups is about 8 to 20 times greater than that in the general population. Relative to UNHS, this increase in base prevalence increases the positive predictive value (PPV) of a screening "refer" result (non-"pass"), and reduces the number needed to screen (NNS) in order to identify an additional case.

However, a limitation of selective screening (in at-risk populations) is that as many as 50% of infants with PCHI have no known risk factors.[1,2,4,5,8,17,18,21,32,10,11,14] Also, risk assessment has been viewed as a documentation-based screening test with poor sensitivity and specificity. A logistical problem is how to identify high-risk infants in a timely and accurate manner, since comprehensive and accurate assessment of risks is a difficult and time-consuming task. Low birth-weight and admission to NICU are easily identified, but it is not always possible to ascertain a family history of hearing impairment or chromosomal abnormality before hospital discharge.

In addition, some major risk indicators, including the asymptomatic cytomegalovirus infection and the manifestations of syndromes known to be associated with PCHI (such as craniofacial anatomical anomalies), may not be routinely determined and documented.[1,8] Many risk indicators are interrelated, their individual predictive values are not well understood, and their evidence base is often less than adequate.

The relatively high incidence of deafness in infants without known risk factors and the introduction of new screening technology over the last 15 years, has led prestigious bodies in many countries worldwide to recommend UNHS as an alternative to selective screening.[1-5,8,18,21,25,30 9,10,14,16] Recent approaches emphasize the use of the risk factors as the primary indicator for newborn hearing screening only in situations where resources for a UNHS program are limited.

Screening tools

Historically, behavioural tests were used for hearing screening in newborns to observe their behaviour in response to auditory stimuli (sound).[1,2,21,26,32,10,11,14,16,22,29,32,33] Behavioural observation audiometry has been discredited because of poor accuracy and reliability. Behavioural testing using operant conditioning, such as visual reinforcement audiometry (VRA) usually becomes feasible at the age of 6 to 9 months, as it requires involvement and cooperation of the child. Automated, microprocessor controlled, and objective tests such as the Crib-o-gram and the auditory response cradle (ARC) were developed to eliminate observer bias associated with behavioural observation of newborns' response to sound. The ARC added detection of physiologic response into behavioural response evaluation of newborns. However, reports conflict on the efficacy and reliability of these screening methods.

Because of the problems associated with the use of behavioural tests for newborn hearing screening (such as low accuracy, need for high operator skills, and their time consuming nature), the research focused on developing electrophysiologic, non-behavioural tests.[1,2,21,26,32,9-11,14,22,29,32,33] A leap forward was taken with the introduction of two non-invasive, objective methods that measure physiological mechanisms related to hearing such as auditory brainstem responses (ABR) and evoked otoacoustic emissions (OAE) (www.otoemissions.org).[1,2,4,5,8,17,20,21,25,34-36]

The ABR testing appeared before the OAE testing in the field of hearing screening in newborns and older infants (www.otoemissions.org).[1,4,5,8,17,20,21,34-36] ABR evaluate the integrity of the peripheral auditory system and the auditory (eighth nerve) pathway up to the brainstem. The ABR are auditory evoked potentials (that originate from the auditory nerve) generated in the brainstem in response to controlled auditory signals (sound/noise), composed of either

clicks or tones. The ABR testing can detect damage to the cochlea, the auditory nerve and the auditory pathways in the stem of the brain.

The ABR testing is a widely accepted proxy gold standard measure of hearing sensitivity in newborns and infants.[1,5,8,18,20,21,24,32] ABR measurements can yield ear-specific, frequency-specific estimates of perceptual threshold, as well as other information about the functional status of auditory neural pathways. The ABR testing has been employed in the initial newborn hearing screening process and is considered the gold standard of hearing tests available for UNHS programs. It is also used for definitive hearing testing in infants. It typically involves manual selection of stimulus and recording parameters, and subjective interpretation of averaged ABR waveforms by an expert. Therefore ABR testing as a screening tool is complex and time-consuming and it has only been feasible as a selective screen of neonates with identifiable risk factors.

OAE evaluate the integrity of the inner ear (cochlea) and are measurements of the response of the outer hair cells to controlled acoustical stimulation (sound/noise), either clicks or tones (www.otoemissions.org).[1,4,5,8,17-19,21,30,36] In response to noise, vibrations of the outer hair cells in the healthy inner ear (normal cochlea) generate electrical responses (faint sounds), which are radiated back through the middle ear to the external canal. OAE presence or absence reflects normal or abnormal hearing sensitivity up to and including the cochlea. Most normal ears yield an OAE, but the likelihood of obtaining a response decreases rapidly in the presence of a PCHI of 25-30 dB HL or greater. OAE testing can detect blockage in the outer ear canal, middle ear fluid, and damage to the outer hair cells in the cochlea.

Currently, the ability to screen large numbers of newborns relies on the use of automated ABR testing and OAE testing devices, specifically designed for this purpose during early 1990s (www.otoemissions.org), (www.infanthearing.org).[1,4,5,8,18,22,30,17,19,36]

Automated ABR and OAE testing as screening tools

Automated ABR (AABR) screening is an adaptation of conventional ABR screening.[1,4,5,8,17,18,20,24,32,37] The AABR device delivers a rapid series of low-intensity clicks (usually at about 35 dB hearing level) through an insert or supra-aural earphone and record electrical activity from the scalp via electrodes/sensors. Averaged electrical waveforms are computed and automated statistical response detection algorithms evaluate the presence or absence of the ABR. AABR systems compare an infant's waveform with that of a template developed from normative ABR infant data and a pass/refer result is determined. The test takes up to 10 minutes per baby.

Automated OAE (AOAE) screening measures either transient-evoked OAE (TEOAE) or distortion-product OAE (DPOAE) (www.otoemissions.org).[1,2,5,8,34,35,38] Both types are frequency-specific measurements of peripheral auditory sensitivity. A transducer placed in the ear delivers the stimuli and records OAE for immediate computer processing. Multiple responses are averaged to get a specific repeatable waveform and a pass/refer result. The test takes less than 5 minutes per baby. Provided that the middle ear function is normal, these measurements can be used to assess cochlear function for 500- to 6000-Hz frequency range. However, the fact that a newborn infant has acceptable OAE at the tested frequencies (a pass case) does not imply that the infant can hear (www.otoemissions.org).

Advantages and limitations

Both AABR and AOAE methods are rapid and easy to perform at bedside in inpatient or outpatient settings (www.infanthearing.org), (www.otoemissions.org).[1,4,5,8,17,18,20,21,32,34-36,38] These tests are performed on any newborn that is asleep or at least at quiet rest (generally after feeding), in a moderately quiet test environment. Neither method needs voluntary responses and can be carried out on newborns without sedation.

The automation of measurement and results interpretation reduced the amount of knowledge and skills required in the screeners (www.infanthearing.org), (www.otoemissions.org).[1,5,8,21,24,34,35,38,9-11,14,39] However, the screeners must understand the limitations of these techniques and some skill is required, especially in choosing an appropriate behavioural state of the newborn when testing, and the correct placement of the recording electrodes and earphone/earprobe. Both technologies allow for a variety of personnel to be trained as screeners, including audiologists, nurses, speech-language pathologists, screening technicians, and volunteers. Ongoing quality control is essential for accurate, consistent test results.

Although the use of AABR and AOAE technologies emerged as an integral part of newborn hearing screening, none provides a direct measure of hearing (www.infanthearing.org), (www.otoemissions.org).[1,4,5,8,20,21,34-36] Both methods test the structural integrity of the auditory pathway. They are not considered true screening tests of hearing, as they do not assess cortical processing of sound.[36] Even if an infant passes screening with these tests, hearing cannot be definitively considered normal until the child is mature enough for a reliable behavioural audiogram to be obtained.

Both OAE and ABR methods are highly correlated with the degree of peripheral hearing sensitivity and the AABR and AOAE screening technologies are not specifically designed to identify infants with central hearing deficits (www.infanthearing.org).[1,4,8,17,18,21,32,36,10,11] Infants with a reverse

slope loss or those with risk factors for central hearing deficits, particularly those who have congenital Cytomegalovirus infection or prolonged severe hypoxia at birth, may pass their hearing screens with either one of these technologies. Infants with precipitous losses, those with mild and very mild losses (25 to 30 dB) as well as those with low frequency losses (below 1kHz) are likely to pass screening with AABR.

AABR can screen for hearing loss due to auditory neuropathy (AN) in newborns whereas AOAE screening does not screen for neural auditory pathology or dysfunction (www.infanthearing.org).[1,4,5,8,17,21,32,9-11,14] AN was recognized relatively recently and may comprise up to 10% of all PCHI in infants. As currently defined, it is not a single entity but a cluster of pathologies that may involve inner hair cells, synapses with primary nerve fibres, and/or the cochlear nerve itself. It appears to be associated with a variety of perinatal insults, including hyper-bilirubinemia and severe hypoxia, but there are also several genetic varieties. The majority of infants with AN are likely to have been in an NICU. Therefore, the use of AABR screening in all NICU graduates is recommended in order to identify most cases.

The AABR lacks frequency-specific information and cannot be used to determine the degree or nature of hearing loss (http://www.infanthearing.org).[4,2,8,11,17,32,9,10,29,39,1,5] AOAE devices have potential for providing frequency specific information. In addition to being used for newborn hearing screening, they can be used in children and adults for monitoring the effects of surgery and drug administration and for various diagnostic applications (http://www.infanthearing.org).[4,1,2,5,8,17,32,34]

However, AOAE screening may require interpretation by the screener while AABR screening does not (http://www.infanthearing.org).[1,2,4,5,8,17,32,34,35] Although TEOAE technology has been used since the early 1990's for newborn hearing screening, there are still many different pass/refer criteria being used in TEOAE-based programs. DPOAE devices are the most recent of the available AOAE techniques and there is still a lot of disagreement about what constitutes a pass or a refer result. Also, there is still no unanimity about what parameters are best for screening with DPOAE (e.g., the different primaries to be used for frequencies, the intensity of the stimulus, or how many data points per octave are required for an adequate test).

Average referral rates for hearing loss of 4% may be achievable using AABR alone (http://www.infanthearing.org).[29] Average referral rates of 8% and 7% may be achievable using DPOAE alone and TEOAE alone, respectively. False-positive results for PCHI from AOAE screening refer results can be caused by any mechanism that interferes with sound transmission from

the earphone to the cochlea and back to the recording microphone (www.infanthearing.org), (www.otoemissions.org).[11,1,2,4,5,8,9,17,18,20,29,32,34-36,38,39] Common problems include debris or fluid in the middle ear or in the external canal, and the latter is more common when AOAE screening is done within 24 hours of birth. AABR results are less affected by middle or external ear debris.

AOAE screening involves only application of a small probe in the outer ear, which makes it acceptable to parents and infants (www.infanthearing.org).[4,5,8,17,32,34,35] Applying electrodes when using AABR screening may be perceived by parents as more invasive.

Screening with AABR devices takes longer in comparison with AOAE devices (http://www.infanthearing.org).[8,17] However, due to improvements in the AABR algorithms the time differences between AABR and AOAE testing are decreasing. The advantages and limitations of AABR and AOAE technologies are summarized in Table 1.

Table 1: Summary of advantages and limitations of AABR and AOAE

Technology	Advantages	Limitations
AABR (measures activity of auditory nerve and brainstem pathways)	Non-invasive Quick, simple operation Provides ear-specific results; response not dependant on infant cooperation Can be carried out on newborns without sedation Can screen for HL due to AN May be administered at bedside Requires no interpretation by screener Average referral rates for HL of < 4% may be achievable using AABR alone Pass/refer results are immediately available Print out of results Results are less affected by middle ear or external ear debris than AOAE A variety of personnel can be trained as screeners	Does not directly measure hearing and is not considered a true screening test of hearing Requires a sleeping or quiet infant May not detect infants with reverse slope loss, or those with risk factors for hearing deficits May not detect infants with mild and very mild HL and those with low frequency HL More susceptible to electrical interference Cannot provide frequency-specific information Initial investment and cost of disposables are relatively high (higher than for AOAE) May be less acceptable to parents

Table 1: Summary of advantages and limitations of AABR and AOAE (continued)

Technology	Advantages	Limitations
AOAE (measures cochlear response to controlled acoustic stimulus; provides information up to and including the cochlea)	Non-invasive Quick, simple operation Provides ear-specific results; response not dependant on infant cooperation Can be carried out on newborns without sedation May be administered at bedside Average referral rates for HL of <4% may be achievable using OAE alone (especially if screened after 24 hours of age) Can provide frequency specific information Motion artefacts interfere less with results Pass/refer results are immediately available Print out of results A variety of personnel can be trained as screeners	Does not directly measure hearing and is not considered a true screening test of hearing Requires a sleeping or quiet infant Does not detect nerve or auditory brainstem pathway dysfunction May not detect infants with reverse slope loss, or those with risk factors for hearing deficits Debris or fluid in the external and middle ear can affect results Screeners may need to decide what constitutes a pass/refer response

AABR and AOAE in newborn hearing screening protocols

Typically, newborn hearing screening programs use multi-stage (2- or 3-stage) protocols, which involve more than one screening test (www.infanthearing.org), (www.otoemissions.org).[1,4,8,17,18,32,40,41,10,22] The multi-stage protocols aim to achieve very low overall false positive rates.

Different approaches have been taken in the well-baby and NICU nurseries (www.infanthearing.org), (www.otoemissions.org).[1,2,4,8,17,18,32,40,9,22] In some programs, infants at high risk of PCHI are screened with AABR only, whereas babies not at risk (or at low-risk) are initially screened by AOAE (either TEOAE or DPOAE) and then by AABR.

AABR and AOAE devices available in North America

In North America several companies offer AABR and/or AOAE screening devices for newborn hearing screening (www.fda.gov/), (www.mdall.ca), (www.infanthearing.org), (www.otoemissions.org).[5,17,42]

Table 2 lists the products that are currently offered, according to the information accessed on their manufacturers'/distributors' websites.

They include various models of portable or handheld (battery-operated) devices, which can be stand-alone (TEOAE, DPOAE, or AABR only) and/or combination units. Combination units configure in multiple ways of TEOAE, DPOAE, and AABR technology in a single device, allowing AOAE/AABR or AABR/AOAE testing sequence in a single screening session. When optimal conditions for screening are met, testing can take 10 to 30 seconds per ear for measuring OAE and 1.5 to 2 minutes per ear for measuring ABR. Test results can be stored in memory for review on the display or printing to the printer which ca be connected directly to the device.

Table 2: AABR and AOAE devices for newborn hearing screening

		Technology		
Manufacturer/ Distributor	Device Name	AABR	DOPAE	TEOAE
Viasys Healthcare Inc., Neurocare Group, Grason Stadler Divisions http://www.viasyshealthcare.com	GSI 70 (Portable devices		x	
	GSI Audioscreener (Handheld device)	x	x	x
	GSI Audera (Portable devices)	x	x	
Interacoustics A/S http://www.interacoustics.com	Otoread (Handheld device)		x	x
	TEOAE 25 (Portable device)			x
	DPOAE 20 (Portable device)		x	
GN Otometrics (Madsen) http://www.gnotometrics.com	Accuscreen (Handheld device)	x	x	x
Maico Diagnostics http://www.maico.com	Ero-Scan (Handheld and portable devices)		x	x
	ALGO 3i (Handheld device)	x		
Natus Medical Inc. http:/www.natus.com	ALGO 3 (Portable device)	x		
Bio-logic System Corp. (a Natus company) http://www.bio-logic.com	Echo-Screen (Handheld device)	x	x	x
	ABaer (Portable device)	x	x	x
	AuDX, AuDX Pro, AuDX Pro II, AuDX Pro Plus (Handheld and portable devices)		x	x
SonaMed Corp. http:/www.sonamed.com	Clarity Screener (Portable device)	x	x	

Safety

According to the manufacturers and distributors of AABR and AOAE technologies currently available in North America (see Table 2), these devices are designed, tested and manufactured to meet the North American, European, and/or International Standards for Medical Electrical Equipment, and comply with the Medical Device Directive. According to Gravel et al.,[39] the stimuli generated by either technology are not harmful and no issues or concerns have been raised about the safety of either AOAE (DPOAE or TEOAE) or AABR.

All manufacturers/distributors emphasize the importance of correct assembly and placement of probe and electrodes/sensors, deemed as crucial to the success of screening newborns for hearing loss. If screeners follow the guidelines for assembling and placing the sensors and probes and take normal care in handling babies there should be no risk associated with performing the test itself. Failure to follow guidelines can lead to cross-infection of infant/screener, and poor probe fit can lead to unnecessarily long testing and the possibility of overly high stimulation. Extreme care is recommended regarding the preparation of the skin for sensors placement.

Risks associated with newborn hearing screening using any of the AABR and/or AOAE devices available on the market include anxiety due to false positive results and possible delayed diagnosis and appropriate treatment due to false negative results.[1-3,5,8,17,43,10,11,14,22,39,44] False positive results may also lead to disease labelling, iatrogenesis from unnecessary testing, and increased costs in terms of time and money.

Regulatory status in Canada

In Canada, the following companies are licensed to market AABR and AOAE devices for newborn hearing screening: Viasys Healthcare Inc., Neurocare Group, Grason Stadler Divisions (GSI 70®, GSI Audera®, and GSI Audioscreener®), Maico Diagnostics (Ero-Scan®); Otodynamics Ltd. (Echocheck® and Echoport®); Interacoustics (OtoRead® and TEOAE 25®); GN Otometrics (Accuscreen®); and Natus Medical Inc. and Bio-logic Systems Corp. (ALGO Portable®, ALGO 3®, ALGO 3i®, Abaer®, Echo-Screen®, AuDX®, AuDX Pro®, AuDX Pro II®, and AuDX Pro Plus®) (Medical Devices Bureau, Health Canada, personal communication, October 2006), (www.mdall.ca), (AIM Technologies, personal communication, November 2006).

Newborn Hearing Screening in Canada

There is evidence to suggest that 6 in every 1000 babies born every year in Canada have some degree of hearing impairment (including unilateral, bilateral, conductive, and sensorineural).[1,7,24,45,32] According to Hyde[8] 2 to 3 in

1000 infants have congenital hearing impairment that merits early detection, which mean up to 1100 new cases annually across Canada.

In the past four decades, the importance of the early identification and management of hearing impairment in children has been the subject of many conferences and task forces in Canada.[1,6,7,14,31,32,33] During this time, recommendations have been formulated addressing the need to identify PCHI early in children, with three main themes recurring consistently. These include: the methods used to identify hearing impairment accurately in newborns and infants; the population to be screened; and the need to educate physicians, other health care professionals, and parents on the signs of hearing impairment in children.

However, before 2000 there was no systematic approach to these issues.[1,8,24,40,45-47] A national survey on Newborn Hearing Screening was conducted in 1998 to determine the state of UNHS programs within Canada.[46] A questionnaire was sent to all birthing hospitals identified in Canada (n=467). Of the 384 hospitals which responded to the questionnaire (approximately 82% return rate), only 35 had newborn hearing screening programs (of any type). The hospitals that had a screening program accounted for 25% of the infants born in Canada during the survey period. Most provinces/territories had at least one program, except Nunavut and Yukon. Fifty-one percent of the programs were situated in rural locations and the remainder in urban hospitals. At the time of the survey, Alberta had two programs situated in urban hospitals.

The majority of centres with screening programs (54%) used either a high-risk registry or confined screening to a defined target population within the hospital.[46] Of the sites using physiological screening protocols, there was an even split in the number using OAE versus ABR. Thirty-eight percent of the centres used conventional ABR while 9% used AABR. The majority of centres that used AOAEs employed DPOAE technology (as the test of choice). Seventy-one percent, 57%, 26%, 9%, and 14% of screening programs used audiologists, nursing staff, volunteers, and other personnel, respectively. Only 31% of NHS programs used a computer-based data management system. These findings suggested that before 2000 little progress was made towards meeting previous recommendations for the identification of hearing impairment in children in Canada.

However, since 2000 there has been a growing awareness and dialogue at the federal level and among provincial governments, professional health associations, educators and other stakeholders about early hearing detection and intervention as an important public health issue.[1,6,8,48,49] In 2000, Alberta initiated a pilot project for UNHS, Ontario implemented a UNHS program, and Health Canada established the Canadian Working Group on Childhood Hearing (CWGCH).

UNHS is now offered in British Columbia, Yukon, Nunavut, eastern part of the Northwest Territories, Manitoba, Ontario, Quebec, New Brunswick, Nova Scotia, and Prince Edward Island.[1,6-8,45,48,49 50] Newborn hearing screening is offered to select populations or by request in Alberta, Saskatchewan, and the western part of the Northwest Territories.[50]

Available research evidence

The research evidence presented in this report is based on a review of published systematic reviews and health technology assessment (HTA) studies conducted on the use of the AOAE and/or AABR technologies for UNHS. The literature search and retrieval methods are outlined in Appendices A and B.

Only published reports of systematic reviews and HTA studies that, by virtue of design and quality of reporting[51-53] were most likely to provide the best level of evidence, were selected for data extraction. Individual primary research studies (of any design) published subsequent to the selected systematic reviews and HTA studies are not included.

Of all retrieved full text articles, only two secondary research studies[2,3] fulfilled the criteria for a systematic review by posing a clear question a priori; by identifying the relevant literature, extracting the data, and assessing the methodological quality of the reviewed primary research in a reproducible fashion; by qualitatively or quantitatively summarizing and analysing the reviewed evidence; and by exploring the sources of variation in the results from study to study.

The following commentary summarizes the findings reported by the selected systematic reviews. Details of these studies are provided in Tables C1 and C2 (see Appendix C).

Efficacy/effectiveness

Thompson et al.[2,21] undertook a systematic review to identify strengths, weaknesses, and gaps in the evidence supporting UNHS and compare the additional benefits and harms of UNHS with those of selective screening of high-risk newborns. They focused their literature search on questions underlying the clinical logic behind newborn hearing screening. The clinical logic assumes that screening tests are accurate; that screening reduces delays in diagnosis and treatment; that earlier treatment results in better language function within the preschool period; and that this improvement in early language function will improve educational, occupational, and social function later in life. For UNHS to be preferred over selective screening, the potential benefits of early detection and treatment must be realized in the subgroup of newborns who have no risk factors and would not otherwise be screened.

The authors used the data accumulated from 19 studies (including one good quality non randomized controlled trial, several cohort studies, of which only two were of good methodological quality, and some case-control analytic studies) to answer four questions:

Question # 1

Can UNHS accurately diagnose moderate-to-profound sensorineural hearing impairment?

Thompson et al.[2,21] found good evidence (from one good quality non-randomized controlled trial and one good quality accuracy cohort study) that AOAE and AABR are accurate screening tests for congenital permanent hearing loss (PHL).

Thompson et al.[2,21] selected 11 publications providing information about the performance of AOAE and AABR when used for newborn hearing screening. These included 10 studies providing information on the yield of UNHS programs (one non-randomized controlled trial, four reports on state-based programs, five reports on hospital-based programs) and one large accuracy cohort study.

Most programs in the selected ten UNHS studies used a 2-stage screening protocol, in which an infant who did not pass the initial test (TEOAE or AABR) was re-tested (TEOAE or AABR) in the hospital or as an outpatient within 12 weeks of discharge, and was referred for audiological evaluation if he/she "failed" the second test. Criteria for defining a "pass" or "fail" on the initial screening test varied, and the results were sensitive to equipment, the tester's training, and the ongoing quality control.

None of the ten UNHS studies evaluated the sensitivity and specificity of neonatal screening against an independent gold standard, although three studies reported the percentage of cases (6% to 15%) that were missed by screening but eventually diagnosed by other means. Among the infants with positive screening test results, the likelihood that the infant had hearing loss varied by study. In the two good quality studies, 2-stage screening detected one case of bilateral, moderate-to-profound PHL for every 925 to 1422 screened newborns. The yield was 2041 to 2794 low-risk and 86 to 208 high-risk screened newborns to find one moderate-to-profound PHL case.

According to **Thompson et al**.[2,21], there was no systematic difference in the performance of TEOAE or AABR when used as the initial test for screening in the UNHS programs described in these studies. Referral rates varied depending on the screening method used in the program, but rates were lower for 2-stage protocols. The referral rate reported by one good quality cohort study for stage 1 of a 2-stage protocol (TEOAE followed by TEOAE or AABR at birth admission) was 6.5%. In one good quality non-randomized controlled study,

the referral rate of a 2-stage protocol (TEOAE followed by AABR) was 1.6%, false negative rate was 15%, and the overall positive predictive value (PPV) for the moderate-to-profound PHL was 6.7%. In the same study, the PPV was 2.2% for well-babies and PPV was 20% for high risk babies.

Thompson et al.[2,21] also selected to review one large good quality accuracy cohort study published by **Norton et al.**[54] in 2000. **Norton et al.**[54] measured the sensitivity and specificity of AOAE (DPOAE and TEOAE) and ABR (not clear if conventional ABR or AABR technology) in 4911 infants who were considered to be at risk for hearing loss. The study population included 4478 graduates from NICUs, 353 well babies with one or more risk factors for hearing loss, and 80 well babies without risk factors who did not pass one or more neonatal tests. The visual reinforcement audiometry (VRA), performed at age 8 to 12 months, was used as an independent gold standard. Of all at-risk infants targeted for follow-up, 64% returned for behavioural hearing testing, and VRA data were obtained in 95.6% of returnees.

Based on their results, **Norton et al**.[54] concluded that all evaluated screening tests performed similarly at predicting behavioural hearing status at 8 to 12 months. The test performances, as measured by the area under a relative operating characteristic curve (ROC), were similar for all three tests when compared with VRA. Performance was similar for all three tests when they were used to identify hearing loss at frequencies of 2 and 4 kHz. However, ABR was more successful at determining auditory status at 1 kHz, compared with the AOAE tests. All three tests resulted in low refer rates, especially if referrals for follow-up were made only for the cases in which stopping criteria were not met in both ears. The use of a 2-stage protocol similar to that recommended in the National Institutes of Health Consensus Conference report (1993) resulted in refer rates that were less than 4%.

According to Thompson et al.2,21 the estimates of accuracy and yield as reported by Norton et al.54 were probably more reliable than those from the actual screening programs on which their other selected 10 studies reported. The evaluated screening tests were found not to be sensitive enough to rule out significant hearing loss. The AOAE technology was very sensitive (98%) for severe hearing loss but was less sensitive (80%) for moderate and profound losses; at this sensitivity, the specificity of the AOAE was 80%21. For ABR, sensitivity and specificity were 84% and 90%, respectively. In approximately 3000 high-risk children who underwent neonatal screening and returned for follow-up testing at 8 to 12 months of age, the 2-stage protocol missed 11% of affected ears. Overall neonatal testing resulted in a final diagnosis of bilateral moderate-to-profound PHL among 1 in 230 high-risk and 1 in 2348 low-risk infants.

Question # 2

In UNHS programs, how many children are identified and treated early (before 6 months)?

According to **Thompson et al.**[2] there is good evidence to suggest that UNHS increases the chance that diagnosis and treatment will occur before 6 months of age. However, no controlled trials of UNHS versus selective screening have been done.

Thompson et al.[2,21] selected one good quality non-randomized controlled study conducted in the United Kingdom and one best quality cohort study conducted in the United States that reported on the frequency of treatment before 6 and 10 months, respectively. These studies' results suggested that UNHS increases early identification between 19% and 42% compared with selective screening in high-risk infants. Other studies did not provide sufficient information, and none reported the proportion of infants who, although screened, were diagnosed and treated late because of loss to follow-up.

Question # 3

Does identification and treatment prior to age of 6 months improve language and communication?

Thompson et al.[2] found no conclusive evidence to answer this question.

The literature search conducted by **Thompson et al.**[2,21] revealed no prospective, controlled study that directly examined whether newborn hearing screening results and early diagnosis and intervention give rise to improved speech, language, and/or educational development. No prospective cohort studies or controlled trials have followed screened and non-screened groups of newborns over time to evaluate language outcomes. None of the state-based programs described in four of the ten selected studies on UNHS reported the outcomes of treatment for infants identified to have hearing impairment.

Thompson et al.[2,21] selected for their review 8 retrospective observational studies, which reported results obtained by three intervention programs (studies which investigated speech and language development in children with PCHI identified through UNHS). Although the studies reported improved language and communicative skills in children who were identified and treated before 6 months, these studies were fair to poor in methodological quality. Selection bias and baseline differences between compared groups were noted. The authors of these studies did not specifically describe outcomes in the subgroup of children who would be identified by UNHS but not by selective screening.

Question # 4

What are the potential adverse effects of screening and of early treatment?

Thompson et al.[2] found no conclusive evidence to answer this question. Most postulated adverse effects have not been evaluated in their reviewed studies. No studies examined whether early screening and intervention adversely affects the child or the parent-child relationship.

As part of their review, **Thompson et al.**[2,21] also constructed a mathematical model of the benefits and harms of UNHS and selective screening in a hypothetical cohort of 10,000 newborns. The results of their literature review were used to estimate prevalence, sensitivity and specificity, compliance, the likelihood of being diagnosed and treated before 10 months, treatment effect size, and other parameters of this model. Base case assumptions were derived from their ten selected studies of UNHS programs.

The sensitivity and specificity of the hypothetical model's 2-stage screening was 85% and 97%, respectively.[2,21] The estimated PPV was 6.7%. Based on this model, it was estimated that with UNHS an additional 7800 screening tests would be done, resulting in the diagnosis of six additional cases of moderate-to-profound hearing loss diagnosed before 10 months of age. Of these, three additional cases would be treated before 10 months of age. Thus, the number needed to screen (NNS) to detect one additional case before 10 months would be 1441 and the NNS to treat one additional case before 10 months would be 2401. With UNHS, 254 newborns would be referred for audiological evaluation because of false-positive second-stage screening test results (versus 48 for selective screening), and 1 of these would also be falsely diagnosed to have PHL at the first post-hospital visist to an audiologist.

Because of the lack of data, **Thompson et al.**[2,21] could not estimate how many of the 6 additional early-diagnosed, low-risk newborns would actually benefit from early treatment. They used a hypothetical example saying that "if 50% of low-risk newborns with PHL would have poor language ability if diagnosed after age 10 months, and early intervention reduced this by 50%, then the NNS to prevent 1additional case of delayed language acquisition would be 6771".

Thompson et al.[2,21] identified several gaps in the information about the effectiveness of UNHS using AABR and/or AOAE. Although these devices can improve identification of newborns with PCHI, as many as 10% of screened newborns with normal or temporarily impaired hearing would require a second screening test. From 1% to 3% of screened newborns would be referred for audiological assessment and over 90% of those referred cases might be false positive results. The consequences of the false positive results have not been adequately evaluated, nor has the reliability of audiological and behavioural assessment used in making treatment decisions.

Thompson et al.[2,21] found false negative rates higher than previously thought (20% to 30% in most programs). These findings called into question the assumption that a newborn who passes a screening test has normal hearing. These findings also suggested that stricter "pass" criteria used to reduce false positives may also reduce the effectiveness of screening.

Puig et al.[3] recently conducted a **Cochrane Systematic Review** to assess the long-term effectiveness (benefits) of a UNHS program (using TEOAE or AABR) and earlier treatment for childhood deafness in comparison with selective screening (by TEOAE or AABR) and treatment. They defined "selective screening" as either "high-risk screening or opportunistic screening". "Opportunistic screening" was defined as "detection of hearing impairment performed in an unsystematic way, e.g. by visiting a pediatrician for other health problems".

None of the studies identified by the searches conducted by **Puig et al.**[3] fulfilled the inclusion criteria and thus no trials were included in their systematic review. The majority of the identified studies were either controlled comparisons of hearing screening versus no hearing screening, comparisons of diagnostic tests for detecting hearing impairment, or description of series or single cohorts of patients undergoing a screening program. No studies were excluded on grounds of poor methodology.

According to **Puig et al.**[3], UNHS programs have proven valuable in increasing detection of infants with hearing loss. However, they found no evidence on the long-term effectiveness of UNHS programs on psychological, language and educational-related outcomes, compared with selective screening programs.

Safety

Neither of the selected systematic reviews[2,3] reported on safety issues or concerns associated with using AABR and/or AOAE technology for UNHS in terms of side effects and complications to the newborn and/or to the screener due to performing the test itself.

Guidelines and consensus documents

No formal guidelines specifically developed on the use of AOAE and/or AABR (alone or in combination) for newborn hearing screening were identified by the literature search conducted for this review. The literature search identified a document[42] developed recently by a group of experts in perinatal audiology which provides information and guidelines for testing infants in the first few months of life by AABR using primarily air conduction

click stimuli to screen for hearing loss. This document discusses data collection parameters, implementation of the test, and scoring algorithms using this technology.

The following sections summarize the recommendations issued most recently by guidelines and consensus statements/position papers developed on newborn hearing screening.

Recommendations in North America

In 2000 in the United States, multiple professional societies, advocacy groups, and government agencies participating on the Joint Committee on Infant Hearing (JCIH) officially endorsed UNHS (using objective, physiologic measures) as an important component of early detection and intervention for infants with hearing loss.[1,2,19,25,26,43 9,11,14,39] The JCIH position statement recommends that infants with hearing loss should have a confirmed diagnosis by 3 months of age and appropriate intervention before age of 6 months. Hearing loss is defined as permanent, bilateral or unilateral, sensory or conductive, and averaging 30dB or more in the frequency region important for speech recognition (approximately 0.5 to 4kHz).

Professional organizations adopting the JCIH position statement include: the American Academy of Pediatrics (AAP), the American Speech-Language-Hearing Association's (ASHA), American Academy of Audiology (AAA), the Council on the Education of the Deaf, and the Directors of Speech and Hearing Programs in State and Health Welfare Agencies.[19,25,30,31,43,9,11,14,39] The Centers for Disease Control and Prevention also supports UNHS through its Early Hearing Detection and Intervention (EHDI) program, which assists states in implementing screening and intervention programs (http://www.cdc.gov).

In 2001, on the basis of the Systematic Evidence Review conducted by Thompson et al.[2,21] the US Preventive Services Task Force (USPSTF) concluded that the evidence was "insufficient to recommend for or against routine screening of newborns for hearing loss during postpartum hospitalization".[43] USPSTF could not determine whether the potential benefit of UNHS "outweigh the potential harms of false-positive tests that many low-risk infants would experience following universal screening in both high-risk and low-risk groups".

The guidelines issued in the United States differed with respect to the screening technology that was endorsed.[19,30,31,36,43] The JCIH recommends that all infants have access to screening using a physiologic measure (either TEOAE or DPOAE and/or ABR).[19] The AAP and the ASHA consider OAE and/or ABR the screening methods of choice and defer on recommendations

as to a preferred screening test.[30,31,36] USPSTF recommends the use of a validated protocol (usually requiring two screening tests) if a newborn hearing screening program is implemented, but it does not recommend a specific screening test.[43]

Currently, most American states have implemented UNHS programs http://infanthearing.org).[1,2,5,8,18,25,27] ASHA recommends that all hearing screening programs be conducted under the supervision of an audiologist holding the ASHA Certificate of Clinical Competence.[30]

In Canada, three national organizations support the American JCIH position statement and guidelines and recommend that all newborns be screened for hearing loss, preferably prior to leaving hospital: the Canadian Association of Speech Language Pathologists and Audiologists (CASLPA), the Canadian Academy of Audiology (CAA), and the Hearing Foundation of Canada (THFC) (http://www.hearingfoundation.ca).[7,45,47] These organizations also recommend the establishment of a well-integrated and structured system of early identification and management for all infants who have hearing loss, which is tailored to the unique geographic, demographic, cultural, and political features of Canada. None recommends a specific screening test or protocol.

The Canadian Working Group on Childhood Hearing (CWGCH) established by Health Canada in 2000 to develop guidelines for early hearing detection and intervention in children with hearing loss, has brought together various stakeholders to ensure a coordinated national approach to the issue and address the following areas:1

- the burden of the disorder, including the number of children affected by hearing impairment (prevalence) and patterns of detection;
- hearing screening tests;
- audiologic assessment;
- medical evaluation and management;
- amplification; and
- effectiveness of different approaches to communication development.

Based on literature reviews, as well as on expert opinion and consultations with a broad range of stakeholders throughout Canada, the CWGCH recently concluded that early hearing and communication development (EHCD) programs incorporating UNHS (similar to EHDI programs in the United States) are feasible and are likely to yield significant overall benefit, relative to traditional methods of identifying permanent hearing impairment in very young children in Canada.[1] Newborn hearing screening leads to early identification of hearing impairment, which leads to improved hearing and facilitates communication development. Loss to follow-up is the largest single

factor limiting the effectiveness of screening. The CWGCH also concluded that there is a need for more research to determine whether UNHS and EHCD programs lead to improved speech, language and education development.

The CWGCH found that AOAE and AABR tests perform well when appropriate protocols are used, but did not recommend a specific screening test or protocol.[1]

The Guidelines Advisory Committee (GAC), which summarizes and endorses existing guidelines for the community of physicians in Ontario, endorsed in 2004 the recommendations and rationales produced by the USPSTF (in 2001) on whether to screen newborns for hearing (www.gacguidelines.ca).

Recommendations in other countries

The European consensus statement on newborn hearing screening, developed in 1998, stated that PCHI was a serious health problem, and recommended hearing screening in all infants immediately after birth to improve quality of life and opportunities for those affected (www.nhs2004.polimi.it).[1-3,5,18,24 29] Since then, an increasing international interest in early identification and related issues has been manifested in three international conferences on "Newborn Hearing Screening, Diagnosis, and Intervention" subsequently held in 2000, 2002, and 2004.

During the last decade, the United Kingdom (UK) has taken the lead in promoting UNHS programs in Europe (www.nhsp.info).[1,4,8,55,56] The Newborn Hearing Screening Program (NHSP) in the UK recommends AOAE detection (up to two AOAE attempts per ear) followed by AABR testing as a 2-stage protocol (www.nhsp.info). All infants nursed in NICU for more than 48 hours should have both tests, whereas "well babies" should only proceed to AABR if clear AOAE responses were not detectable in one (or both) ears in the first step of the screen or if AOAE is not appropriate.

In 2001, a National Forum for Consensus and Implementation held in Australia on UNHS also identified hearing impairment as a significant condition in newborns.[57] At this forum, participants from all states and territories of Australia (including audiologists, teachers of the hearing impaired, neonatologists, paediatricians, ear, nose and throat surgeons, nurses, epidemiologists, and parents of children with hearing impairment) agreed that UNHS is feasible, beneficial, and justified. The Public Health Association of Australia also endorsed UNHS as feasible, beneficial and justifiable.[18] No specific screening test(s) or protocol(s) are recommended.

Discussion

During the last 20 years, the ability to screen infants using UNHS programs has progressed at different levels in various countries in North America, Europe, Australia, and Asia. According to the reviewed literature, although UNHS is currently endorsed by a broad consensus of professional opinion, its safety and clinical efficacy has not been established by well-designed clinical trials as required by current standards for evidence-based health care.[1-3,19,30,31,36,43] The selected systematic reviews[2,3] compared UNHS programs with selective newborn hearing screening programs and revealed the paucity of well-controlled studies examining and evaluating the overall effectiveness of UNHS. Data are lacking to directly compare the short- and long-term benefits and harms of UNHS versus those associated with selective screening.

The enthusiasm of advocates of UNHS in North America is in contrast with the more sober position of the US Preventive Services Task Force (USPTF)[43] which questioned whether UNHS results in better outcomes than selective screening. USPTF could not determine from the data reviewed by Thompson et al.[2] whether the potential benefits of early identification and intervention outweigh the potential harms of false positive test results that some low-risk infants and their families may experience as participants in UNHS.

The lack of consensus on the benefits UNHS has partially been attributed to the emphasis on the developmental outcomes as the primary outcomes.[15,1-4,8,10,11,13,14,22,39,43] Research on improved speech and language, cognitive ability, communication, and other developmental outcomes in the context of newborn hearing screening is complex and difficult to conduct. Newborn hearing screening (either universal or selective) and early detection by itself do not result in improved developmental outcomes. Many of the factors that have the potential to affect the developmental outcomes, including the degree of PCHI, additional morbidities and/or handicapping conditions, the quality of diagnostic and intervention services provided immediately after screening, and parental/family involvement, are still poorly understood. Also, there has been relatively little research on other potential important benefits from early identification of infants with PCHI, such as its impact on family communication, decision-making, and quality of life.

Young and Andrews[58] recently explored how parents experience the process and outcomes of UNHS and concluded that there is not enough evidence to support the argument that UNHS is not justified because of long-term damaging effects on families, particularly of the false positive test results. However, the evidence surrounding the anxiety associated with UNHS at various points and its determinants remains contradictory and incomplete.

The overall appraisal of UNHS by mothers is positive. However, the experiences of parents whose babies fail the first stage of (inpatient) screening and have to return for stage 2 (outpatient screening) raises the most unanswered questions.

The proponents of UNHS responded to criticisms on the efficacy and costs associated with UNHS by developing new screening technologies and protocols.[19,30,31,36,43,4,8-11,14,15,17,22,39] UNHS is currently based on electrophysiological screening using AOAE (DPOAE or TEOAE) and/or AABR technologies. Many different UNHS programs use devices in each of these categories, in single-or multiple-stage protocols.

In North America, various companies currently offer stand-alone (TEOAE, DPOAE, or AABR only) and/or combination units (configuring TEOAE, DPOAE, and AABR technology within a single device) for UNHS. Most of these companies have received marketing approval from Health Canada. Screening with these devices is non-invasive, and can be performed at bedside in inpatient or outpatient settings. According to their manufacturers/distributors, the available devices are relatively safe for the newborn and screeners, are easy to use and do not require highly trained staff. Therefore, these devices have the theoretical potential to become useful tools in the clinical practice for population-based newborn hearing screening.

Efficacy/effectiveness of AOAE and AABR devices

According to the available evidence,[2,3] UNHS, using AABR and/or AOAE (either alone or in combination in 2-stage protocols), increases early identification of moderate to profound PCHI and may lead to early intervention in diagnosed infants (before 6 months). However, loss to follow-up is a limiting factor for program sensitivity.

Evidence from one good quality non-randomized controlled trial and one good quality large accuracy cohort study suggests that AOAE (TEOAE or DPOAE) and AABR are equally accurate screening tests for moderate to profound PCHI.[2] A 2-stage protocol using TEOAE followed by AABR, may achieve better specificity (>97%) and lower overall referral rates (<2%) than 1 stage protocols using either technology. However, this type of protocol may fail to screen for hearing loss due to auditory neuropathy in infants who pass TEOAE screening.

The long-term efficacy/effectiveness of UNHS using AOAE and/or AABR for PCHI in terms of improved developmental outcomes (such as language and communication development) has yet to be established.[2,3] The existing evidence that early detection and start of habilitation promotes improved communication and language development in the infant diagnosed with PCHI is limited.[3,2,18,37,38]

Other important questions related to the efficacy/effectiveness of using AOAE and/or AABR for UNHS could not be answered based on this review's findings:

- Does UNHS using AABR and/or AOAE devices affect the treatment decisions for PCHI in infants within their first 6 months of life and lead to effective interventions? and
- Does early identification of PCHI using AABR and/or AOAE improve long-term health outcomes when compared to later identification using conventional methods?

Further specific research is needed to adequately address these issues, ideally by means of prospective controlled trials. Future studies should use relevant, validated measures of the various developmental outcomes. Confounding factors such as age at diagnosis, age at initiation of management, characteristics of referral patterns, and management undertaken, should be controlled.

Safety of AOAE and AABR devices

Neither of the two selected systematic reviews[2,3] reported on safety issues or concerns associated with using AABR and/or AOAE technology for newborn hearing screening in terms of side effects and complications to the newborn and/or screener due to performing the test itself. However, little is known about the most postulated adverse effects of newborn hearing screening and early diagnosis and treatment. The frequency of misdiagnosis in everyday practice settings and the likelihood that infants will be subjected to inappropriate procedures have yet to be determined.[2,59]

Referral rates vary depending on the method of screening used in the program.[2,1,5,9-11,14,22,39] Higher referral rates have been encountered when less experienced screeners administer the test, when the screening was conducted in environments with high noise level and when screening was performed in newborns less than 24 hours old (for these cases AOAE appears to be more affected than AABR). Conclusive evidence regarding the impact of false positives on the child, parent, or the parent-child relationship has yet to be established.[17,1-4,8,10,15,58]

One important concern is associated with the number of infants with moderate to profound PCHI who may pass screening with AOAE and/or AABR devices but who emerge later and are diagnosed with PCHI late because of a false sense of security generated in their families and physicians by the apparently normal results from screening.[39,1,2,8,10,22,59,60] Are the false negative results from screening due to a problem in the screening device(s), the protocol used, or the screener's training and experience? Was the diagnosed PCHI truly acquired after the screening? These questions remain to be answered.

Further specific research is needed to adequately address the issues associated with the safety and efficacy/effectiveness of using AOAE and/or AABR devices for UNHS , ideally by means of prospective controlled trials.

Considerations on the performance of AOAE and/or AABR

The main purpose of using AOAE and/or AABR for UNHS is to differentiate the newborns with normal hearing from those who are most likely to have PCHI and need referral for diagnostic evaluation. The uncertainties related to the differentiation between impaired and normal hearing in newborns and older infants prevent objective calculations of sensitivity and specificity of the available screening tests.[12 1,4,8-11,14,22,33,39] The change in the infant's hearing status in the interval between screening and gold standard assessment may bias estimates of test performance. Some hearing impairment in detected newborns improves naturally during infancy, but the prevalence and the responsible risk factors remain uncertain. Not all PCHI can be detected by newborn hearing screening and some infants suffer progressive hearing loss, the prevalence of which is also unknown.

Estimates of sensitivity require ascertainment of all true cases, which is not possible until school age.[33,1,2,4,8,10-12,15,22,39,60] These estimates will include some cases of acquired, late-onset and/or progressive PCHI and will not include diagnostic assessment of all those who screened negative. Estimates of specificity include the assumption that detection of "false positive" cases of mild, unilateral, or non-permanent hearing impairment is no more desirable than a false positive screen in a child with normal hearing.

The use of an audiometric test (a reliable behavioural audiometry or conventional ABR) in the entire population of newborns who had received AOAE and/or AABR is necessary to reliably estimate the test sensitivity for detecting PCHI in infancy.[10,1,2,4,8,11,22,33,39,60] Only Norton et al.[54] conducted such a study in a large population, but they included only at risk newborns. The less than perfect accuracy of the gold standard assessment itself may bias the estimates of the evaluated screening tests.

The reviewed literature indicated that the performance of a screening test or protocol for UNHS should be interpreted in the context of the prevalence of the target disorder, the administration of the screen, the extent to which newborns are successfully accessed for screening and are successfully followed up after a referral result, the efficacy of the intervention following identification/diagnosis, the current hearing and child health services delivered, as well as the costs of identification and habilitation.[19,30,31,36,43,4,8,10,11,14,22,28,33,39,59-64] Whether UNHS is worth implementing ultimately depends upon public

services rising to the challenge of earlier diagnosis and initiation of appropriate interventions. Educational and support services must provide habilitation appropriate for newly identified infants and their families.

Good prevalence estimates of PCHI are needed for an accurate estimation of the performance of the screening tests, protocols, and programs used for newborn hearing screening.[19,1-3,8, 10 12,14,22,28,39,43,44,59] Currently there is a relatively large range of prevalence estimates reported by epidemiological studies and reports of UNHS programs. Some may be describing a difference in prevalence for populations with different ethnic, cultural, and genetic backgrounds, or a difference over time. Others may be due to methodological differences in the source of collected data. Some of the difference may be due to inclusion or exclusion of infants with various cut-off impairment levels (such as ≥20, >30dB, ≥35dB; >40dB, ≥40 dB; ≥50dB), at various frequencies (0.5 to 4KHz). These issues make comparisons difficult. The audiological criteria can be addressed by establishing a universally agreed upon standard for reporting the severity level and the frequency inclusion.

Knowledge of the acquired, late-onset, and/or progressive PCHI is needed to estimate the proportion of children in these categories.[12 22,39] Knowledge of the number of children who have a degree of PCHI which could not be identified within the neonatal period and would need to be identified later, is also important for the implementation of newborn hearing screening.

Technical considerations

Several technical considerations affect the validity of AOAE and/or AABR technologies as screening tools for optimal UNHS. The AOAE and AABR technologies emerged as integral parts of UNHS although none provides a direct measure of hearing or is considered a true screening test of hearing. AOAE and AABR technologies measure slightly different physiological mechanisms related to hearing and are most often used in multiple-stage screening protocols to reduce the number of false positive results and test all possible aspects of the structural integrity of the auditory pathway. However, even if an infant passes screening with these tests and protocols, hearing cannot be definitively considered normal until the child is mature enough for a reliable behavioural audiogram.

In practice, the operating characteristics of feasible screening tests influence the target disorder criteria (http://www.otoemissions.org), (http://www.infanthearing.org).[1,8-12,14,19,34,39,65] The AOAE and/or AABR devices are not designed to detect central hearing deficits. The lowest limit of impairment that appears to be detectable with reasonable accuracy is typically reported

to be about 30 dB hearing loss. Milder degrees PCHI (<30 dB) tend to give high rates of screening errors. The evaluated AOAE and/or AABR devices (either alone or in combination in a 2-stage protocol) perform better for infants with moderate to profound PCHI, for whom there is little debate that intervention needs to occur early in life to improve developmental outcomes.[19] [1,2,4,8,33,39] However, there is a growing concern over the number of children with unilateral and mild to moderate degrees of PCHI who are not being identified at birth using AOAE and/or AABR screening devices (alone or in combination in a 2-stage protocol).[1,8,39]

The use of AABR and /or AOAE devices for UNHS is still evolving as the algorithms used in the evaluated protocols to differentiate newborns who are most likely to have PCHI from newborns with normal hearing have yet to be optimized or standardized (http://www.otoemissions.org), (http://www.infanthearing.org).[11,1,1,9,10,34,39,59,64,65] There are several unresolved technical issues relating to the meaning of hearing level in the context of screening newborns. The hearing level scale reference zero level is defined in relation to adult ears, and the effect of delivering a given stimulus to the ear of a newborn may differ from that in an adult, because of differences in anatomy and function of the immature ear. Compounding the lack of a uniform standard for the calibration of AOAE or AABR devices, manufacturers may not provide sufficient supporting evidence that would allow professionals to determine the validity of the specific pass/refer criteria and/or automated algorithms incorporated in the instruments.

The available evidence was obtained from studies evaluating earlier versions of the AOAE and AABR devices and may underestimate the capabilities of the newer devices currently available on the market in North America. The devices that combine AOAE and AABR technologies into a handheld unit hold promise for rapid testing with a multi-stage protocol for all infants, in terms of reducing refer (false positive) rates associated with transient external or middle ear dysfunction, and improving identification in infants with more unusual forms of hearing impairment such as AN. However, whether these devices would result in an improved discriminating ability between newborns with normal hearing and those with PCHI is yet to be determined.

This report is limited since it summarizes only the results from two systematic reviews and results from subsequently published primary research studies (which may have addressed some of the outstanding issues associated with the use of AOAE and/or AABR for UNHS) are not included.

Future directions in electrophysiological hearing testing for UNHS

The impetus for UNHS has pushed forward the development of other electrophysiological technologies not based only on information from the auditory periphery (http://www.otoemissions.org).[34,11,35] One of these new technologies is the auditory steady state response (ASSR) testing. Although initially the technology behind the ASSR was not intended as a new application for newborn hearing screening /monitoring, the progresses in the field are important. In the future ASSR protocol may have a role in the UNHS and EHCD/EHDI programs.

In the future it may be feasible to use protocols offering more information about the tested newborns, which can be used either for screening purposes or for diagnostic statistics.[34,35] Several recent reports indicate the trend to encapsulate in one device many testing protocols, both for screening and diagnosis.

The recent advances in genetics research and the identification of numerous genes responsible for many types of hearing impairment are promising a near-by future where the majority of hearing testing may be conducted via genetic probes from a small blood sample.[20,11,12,25,35] Combining genetic screening for more common forms of genetic hearing loss as well as genetic screening for presence of congenital cytomegalovirus infection with electrophysiological hearing testing may reduce false positive and false negative rates of current screening methods and improve identification of infants at risk for late-onset hearing loss.

Conclusions

Based on the results reported by two systematic reviews, it can be concluded that UNHS using AOAE (TEOAE or DPOAE) and/or AABR technology (either alone or in combination in a 2-stage protocol), is effective in terms of increasing early identification of moderate to profound PCHI and may lead to early intervention in diagnosed infants (before 6 months). However, there is no direct evidence that compares selective versus universal screening for these outcomes.

If UNHS is implemented, those considering AOAE and/or AABR technologies (either alone or in combination in a 2-stage protocol) should be aware that:

- AOAE and/or AABR devices have been shown to affect detection rates only for moderate to profound PCHI. Not all types and degrees of PCHI can be detected by these technologies.
- The accuracy of AOAE and/or AABR as screening tools depends on many factors including the cut-off impairment levels (dB hearing level, frequency range), the age of the newborn at screening, the screening protocol used, and the environment in which the screening is performed.

- The efficacy/effectiveness of AOAE and/or AABR in terms of longer-term outcomes (such as development of speech and language, cognitive ability, and communication skills) may be difficult to establish because the impact on developmental outcomes is related to more factors than just accuracy of screening technologies.
- The AOAE and/or AABR technologies are still evolving. There is no definitive data to determine which of the AOAE and/or AABR devices currently available on the market in Canada are the best and which of the protocols used to screen newborns for PCHI should be considered optimal for a UNHS program. The available devices still await prospective validation against an accepted gold standard.

The advent of new technology and screening devices will continue to allow for new and different opportunities for detection of PCHI during the first 6 months of life. However, screening tests represent only one component of a properly coordinated newborn hearing screening program and should not be introduced until there is evidence that the potential benefit of the whole program outweigh the harm. Little is known about the other factors that may affect the development of optimal UNHS programs.

Resources need to be available for diagnosis and intervention before UNHS can be considered.

Appendix A: Search Strategy

The literature search was conducted by a Research Librarian from the Alberta Heritage Foundation for Medical Research between June 14, 2006 and August 10, 2006. Major electronic databases used include: The Cochrane Library, NHS Centre for Reviews and Dissemination (CRD Databases: NHS EED, HTA, DARE), PubMed, and EMBASE. In addition, relevant library collections, web sites of practice guidelines, regulatory agencies, evidence-based resources and other HTA related agency resources (AETMIS, CCOHTA, ECRI) were searched (see Table A1). Internet search engines were also used to locate grey literature. Medical Subject Headings (MeSH) terms relevant to this topic are: mass screening; infant, newborn; infant; hearing; evoked potentials, auditory, brain stem (see Table A1).

Table A1: Search strategy See below for limits[†]

Database	Edition or date searched	Search Terms [††]
Databases		
The Cochrane Library http://www.thecochranelibrary.com	Issue 2, 2006 June 16, 2006	(infan* OR newborn*) AND ((hearing AND screening) OR OAE OR DPOAE OR TEOAE OR AABR OR ABR OR otoacoustic emission* OR auditory brainstem response) in Title, Abstract or Keywords
PubMed http://www.pubmed.gov	June 16, 2006	#1: (Infan* OR newborn* OR neonat*) AND (OAE OR DPOAE OR TEOAE OR AABR OR ABR OR otoacoustic emission* OR auditory brainstem response OR hearing screening) Limits: English, Publication Date from 2001 #2: #1 Limits: Animals #3: #1 NOT #2 #4: #3 Limits: Editorial, Letter, Meta-Analysis, Practice Guideline, Review, Consensus Development Conference, "Consensus Development Conference, NIH", Evaluation Studies, Government Publications, Guideline #5: in process[sb] OR publisher[sb] #6: #3 AND #5 #7: #4 OR #6
CRD Databases (DARE, HTA & NHS EED)	June 16, 2006	(infant OR newborn OR neonat) AND ((hearing AND screening) OR OAE OR DPOAE OR TEOAE OR AABR OR ABR OR otoacoustic emission* OR auditory brainstem response)
EMBASE –Ovid platform (Licenced resource)	(2006 Week 23) June 16, 2006	1. (Newborn/ or Infant/) and ((hearing and screening).mp. or exp Otoacoustic Emission/ or auditory brainstem response. mp. or (OAE or DPOAE or TEOAE or AABR or ABR).mp.) 2. limit 1 to (human and english language and yr="2001 - 2006") 3. (meta-anal$ or metaanal$).mp. or review.pt. or (review$ or overview$).mp. or (hta$ or health technology assessment$ or biomedical technology assessment$). mp. or exp CONSENSUS DEVELOPMENT/ or exp CONSENSUS/ or exp Practice Guideline/ 4. 2 and 3
Web of Science – ISI platform (Licensed resource)	June 16, 2006	1. TS=(newborn* or infan* or neonat*) AND TS=(OAE OR DPOAE OR TEOAE OR AABR OR ABR OR otoacoustic emission* OR auditory brainstem response OR (hearing AND screening)) Language=English; Databases=SCI-EXPANDED, SSCI, A&HCI; Timespan=2001-2006 2. #1 DocType=Review; 3. #1 AND TS=(review* OR overview* OR guideline* OR clinical pathway OR consensus OR meta analysis OR meta-analysis OR HTA OR technology assessment) 4. #2 OR #3

Table A1: Search strategy (continued)

Database	Edition or date searched	Search Terms ††
Library Catalogue		
NEOS (Cenral Alberta Library Consortium)	June 16, 2006	(newborn$ or infant$ or neonat$) and hearing and screening; otoacoustic emission$ or auditory brainstem response
Guidelines		
AMA Clinical Practice Guidelines http://www.topalbertadoctors.org/TOP/CPG/	June 14, 2006	Browsed list of guidelines
CMA Infobase http://mdm.ca/cpgsnew/cpgs/index.asp	June 16, 2006	Hearing; otoacoustic; auditory brainstem
National Guideline Clearinghouse http://www.ngc.gov	June 14, 2006	(newborn* OR infant*) and hearing and screening
Coverage/Regulatory/Licensing Agencies		
Alberta Health and Wellness http://www.health.gov.ab.ca	June 14, 2006	Infant +hearing +screening; newborn +hearing +screening
Medical Devices Active Licence Listing http://www.mdall.ca/	June 16, 2006	**Device name:** otoacoustic **Device name:** auditory brainstem
Health Canada http://www.hc-sc.gc.ca	June 16, 2006	"newborn hearing screening"; "infant hearing screening"; "otoacoustic emissions"; "auditory brainstem"
US Food and Drug Administration Databases http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/search/search.cfm	June 16, 2006	otoacoustic; auditory brainstem response
Aetna Clinical Policy Bulletins http://www.aetna.com/about/cov_det_policies.html	June 14, 2006	"otoacoustic emissions"; "auditory brainstem response"

Table A1: Search strategy (continued)

Database	Edition or date searched	Search Terms ††
HTA resources		
AETMIS http://www.aetmis.gouv.qc.ca	June 14, 2006	otoacoustic; "auditory brainsterm"; "hearing screening"
CADTH http://www.cadth.ca/index.php/en/hta/reports-publications/search	June 14, 2006	Browsed list of guidelines
Institue for Clinical and Evaluative Sciences (ICES), Ontario http://www.ices.on.ca/	June 15, 2006	otoacoustic; auditory brainstem; hearing
Health Technology Assessment Unit At McGill http://www.mcgill.ca/tau/v	June 15, 2006	Browsed list of topics
Medical Advisory Secretariat http://www.health.gov.on.ca/english/providers/program/mas/mas_mn.html	June 15, 2006	Browsed list of reviews
CCE http://www.med.monash.edu.au/healthservices/cce	June 15, 2006	Browsed list of reviews
ECRI http://www.ecri.org (Licenced Resource)	June 15, 2006	(infant* OR newborn*) AND hearing AND screening; otoacoustic; auditory brainstem
Health Quality Council, Saskatchewan http://www.hqc.sk.ca/	June 15, 2006	"auditory brainstem response"; otoacoustic
BlueCrossBlue Shield http://www.bluecares.com/tec/index.html	June 14, 2006	Browsed list of assessments
MHRA (UK) http://www.mhra.gov.uk	June 15, 2006	Browsed list of assessments
NZHTA http://nzhta.chmeds.ac.nz/publications.htm	June 15, 2006	Browsed list of publications
NICE (UK) http://www.nice.org.uk/	June 15, 2006	otoacoustic; auditory brainstem response

Table A1: Search strategy (continued)

Database	Edition or date searched	Search Terms ††
Search Engines		
Google http://www.google.com	August 10, 2006	1. Newborn hearing screening auditory-brainstem-response OR otoacoustic-emission –pubmed; 2. Newborn hearing screening auditory-brainstem-response OR otoacoustic-emission –pubmed Technology assessment (first 50 results of each)

Note:

† **Limits:** Searches were limited to **publication dates** 2001-2006; **language:** English only; **studies:** human studies only. These limits are applied in databases where such functions are available.

†† "*", "# ", and "?" are truncation characters that retrieve all possible suffix variations of the root word e.g. surg* retrieves surgery, surgical, surgeon, etc.

Semicolons are used to separate terms that were searched separately.

In addition to the above-mentioned searches, the bibliographies and reference lists of all retrieved articles were examined.

Canadian specialists in paediatrics and in paediatric audiology were contacted for expert opinion on the best practice for newborn hearing screening and the current status of using AOAE and/or AABR testing for this indication. At the time this report was completed, no advice was received from the Canadian specialists.

The companies offering AOAE and AABR devices for newborn hearing screening in North America (see Table 1) were contacted for information on regulatory status, availability, and coverage in Canada. At the time this report was completed, responses were received from two companies (Viasys Healthcare Inc., Neurocare Group, Grason Stadler Divisions and Otodynamics Ltd.) through their Canadian distributor (AIM Technologies).

Health Canada was contacted for information on regulatory status of the available AOAE and AABR screening devices in Canada.

Appendix B: Screening and Reviewing the Literature

Two reviewers individually conducted the initial study selection based on the study titles and abstracts only. Copies of the full text of potentially eligible studies were then retrieved and individually assessed by the same reviewers. The selection was determined on the basis of a list of inclusion and exclusion criteria developed for this review. In some cases, when the full text of the article was retrieved, closer examination revealed that it did not meet the inclusion criteria specified by the review protocol. Consequently, these papers were not used to formulate the evidence base for the systematic review (the reasons for their exclusion are listed in Table B1). However, where appropriate, relevant information contained in the excluded papers was used to inform the section on "Introduction"/"Background" and to expand the review "Summary"/"Discussion".

Inclusion criteria

Type of studies

Published reports of systematic reviews (quantitative and/or qualitative) conducted to evaluate the efficacy/effectiveness and safety of AOAE and/or AABR when used as tools for newborn hearing screening were considered for inclusion.

Studies were included in the review if:

- the published report was publicly available;
- they included newborns (from birth through 3 months) at an inpatient or outpatient setting (urban or rural);
- they reported on the use of the AOAE and/or AABR device as a tool for newborn hearing screening (either universal or selective);
- they compared the AOAE and/or AABR with other screening tests used for this indication, or with no testing;
- they measured efficacy/effectiveness and safety of using the using AOAE and/or AABR devices in a newborn hearing screening program (either universal or selective) in terms of :
  - screening accuracy in terms of sensitivity, specificity, and predictive value of screening tests;
  - impact on age at diagnosis of PCHI;
  - impact on the number of infants diagnosed with PCHI;
  - impact on usage of diagnostic tests;
  - impact on age at start of treatment for PCHI;
  - impact on treatment decisions (such as type of treatment)

- impact on usage of interventions to treat PCHI;
- impact on speech and language acquisition and development in children diagnosed with PCHI;
- impact on social and emotional development, and other developmental milestones (such as scholastic achievement) in children with PCHI;
- risks and complications to the newborns and/or screeners from performing the test itself; and
- adverse effects of false positive and false negative test results.

Using criteria from **Cook et al.**[51], a review was considered to be systematic if it met four of the following five criteria:

- focused clinical question;
- explicit search strategy;
- use of explicit, reproducible and uniformly applied criteria for article selection;
- critical appraisal of the included studies;
- qualitative or quantitative data synthesis.

Only full peer-reviewed articles were included because abstracts do not provide adequate detail on the review methodology. However, where appropriate, relevant information contained in abstracts of primary research studies was used to inform the section on available evidence.

In the case of duplicate publications, the most recent and complete version was included.

Exclusion criteria

Published reports of primary research studies (such as randomised controlled trials, non-randomized controlled trials, cohort studies, case series and case reports), editorials, letters and technical reports **were excluded**.

Published reports of systematic reviews **were excluded from data extraction if**:

- they focused on the use of AOAE and/or AABR for hearing screening in infants older than 3 months and in young children;
- they involved both newborns and infants older than 3 months or young children but did not separately report on the use of the AOAE and/or AABR for detecting hearing impairment/loss in newborns;

Published reports of narrative and descriptive reviews, which summarized the research on the topic but lacked an explicit description of a systematic approach to the identification and interpretation of evidence, **were excluded** from data extraction. They were considered only as a source of background information.

Table B1: Excluded studies

Study	Reason for exclusion
Malaysian Health Technology Assessment Unit (2004)[18] Screening for hearing loss in infants.	This study did not meet all criteria for a systematic review (the published report does not provide clear information on how the studies were selected for the review, or how many reviewers performed the selection; no statement on whether validity/quality of reviewed studies was assessed as well as how the selected studies were assessed for validity, or how many reviewers performed the validity assessment; no critical appraisal tool is described; no quantitative analysis). No reply received to the request for information on review methodology.
Kunze et al. (2004)[37] Screening of the hearing of new-borns - a systematic review. Germany	Only the executive summary is available in English.
Swedish Council on Technology Assessment in Health Care (2004)[38] Universal newborn hearing screening - early assessment briefs (Alert). Sweden	Only the executive summary is available in English.
Guimera et al. (2002)[66] Proposal for a programme for the early detection of infant deafness in the Basque Autonomous Community Basque region of Spain	Only the executive summary is available in English.
Medical Services Advisory Committee[67] Neonatal hearing screening Australia	The published report of this study was not publicly available (assessment awaiting editing).
Okubo et al.[22] Evaluation of universal newborn hearing screening in Japan: an analysis of the literature	This study does not meet all criteria for a systematic review (it searched only 2 Japanese databases for original and review articles; the authors commented on the methodological quality of included studies but no specific critical appraisal tools were used; no data synthesis or quantitative analysis performed)
HAYES and Inc.[21] Neonatal hearing screening USA	The published report of this study was not publicly available.
ECRI[26] Hearing Screening for infants USA	This Hotline Response does not meet all criteria for a systematic review (it is a summary of relevant literature based on a review of abstracts of published articles; no critical appraisal of the methodological quality of the selected studies; no qualitative or quantitative analysis).

Guidelines and consensus documents

The section on "Guidelines and consensus documents" summarizes recommendations from reports of relevant clinical practice guidelines, position papers, and consensus statements issued on newborn hearing screening (either universal or selective) and/or on the use of AOAE and/or AABR devices as tools for newborn hearing screening.

Background information

Where appropriate, relevant published material in the form of overview materials, clinical reviews, narrative and descriptive reviews, letters, conference material, commentaries, discussion papers, editorials, and abstracts were included as background information to inform the sections of the report.

Data extraction

Two reviewers individually abstracted in tabular form data from published reports of the selected systematic reviews. Main characteristics, findings, and conclusions from these studies and details of their methodology were summarized in Table C1 and Table C2 (Appendix C).

For studies in which the reporting of the review methodology was unclear, their authors or the agencies which produced the published reports, were contacted by e-mail for further information. If no reply was received, these studies were excluded from data extraction for not meeting all criteria for a systematic review (see Table B1).

Methodological quality assessment

The methodological quality of the selected systematic reviews was not critically appraised and no attempt was made to assess the validity of their findings.

Appendix C: Results Reported by Two Systematic Reviews

Abbreviations

AABR – Automated Auditory Brainstem Response
ABR - Auditory Brainstem Response
AHRQ – Agency for Healthcare Research and Quality
AOAE – Automatic Otoacoustic Emissions
CI95 - 95% confidence interval
HI – hearing impairment
HL – hearing loss
mo – month(s)
NHS – Newborn Hearing Screening
NNS – Number Needed to Screen
NPV – negative predictive value
OAE – Otoacoustic Emissions
PHL – Permanent Hearing Loss
PPV – positive predictive value
RCT – randomized controlled trial
ROC – receiver operating characteristic(s)
Sn – sensitivity
Sp – specificity
TEOAE – Transient Evoked Otoacoustic Emissions
UK – United Kingdom
UNHS – Universal Newborn Hearing Screening
USA – United States of America
USPTF – US Preventive Services Task Force
VRA – visual reinforcement audiometry
WBN – well-baby nursery
wk – week(s)

Table C1: Selected systematic reviews (characteristics, main findings, and conclusions)

Study	Study's characteristics
Thompson et al. (2001)[2] AHRQ Evidence Report USA	**Included studies:** controlled and observational studies (descriptive and cohort studies) **Excluded studies:** criteria not stated **Participants:** newborn population **Intervention:** UNHS; OAE and/or ABR **Comparator(s):** selective screening (of high-risk newborns); independent gold standard test for NHS (such as VRA) **Outcome(s) and outcome measures:** accuracy, yield, and harms of NHS; effects of screening or early identification and treatment on l anguage outcomes;
Puig et al. (2005)3 Universal neonatal screening versus selective screening as part of the management of childhood deafness Cochrane Systematic Review Iberoamerican Cochrane Centre	**Included studies:** RCTs (regardless of whether the unit of randomization was population, institution, or individual) **Excluded studies:** criteria not stated Participants: all newborns screened for HL and children of any age opportunistically screened for HI by any method **Intervention:** universal neonatal auditory screening by a TEOAE test or an AABR test **Comparator(s):** high-risk neonatal auditory screening by a TEOAE or AABR; opportunistic screening **Outcome(s) and outcome measures:** - primary outcomes included reduced delay in acquisition of verbal skills; reduced delay in language acquisition; language level; education level; level of social integration; any other measure of effectiveness of treatment that the authors included in their studies; - secondary outcomes or confounding variables included Sn and SP of screening programs; age at diagnosis; age at start of treatment; type of treatment; cost-effectiveness of the program (screening as well as treatment)

* Main findings regarding the use of AOAE and/or AABR for newborn hearing screening;
** Conclusions stated by the author(s) and quoted directly from the published report

	Study's main findings* and conclusions**
	Main Findings* Ten studies of UNHS programs, 1 study of the accuracy of AOAE and AABR devices, and 8 studies of language outcomes met the inclusion criteria. Evidence from 10 studies of UNHS programs (only 2 of them evaluated as good quality studies) : - No study evaluated Sn and Sp of screening test(s) against an independent gold standard. - Estimated Sn of 2-stage protocol: 85% (data from all 10 studies); - Estimated Sp of 2-stage protocol: 97% (data from all 10 studies); - Estimated overall PPV of 2-stage protocol was 6.7% (data from 1 good-quality controlled study) - The refer rate of 2-stage protocol was 1.6% (data from 1 good quality controlled study); - The refer rate was 6.5% for stage 1 (TEOAE followed by TEOAE or ABR at birth admission) of a 2-stage protocol (data from 1good quality cohort study). Evidence from 1 large good quality cohort study of accuracy of AOAE and ABR: - No test was sensitive enough to rule out significant HL. - Sn of AOAE ranged from 80% for moderate PHL to 98% for profound PHL; Sp of 80% - Sn and Sp of ABR were 84% and 90%, respectively; - The 2-stage protocol missed 11% of affected ears; - Overall, screening resulted in a final diagnosis of bilateral moderate-to-profound PHL among 1 in 230 high-risk and 1 in 2348 low-risk infants. Benefits of UNHS (evidence from 1 cohort study in USA and 1 good quality controlled study in UK) - UNHS increases the chance that diagnosis and treatment will occur before 6 mo; UNHS increases early identification between 19 and 42% over selective screening in high-risk childrenSafety - No reporting on risks and complications due to performing AOAE and/or AABR testing itself; - Most postulated adverse effects of NHS have not been evaluated /reported in reviewed studies. **Conclusions**** "Modern screening tests for hearing impairment can improve identification of newborns with PHL, but the efficacy of UNHS to improve long-term language outcomes remains uncertain."
	Main Findings* No trials/studies were included in this review. No data on randomised comparisons between universal and selective screenings for childhood deafness. **Conclusions**** "The long-term effectiveness of universal newborn hearing screening programmes has not been established to date. There is a need for controlled trials and before and after studies to address the issues further."

Table C2: Selected systematic reviews (objective and methods)

Study	Study's objective and methods
Thompson et al. 20012 AHRQ Evidence Report USA	**Objective:** To identify strengths, weaknesses, and gaps in the evidence supporting UNHS and to compare the additional benefits and harms of UNHS with those of selective screening of high-risk newborns. **Methods:** MEDLINE®, CINAHL, and PSYCINFO were searched for relevant papers published in English from 1994 to September 2000, using the keywords hearing disorders and infant or newborn combined with terms for screening and relevant treatments, such as early intervention, amplification, and American Sign Language. The search was updated quarterly through August 2001. To identify additional articles, the reviewers contacted experts and examined reference lists of review articles. To identify articles published before 1994, the reviewers relied on systematic reviews published in 1996 and 1997. Two authors reviewed titles and abstracts of original searches. They selected to include in evidence tables: (1) controlled trials; (2) reports on accuracy, yield, and harms of screening using AOAE, AABR, or both in the general newborn population, or (3) reports of the effects of screening or of early identification and treatment on language outcomes. Two authors abstracted data on population, test performance, outcomes, and methodological quality from each included study. For studies of accuracy of screening tests, Sn was defined as the number of infants with HL who screened positive divided by the actual number of infants with HL. Sp was defined as the number of infants with normal hearing who screened negative divided by the total number of infants with normal hearing. The PPV was defined as the number of infants with HL who screened positive and later proved to have permanent bilateral PHL divided by the number of infants who screened positive. With input from the Task Force, the authors defined tests performed in the hospital during the birth admission as screening tests, and defined subsequent testing performed as part of an effort to establish the final diagnosis to be part of the follow-up evaluation. Each study was classified as "good," "fair," or "poor" using pre-specified criteria developed by the USPSTF for grading the internal validity of studies and the overall evidence for each link in the analytic framework. When necessary, the reviewers sought additional information needed to apply the criteria from authors of the selected studies. The USPSTF discussed the review and rated the quality of 4 key studies of early intervention and provided overall guidance. A mathematical model of the likely benefits and harms of UNHS versus selective screening of 10,000 newborns, estimating prevalence, sensitivity and specificity, compliance, treatment effect size, and other model parameters from the included studies was constructed. Excel 97 (Microsoft Corp, Redmond, Wash) was used for all analyses.

Table C2: Selected systematic reviews (objective and methods) (continued)

Study	Study's objective and methods
Puig et al. (2005)3 Cochrane Systematic Review Iberoamerican Cochrane Centre	Objective: to compare the long-term effectiveness of a universal neonatal screening and early treatment program for hearing impairment with (1) screening and treatment only of high-risk neonates and (2) opportunistic screening and treatment in reducing the short and long term psychological, linguistic and educational sequelae associated with childhood hearing impairment **Methods:** An electronic search conducted to identify suitable RCTs using MEDLINE (1966 to 2003), EMBASE (1974 to 2003), the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library Issue1, 2004) and registers of health technology assessment agencies as well as registers of clinical guidelines. Medical Subject Headings (MeSH) included Deafness [*diagnosis]; Hearing; Hearing Disorders [diagnosis]; Hearing Tests; Infant, Newborn; Neonatal Screening [*methods]. MeSH check words included Humans. Two reviewers independently analysed the summaries of the studies obtained by the searches to decide their eligibility for inclusion. Studies considered as potentially eligible were retrieved in full text for in-depth analysis. Disagreements between reviewers were resolved through discussion or through involvement of a third reviewer. The quality of the included studies was to be evaluated according to valid parameters (not specified) and depending on the results observed they were to be classified as trials with low, moderate, and high risk of bias. In addition the 1990 criteria for evaluating a screening procedure was to be used. The application of the quality criteria was to be conducted independently by two reviewers (preferably one of who would be specialized in research into the diagnosis and treatment of childhood hearing impairment) without knowing the author(s), institution(s), source of reference, or study results. Any disagreement was to be discussed in order to reach consensus. A table of evidence was to be created to describe the selected studies by study quality, design, participating populations, method of screening, outcome variables collected, results observed and other relevant information for the interpretation of the systematic review. If possible a pooled analysis of the results would be conducted in which estimates of the combined effects for the group of selected studies would be calculated by meta-analysis techniques. Before undertaking the meta-analysis, the presence of clinical and statistical heterogeneity between the studies (which might constitute a formal impediment to the data combination) would be evaluated. If a pooled analysis would have been possible, a sub-group analysis would have been considered by type of treatment administered after detection of HI.

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SECTION THREE
ECONOMIC EVALUATION

Prepared by Ken Eng and Doug Lier

COST EFFECTIVENESS OF 1-STAGE AND 2-STAGE PROTOCOLS OF UNIVERSAL NEWBORN HEARING SCREENING

Introduction

This report conducted a cost effectiveness study on the screening alternatives of 1-stage and 2 stage protocol of universal newborn hearing screening. The technologies examined are Automatic Otoacoustic Emissions (AOAE) and Automated Auditory Brainstem Responses (AABR). In total, there are three screening protocols to examine. The 1-stage protocol involves the use of either AOAE or AABR separately. The 2-stage protocol uses the AOAE in the first stage and the AABR in the second stage of testing. The objective was to determine which screening protocol was the most cost-effective alternative.

Objective

This report outlines the economic component on universal screening for newborn hearing. Screening for newborn hearing is conducted using the following technologies: Automated Otoacoustic Emission (AOAE), Automated Auditory Brainstem Response (AABR) and a 2-stage protocol that uses AOAE and ABBR together. The report is divided into three parts. Part 1 is a review of the literature on the economic evaluation of hearing screening using the technologies. Part 2 presents the economic evaluation of the technologies. An economic model is given that captures the cost effectiveness of each screening protocol. Data in the model were obtained from the literature and the Alberta Universal Newborn Hearing Screening Project: Research Outcomes Final Report 2004.[1] A summary of the findings from the economic model on the cost- effective alternative is given. Part 3 is a discussion and conclusion of the report.

PART 1: LITERATURE REVIEW

Literature search findings

A total of eight articles were selected for review.[2-9] Four of these articles were on the economic evaluation of 1-stage and 2-stage screening.[2-5] Four of the articles only examined the 1-stage screening.[6-9]. Inclusion criteria were English language studies on the economic evaluation, economic costing and cost effectiveness of AOAE, AABR 1-stage protocol and 2-stage protocol. Inclusion criteria focused on the economic evaluation of the technologies. Exclusion criteria excluded articles that examined screening programs and did not incorporate the technologies. A summary of the search terms and databases are provided in Appendix A.

Literature findings on economic evaluation of 2-stage screening

Kezirian et al., 2001[2]

The study by Kezirian et al. defined cost effectiveness as the ratio of cost and the number of infants identified with hearing loss. This is an inaccurate definition. A formal cost effectiveness should use an Incremental Cost Effectiveness Ratio (ICER) where it calculates the difference of the costs and effectiveness of competing screening technologies. Kezirian et al. used a loose definition and did not calculate the incremental costs or effectiveness between technologies.

The objective of the authors' study was to estimate the cost and cost effectiveness of UNHS using OAE, S-ABR and 2-stage screening. The authors treated Transient Evoked OAE (TEOAE) and Distortion-Product OAE (DPOAE) as a single entity OAE and S-ABR was described as a shorter screening version of ABR. It was not explained whether this was the AABR.

The authors incorporated lost to follow up in their model and defined hearing loss as bilateral and unilateral. The decibel was not specified. Costs per screening and cost per identified infant (cost effectiveness) were estimated. Costs per screening in US dollars were as follows: S-ABR $20.48, OAE $12.91 and 2-stage $20.19. Cost effectiveness were $8112, $5113 and $7996 for S-ABR, OAE and 2-stage. The principal finding by Kezirian et al. demonstrates that OAE has the lowest cost and is cost effective, versus the comparators. The estimates on costs per screening are useful. However, it is worth reiterating that the cost effective definition and thus conclusion on the cost effective technology is misleading. The authors did not perform incremental cost or effectiveness accurately. Cost effectiveness by Kezirian et al. is simply the ratio of a single technology without comparators. It is erroneous by not taking the difference between technologies. The authors do not perform incremental analyses of the costs and effectiveness between technologies.

Keren et al., 2002[3]

Keren et al. did not directly compare the cost effectiveness of 1-stage versus 2-stage screening and did not evaluate which screening technology is more cost effective. Rather, the principle objective in the authors' study was an economic evaluation and comparison of Universal Newborn Hearing Screening (UNHS) and selective screening. It is under the modeling of each screening protocol the authors provided an economic evaluation of each screening technology by examining incremental cost and incremental effectiveness.

In the 1-stage screening only the cost effectiveness of AABR was examined. The authors did not conduct an economic evaluation of AOAE in the single stage screening. The model used in UNHS was a 2-stage protocol with the

TEOAE used in the first stage and AABR in the second stage. Lost to follow up were incorporated in the model. A highlight of the model is that Keren et al. were the only authors who incorporated the lifetime costs of untreated deaf infants. Deaf infants with no early intervention were modeled to have delayed language with an associated lifetime cost. Those deaf infants with early intervention were modeled to have normal language skills with an associated lifetime cost.

Lifetime costs include lost to productivity, special education, vocational rehabilitation, and medical costs. Lifetime costs for deaf infants without early intervention were estimated at approximately $1.1 million (US dollars). Most of these costs were from special education and lost productivity. Lifetime costs for deaf infants with early intervention were estimated at approximately $700,000 (US dollars).

Keren et al. found that the incremental cost of diagnosing an infant with bilateral moderate to profound deafness at 40dB by 6 months was approximately $16,000 (US dollars) using selective screening (1-stage) and $44,000 (US dollars) using UNHS (2-stage). The authors did not directly examine which technology is preferred over the other. Rather, the technologies adopted were implied based on the screening protocol- selective screening (1-stage) versus UNHS (2-stage). The authors implied that under UNHS, using a 2-stage protocol, may be beneficial if early identification results in improved language skills, lower educational and vocational costs and increased lifetime productivity resulting in long-term cost savings.

Lin et al., 2005[4]

Lin et al. compared the differences in referral rates and the cost effectiveness of 1-stage and 2-stage screening. However, in the 1 stage screening the authors only examined TEOAE and did not explore AABR as a separate 1-stage test. Hearing loss was identified by the authors as both unilateral and bilateral loss. The decibel was not specified.

The authors found that the referral rates were lower in the 2-stage screening, 1.8%, compared to the 1 stage screening, 5.8%. The total cost of screening in US dollars per infant was $10.10 for the 1-stage and $8.90 for the 2-stage. Both screening costs per infant and referral rates were lower for the 2 stage screening. The use of the 2-stage screening was able to reduce the number of infants sent for additional diagnostic testing, thereby reducing the overall expense.

Similar to the study by Kezirian et al.[1] the study by Lin et al. did not adequately provide a formal economic evaluation of the cost effectiveness of the screening protocols. Formal incremental costs and effectiveness were not examined.

Vohr et al., 2001[5]

Vohr et al. investigated the costs and referral rates of three universal screening programs: TEOAE, ABBR and 2-stage TEOAE+AABR. The authors only modeled pass and fail rates of screening. They did not incorporate lost to follow up, the diagnostic evaluation, or define deafness.

A comprehensive estimation of total costs, cost per infant and cost per identified deaf infant was examined. However, direct incremental cost and effectiveness were not performed. Costs per infant screened in US dollars were AABR $32.81, TEOAE $28.69 and 2-stage $33.05. Costs per identified deaf infant were AABR $16,405, TEOAE $14,347 and 2-stage $16,527. Vohr et al. found that costs among the three screening protocols were similar. AABR has higher costs but has lower referral rates than TEOAE and TEOAE+AABR. Referral rates were 3.21% for AABR, 6.49% for TEOAE and 4.67% for 2-stage test.

Vohr et al. did not directly examine cost effectiveness by performing incremental cost, incremental effectiveness or ICER. However, incremental analyses are implicit in the study if the reader takes the difference between each screening protocol's per screening costs and referral rates. The authors did not explicitly state which screening protocol is cost effective. The study's findings were that costs among the three screening protocols were similar. Screening costs per infant were especially similar between AABR and 2-stage where AABR has the lowest referral rate.

Literature summary on economic evaluation of 1-stage versus 2-stage screening

A summary of the literature is in Table 1. Of the four articles[1-4] selected for review, two articles[3,4] did not compare the 1-stage AOAE and AABR tests. Keren et al. examined the use of AABR in the 1-stage screening. It did not evaluate AOAE in the 1-stage screen. Lin et al. evaluated the TEOAE in the 1-stage screening but excluded the AABR.

The remaining two articles[2,5] evaluated all technologies in both the 1-stage and 2-stage screening. Results from those studies suggest AOAE has the lowest per infant screening costs but also has the highest referral rates which may lead to higher overall costs. However, it is important to note those studies did not provide an adequate estimation of cost effectiveness. Formal incremental costs and effectiveness were not examined. Cost effectiveness with estimates of ICER was not conducted. The conclusions from the literature are mixed as formal cost effectiveness was not examined.

Table 1: Summary of literature findings of 1- and 2-stage screening

Study	Study Characteristics	Findings and conclusions
Kezirian et al. (2001)[2] United States	**Method:** Estimate cost effectiveness of UNHS Cost effectiveness defined as ratio of costs and the number of identified deaf infants **Intervention:** 1-stage using S-ABR and OAE and 2-stage with a combination of S-ABR and OAE.	**Results:** Costs per screening were as follows: S-ABR $20.48, OAE $12.91 and 2-stage $20.19. Cost effectiveness were $8 112, $5 113 and $7 996 for S-ABR, OAE and 2-stage. **Conclusions:** OAE has the lowest cost and most cost effective
Keren et al. (2002)[3] United States	**Method:** Cost effectiveness analysis of alternative screening programs: 1) UNHS 2) selective screening 3) no screening **Intervention:** 1-stage only using AABR and 2-stage using TEOAE and AABR.	**Results:** Lifetime costs for deaf infants without early intervention were estimated at approximately $1.1 million. Incremental cost of was approximately $16,000 using selective screening (1-stage) and $44,000 using UNHS (2-stage). **Conclusions:** Using a 2- stage protocol under UNHS may be beneficial if early identification results in improved language skills, lower educational and vocational costs and increased lifetime productivity resulting in long-term cost savings.
Lin et al. (2005)[4] Taiwan, costs in US dollars	**Method:** Compare the referral rate and costs of 1-stage and 2-stage screening. **Intervention:** 1-stage with only TEOAE and 2-stage using combination of TEOAE and AABR	**Results:** Referral rates in the 2-stage screening are 1.8% and the 1-stage screening is 5.8%. Total cost of screening per infant was $10.10 for the 1-stage and $8.90 for the 2-stage. **Conclusions:** 2-stage screening was able to reduce the number of infants sent for additional diagnostic testing, thereby reducing the overall expense.
Vohr et al. (2001)[5] United States	**Method:** Investigate the costs and referral rates of 1-stage and 2-stage screening. **Intervention:** UNHS comparing 1-stage with TEOAE, AABR and 2-stage using a combination of TEOAE and AABR.	**Results:** Referral rates are 3.21% for AABR, 6.49% for TEOAE and 4.67% for 2-stage. Costs per infant screened are $32.81 for AABR, $29.68 for TEOAE and $33.05 for 2-stage. **Conclusions:** Costs among the three screening protocols were similar. AABR has higher costs but has lower referral rates than TEOAE and TEOAE+AABR

Literature summary on economic evaluation of 1-stage screening

Results of the literature for 1-stage testing are shown in Table 2. Four articles were based on the economic evaluation of 1 stage screening.[6-9] This evaluated AABR and TEOAE. However, two of the articles only examined TEOAE itself and did not have comparisons to AABR.[6] This report will not discuss each article in detail separately for several reasons. First, none of the articles examined the 2-stage screening. A comparison of the 1-stage and 2-stage

screening cannot be made and therefore does not merit a complete description of the articles by themselves. Second, the articles did not perform full economic evaluations and provided few elements of an economic analysis. The articles provided elements of costing and economic modeling of costing alternatives. Only a brief description of its findings is relevant for clarity and conciseness.

Table 2: Summary of literature findings on 1-stage screening

Study	Study Characteristics	Findings and conclusions
Grill et al. (2005)[6] England	**Method:** Markov modelling and clinical effectiveness of three screening programs: 1) UNHS 2) Selective screening based on risk factor 3) no screening. Costs were not thoroughly examined. **Intervention:** TEOAE only. Health effects used were Quality weighted detected Child Months (QCM). Quality reflects that early detection of impairment is a better and desired outcome.	**Results:** UNHS detected the most deaf infants, selective screening detected less infants than UNHS and no screening detected the least infants. **Conclusions:** UNHS leads to an earlier age of confirmed diagnosis compared to selective screening. UNHS has higher clinical effectiveness.
Lemons et al. (2002)[7] United States	**Method:** Costs and performance characteristics of AABR and TEOAE. AABR performed by neonatal nurses and TEOAE by master's level audiologists. **Intervention:** UNHS; TEOAE and/or AABR	**Results:** Costs per infant screened using AABR and TEOAE are $33.68 and $32.23. Referral rates for AABR and TEOAE are 6.5% and 15.7%. Total costs per infant screened using AABR and TEOAE are $45.85 and $58.07 including post discharge screening and diagnostic evaluation. **Conclusions:** AABR appears to be the preferred screening protocol. AABR was associated with lower costs and achieved the lowest referral rates at hospital discharge.
Boshuizen et al. (2001)[8] Netherlands	**Method:** Cost analyses with a simulation model. Comparisons of the cost per child detected for each screening protocol for bilateral and unilateral hearing loss **Intervention:** UNHS; OAE and/or AABR	**Results:** Costs per child detected using AABR and OAE are €39 and €25. **Conclusions:** Screening with OAE is recommended.
Grill et al. (2006)[9] England	**Method:** Markov modelling and costs of UNHS on hospital versus community settings. **Intervention:** TEOAE only. Health effects used were Quality weighted detected Child Months (QCM). Quality reflects that early detection of impairment is a better and desired outcome.	**Results:** Cost per child detected for TEOAE was €25.81 in a hospital setting and €23.39 in a community setting. Sensitivity analyses also demonstrate costs are higher in a hospital setting. **Conclusion:** Lack of definitive conclusion. Further evaluation of cost effectiveness should focus on differences in test parameters between hospital and community settings.

Of the four articles, only two compared the costs of 1-stage screening between AABR and AOAE.[7,8] Both studies found AABR more costly than OAE. Lemons et al.[7] found small cost differences between the two screenings at $1.45 (US dollars) (AABR $33.68 and TEOAE $32.23). Boshuizen et al.[8] found greater costs differences of €14 (AABR €39 and TEOAE €25).

Of the remaining two articles[6,9] only one examined costs.[9] However, costs were only estimated for TEOAE itself. Grill et al.[9] calculated costs of AOAE between a hospital and community setting. Cost per child detected in a hospital and community were £25.81 and £23.39, respectively.

PART 2: ECONOMIC EVALUATION

Economic Model

The economic model assumes universal screening for newborn hearing is conducted.

The economic objective is to determine which screening technology is cost-effective given that screening must occur under a universal screening program. The perspective is societal because the report has included costs (e.g. education) outside the health sector. The model incorporates only direct costs and specifically excludes the costs of lost productivity. Direct costs include screening costs and downstream costs of deaf infants.

In economic assessment, a decision tree modeling the components of screening is an effective method that captures the various outcomes of screening. For each screening alternative, the ratio of incremental cost to effectiveness is provided. All infants are assumed to be diagnosed by 3 months and receive treatment by 6 months.

This model does not make a distinction on the types of hearing loss. Rather, the model ends at the diagnostic terminal node where hearing loss will be confirmed. Hearing loss is defined as bilateral moderate to profound hearing loss tested at 40dB. A review of the literature found only one article where it provided test characteristics of screening and a definition of hearing loss at specific decibel.[2]

The model distinguishes between those with impaired hearing from those with normal hearing and their associated test outcomes. The impaired hearing group includes infants who are truly positive (T+) and, also, those who are false negative (F-) whereas the normal hearing group include infants who are truly negative (T-) and also those who are false positive (F+). The screeners only see positive or negative test results. The screening protocol requires that all infants who test positive undergo a follow up screening. These positive

tests include T+ and F+. The screeners do not know whether test outcomes are T+ or F+ but the model is designed to capture these outcomes.

It is important to describe the model characteristics and probabilities. An illustration of the decision tree shown in Figure 1 highlights the economic model of the 2-stage screening.

Model Characteristics

A circle node represents a chance node and a triangle node represents a terminal node or a final outcome. The expected cost (average cost) of each screening alternative is calculated as the weighted average of the cost of each pathway. The weight assigned to each pathway is the product of all the probabilities along the pathway. For example, the following section shows that the probability of the first pathway (Path_A) is the product of the prevalence rate multiplied by the first lost to follow up rate. The probability of the other pathways is calculated in a similar manner. All newborns/infants are assumed to be diagnosed by 3 months and receive treatment by 6 months.

Model probabilities

Prevalence

Prevalence estimates are used to determine the number of newborns or infants who have impaired hearing. Estimates on the number of newborns with normal hearing are calculated by taking the difference of one minus prevalence of the newborns/infants with impaired hearing.

Lost to follow up (LTFU)

Lost to follow up are newborns who do not undergo screening. The costs of infants who are lost to follow up are different. This depends on whether the infant has normal hearing or impaired hearing.

Impaired hearing

The model assumes infants with impaired hearing that are lost to follow up will develop hearing loss with delayed language skills and incur downstream costs. The model assumes downstream costs are the same for each lost to follow up pathway. However, the final cost of each pathway is different because of the different number of screening tests performed.

Normal hearing

The model assumes there are no downstream costs for infants with normal hearing who are lost to follow up. These infants have normal hearing and will not require medical or treatment costs as they are lost to follow up.

Test characteristics

True positive T+:	Those who test positive for the condition and have the condition.
False negative F-:	Those who test negative for the condition but have the condition.
True negative T-:	Those who test negative for the condition and do not have the condition.
False positive F+:	Those who test positive for the condition but do not have the condition.

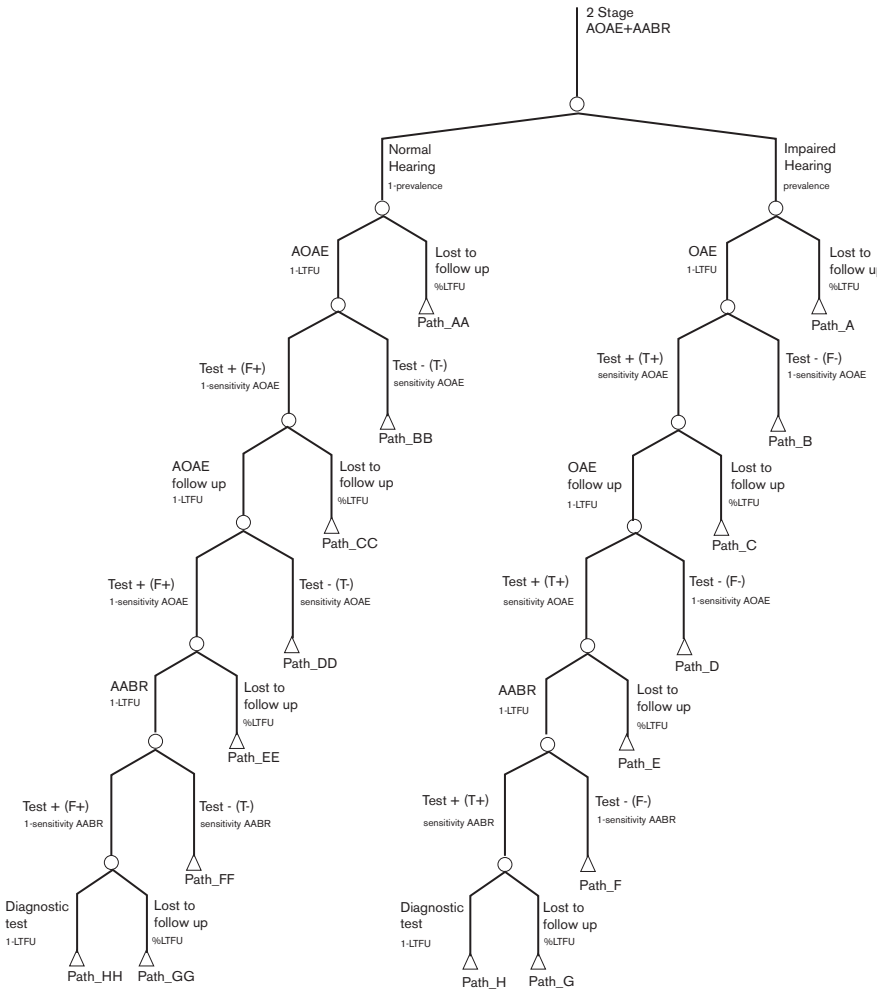
Diagnostic test

The diagnostic test is the final test performed after infants fail (T+ and F+) all of their screening tests. The test is performed by an audiologist and the model assumes that the diagnostic test has 100% accuracy.

Health Outcome

The health outcome of the model calculates the proportion of newborns whose hearing status is correctly identified. This is the definition of effectiveness as used in the model. It is the proportion of infants identified as hearing impaired/true positives (T+) and normal hearing/true negatives (T-).

Figure 1: 2-stage AOAE+AABR protocols



2-Stage AOAE + AABR

The decision tree shown as Figure 1 outlines the 2-stage screening test.

For all newborns screened, a portion (prevalence) of newborns has impaired hearing and a portion (one minus prevalence) has normal hearing. For either cohort an initial screening is performed. The model captures lost to follow up before screening is conducted. This highlights the fact that even under universal screening some newborns may not be screened.

Impaired hearing

Newborns who undergo the initial AOAE screening will have test outcomes that are either test positive (T+) or negative (F-). The infants that test positive (T+) undergo a follow up AOAE screening. Test results for these follow up infants are either positive (T+) or negative (F-). For those who have a positive test (T+) a second stage AABR screening is conducted. Test results for those infants are either positive (T+) or negative (F-). Therefore, sequential and F+ testing increases the number of false negatives. Infants who are positive (T+) undergo a diagnostic test where the infant is diagnosed with hearing loss: bilateral moderate to profound hearing loss tested at 40dB.[3]

Normal hearing

Newborns who undergo the initial AOAE screening will either test negative (T-) or positive (F+). The infants that test positive (F+) undergo a follow up AOAE screening. Test results for these follow up infants are either negative (T-) or positive (F+). For those who have a positive test (F+) a second stage AABR screening is conducted. Test results for those infants are either negative (T-) or positive (F+). Sequential testing in this cohort increases the number of true negatives. Infants who are positive (F+) undergo a diagnostic test where the test will show the infant does not have impaired hearing.

For those with impaired hearing there are four pathways that represent lost to follow up (Path_A, C, E and G). The model assumes the downstream costs for these infants are the same. However, each pathway has different total costs because of the different number of screening tests performed at each pathway. Newborns with normal hearing that are lost to follow up are in four pathways (Path_AA, CC, EE, and GG). The model assumes that newborns with normal hearing do not have downstream costs because there are no medical or treatment costs required for normal hearing. The only costs these infants have on the medical system are screening costs.

1-Stage AABR or AOAE

The 1-stage protocol is presented as Figure 2. The logic is similar to the 2-stage protocol. The single test ends at an earlier terminal node with no additional second stage test.

Impaired hearing

Some newborns are lost to follow up before a screening test is performed. For those newborns who undergo an initial screening the test outcomes will either have the infant test positive (T+) or negative (F-). The infants that test positive (T+) undergo a follow up screening test. Test results for these infants are either positive (T+) or negative (F-). For those who have a positive test (T+) they are referred to undergo a diagnostic test. Some infants will be lost to follow up and those who have the diagnostic test will be diagnosed with hearing loss: bilateral moderate to profound hearing loss tested at 40dB.[3]

Normal hearing

The same logic that applies to the cohort of impaired hearing applies to this cohort. However, the test characteristics are different when examining cases of T- and F+. For those newborns who undergo an initial screening the test outcomes will either have the infant test negative (T-) or positive (F+). The infants that test positive (F+) undergo a follow up test where the infants are either negative (T-) or positive (F+). For those who have a positive test (F+) they undergo a diagnostic test where the test will show the infant does not have impaired hearing.

Methods

Inputs in the model include the following and are summarized in Table 3:

- downstream costs of untreated infants with hearing loss;
- costs per screening for each technology;
- prevalence rate of hearing loss;
- sensitivity and specificity of AOAE and AABR;
- lost to follow up (LTFU) rates.

Downstream costs

Estimated downstream costs were derived for infants with and without treatment of hearing loss.[3] Keren et al. classified hearing impaired infants without early treatment as having delayed language skills and those with early treatment as having normal language. This report estimated these downstream costs adjusting for inflation and converting into 2003 Canadian dollars, which is the same year as the pilot study Alberta Universal Newborn Hearing Screening Project: Research Outcomes Final Report 2004.[1] Estimates

are conservative as it omits lost productivity costs and only direct costs are included. Estimated lifetime treatment costs include special education, vocational rehabilitation and assistive devices and medical costs. The cost of infants with delayed language skills were $933,435 and the cost of infants with normal language were $838,365.

Figure 2: 1-stage protocol

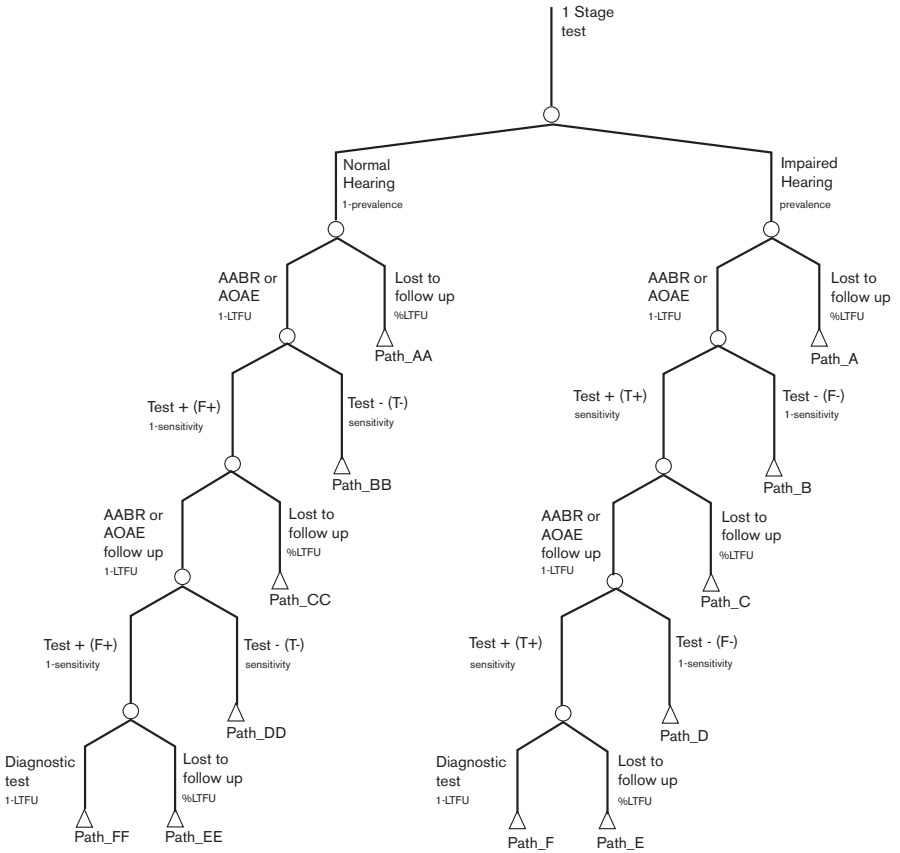


Table 3: Model inputs

Input	Estimate	Reference Sources
Downstream Costs		
Delayed language (untreated deaf infants)	$933,435	3
Normal language (treated deaf infants)	$838,365	3
Costs per screening		
AOAE	$23.13 (Cdn dollars)	9
AABR	$35.84 (Cdn dollars)	9
Prevalence	0.004 (49/12,178)	9
Sensitivity		
AOAE	0.90	2, 3, 10
AABR	0.95	2, 3, 10
Specificity		
AOAE	0.85	2, 3, 10
AABR	0.90	2, 3, 10
Lost to follow up		
LTFU1	0.1048 (1503/14,348)	9
LTFU2	0.041 (590/14,348)	9
LTFU3	0.0025 (36/14,348)	9
LTFU4	0.00098 (14/14,348)	9

Costs per screening

Estimated costs per screening for each technology include the cost of the equipment, personnel, testing supplies, and general supplies. The costs are in 2003 dollars as it is the year of the pilot study.[1] Data was obtained from the Alberta Universal Newborn Hearing Screening Project: Research Outcomes Final Report 2004.[1]

AOAE

Estimated cost for per screening of the AOAE is $23.13. The equipment used in AOAE testing is the Ero scan. The per equipment cost of the Ero-scan is estimated at $6079. The annual cost with depreciation is $1013, based on a 6 year lifespan.

AABR

Estimated cost for per screening is $35.84 for AABR. Screening time for AABR is longer relative to AOAE. This relative time factor was adjusted in the screening costs. The equipment used in AABR testing is the ABaer. The cost of the ABaer equipment is estimated at $20,280. The annual cost with depreciation is $3380, based on a 6 year lifespan.

Prevalence of hearing loss

Prevalence of hearing loss is 0.004 (49/12,178). This is derived from The Alberta Universal Newborn Hearing Screening Project: Research Outcomes Final Report 2004.[9]

Sensitivity and specificity

The sensitivity for AOAE is 0.90 and AABR is 0.95. The specificity for AOAE and AABR is 0.85 and 0.90, respectively. These estimates were obtained from the literature.[2,3,10]

Three studies provided AOAE sensitivities.[2,3,10] Norton et al. reported a sensitivity of 0.80.[10] Kezirian et al. and Keren et al. both found sensitivities of 0.95.[2,3] However, the studies by Kezirian et al. and Keren et al. had AOAE sensitivity equal to that of the AABR. AABR is more sensitive than AOAE as the former screens in newborns/infants with auditory neuropathy. In the sensitivity analysis conducted by Kezirian et al. and Keren et al. the authors used 0.90 as the lower bound limit. A sensitivity of 0.80 as used by Norton et al. is low compared to other studies. This report used an AOAE sensitivity of 0.90.

Lost to follow up rates (LTFU)

The LTFU rates were estimated from data based on the Alberta Universal Newborn Hearing Screening Project: Research Outcomes Final Report 2004.[1] There are four LTFU rates. The first LTFU rate is 0.1048 (1503/14,348) and represents the first LTFU before any screening is conducted. The second LTFU rate is 0.041 (590/14,348) and occurs after the first screen test is performed. The third LTFU rate is 0.0025 (36/14,348) occurring after the second screen test. The fourth LTFU is only for the 2-stage test where infants are LTFU after conducting the second stage AABR test and they are referred for a diagnostic test. This rate is 0.00098 (14/14,348).

Model Assumptions

The following is a list of the assumptions used in the model:

- Universal hearing screening for all newborns/infants in Alberta.
- Infants in NICU and in well-baby nurseries are tested following the same protocol.
- An audiologist spends an hour for the diagnostic evaluation. This includes time conducting the test and counseling parents.
- Diagnostic evaluation performed by an audiologist after all screenings is 100% accurate.
- Hearing loss is defined as moderate to profound bilateral permanent hearing loss at 40dB.

- Infants with impaired hearing that are lost to follow up will develop hearing loss with delayed language skills and incur downstream costs.
- Infants with impaired hearing that are diagnosed and treated within 6 months will develop normal language skills. Infants with impaired hearing who are not treated within 6 months will develop delayed language skills.
- There are no downstream costs for infants with normal hearing who are lost to follow up. These infants have normal hearing and will not require medical or treatment costs as they are lost to follow up.

Cost Effectiveness

Cost effectiveness is based on estimates of downstream costs, costs per screening and probabilities in the lost to follow up rate and the sensitivity and specificity of each test. Cost effectiveness determines both expected costs and effectiveness (outcomes).

Concepts

Expected costs

The expected cost (average cost) of each screening alternative is calculated using costs of each screening protocol and probabilities along the model. These probabilities include the sensitivity and specificity of each screening technology and the lost to follow up rates.

Incremental cost and effectiveness

Incremental cost and effectiveness is calculated taking the difference in costs and effectiveness between two technologies. For example, the incremental cost between AABR and AOAE is the difference in cost between the two strategies.

Incremental cost effectiveness ratio (ICER)

An ICER is taken as the ratio of the incremental cost and effectiveness between competing technologies. A technology is dominated if it costs more and is less effective compared to the alternative. An ICER is not calculated if an alternative is dominated by another technology. An ICER is interpreted as the additional cost per identified infant between screening alternatives.

Results

Costs of 1-stage and 2-stage

Table 4 highlights estimates of the model and lists screening alternatives in ascending expected costs. Effectiveness is not in ascending order. The 1-stage AABR has the lowest expected cost ($3475.50) and the 2-stage protocol has the highest ($3508.06). The 2-stage protocol has the highest effectiveness (0.886901) and the 1-stage AOAE has the lowest (0.869769). Effectiveness is

the proportion of births whose hearing status, normal hearing (T-) or hearing loss (T+), is correctly identified by the test. The effectiveness in the 2-stage protocol translates to 0.886901 proportion of births who have their hearing status correctly identified as normal hearing (T-) or hearing loss (T+).

The 1-stage AABR test dominates the 1-stage AOAE protocol since the former has lower costs and greater effectiveness. This eliminates the 1-stage AOAE as a cost effective alternative. The ICER is not calculated between screening protocols when an alternative is dominated by another. The 2-stage protocol is, therefore, compared to the 1-stage AABR protocol.

The incremental expected cost and effectiveness between the 1-stage AABR and 2-stage protocol are positive. This indicates an increase in both the expected cost and effectiveness if we switch from a 1 stage AABR to a 2-stage protocol. The ICER between the 1-stage AABR test and 2 stage protocol is $7574.78. This means that an additional cost of $7574.78 will be incurred to correctly identify the hearing status, T+ and T-, of one additional infant between the two protocols.

Table 4: Costs of 1-stage and 2-stage tests

Technology	Expected Cost Cdn 2003 $	Incremental Cost Cdn 2003 $	Effectiveness	Incremental Effectiveness	ICER
1-stage AABR	$3475.50		0.882603		
1-stage AOAE	$3494.49	$18.99	0.869769	-0.012834	(Dominated)
2 stage protocol	$3508.06	$32.56	0.886901	0.004298	7574.78

Sensitivity Analysis

Sensitivity analyses were performed on the sensitivity and specificity of each screening alternative. Additional analysis was also performed on downstream costs and the LTFU rates.

AOAE test characteristics

Table 5 displays the AOAE sensitivity analysis results. The sensitivity and specificity values ranged from 0.80-0.96.[2,3,10] Of the 1-stage protocols, the AABR dominates the AOAE alternative if the sensitivity of AOAE is 0.92 or less. In addition, the 2-stage protocol has the highest effectiveness where the ICER between the 1-stage AABR and 2-stage protocol varies from 4827 22,709. If AOAE sensitivity was 0.96 it becomes the cost effective alternative compared to the AABR. At 0.96 sensitivity, the 1-stage AABR is dominated by the 1-stage AOAE. Also, the ICER between the 1-stage AOAE and 2-stage protocol is 902.

If AOAE specificity is less than 0.88 the 1-stage AABR dominates the 1-stage AOAE. The ICER between the 1-stage AABR and 2-stage protocol varies depending on the specificity. At specificities of 0.92 and 0.96 the 1-stage AABR still has the lowest expected cost. However, it does not dominate other screening protocols given the various values of ICER.

Table 5: Sensitivity analysis of AOAE

Sensitivity AOAE	Protocol	Cost	Incremental Cost Cdn 2003 $	Effectiveness	Incremental Effectiveness Cdn 2003 $	ICER
0.80	1-stage AABR	3475.50		0.8826		
	1-stage AOAE	3549.80		0.8692		(Dominated)
	2-stage	3560.60	85.00	0.8863	0.0037	22,709
0.84	1-stage AABR	3475.50		0.8826		
	1-stage AOAE	3528.50		0.8694		(Dominated)
	2-stage	3540.30	64.80	0.8866	0.004	16,368
0.88	1-stage AABR	3475.50		0.8826		
	1-stage AOAE	3506.10		0.8696		(Dominated)
	2-stage	3519.10	43.50	0.8868	0.0042	10,413
0.92	1-stage AABR	3475.50		0.8826		
	1-stage AOAE	3482.60		0.8699		(Dominated)
	2-stage	3496.80	21.30	0.8870	0.0044	4827
0.96	1-stage AOAE	3458.20		0.8702		
	2-stage	3473.60	15.40	0.8873	0.0171	(Dominated)
	1-stage AABR	3475.50		0.8826		902
Specificity AOAE	**Protocol**	**Cost**	**Incremental Cost Cdn 2003 $**	**Effectiveness**	**Incremental Effectiveness Cdn 2003 $**	**ICER**
0.80	1-stage AABR	3475.50		0.8826		
	1-stage AOAE	3496.00		0.853		(Dominated)
	2-stage	3509.60	34.10	0.8835	0.0009	36,325
0.84	1-stage AABR	3475.50		0.8826		
	1-stage AOAE	3494.80		0.8668		(Dominated)
	2-stage	3508.40	32.90	0.8863	0.0037	8,975
0.88	1-stage AABR	3475.50		0.8826		
	1-stage AOAE	3493.60		0.8778		(Dominated)
	2-stage	3507.20	31.70	0.8887	0.0061	5,192
0.92	1-stage AABR	3475.50		0.8826		
	1-stage AOAE	3492.60	17.10	0.8861	0.0035	4,892
	2-stage	3506.10	13.50	0.8909	0.0048	2,837
0.96	1-stage AABR	3475.50		0.8826		
	1-stage AOAE	3491.60	16.10	0.8917	0.0091	1,782
	2-stage	3505.20	13.50	0.8928	0.0011	12,447

AABR test characteristics

Table 6 presents the results of the AABR sensitivity analysis. The sensitivity ranged from 0.84-0.98 and the specificity from 0.80-0.99.[2,3,10] At a sensitivity of 0.84 the AABR is dominated by the AOAE. If the sensitivity of AABR was 0.91 or less the lowest cost alternative is the 1-stage AOAE with various ICER values between the screening alternatives. At a sensitivity of 0.945 or higher the 1-stage AABR dominates the AOAE alternative. At this sensitivity and higher, the ICER values are 7133 and 10,399 with the 2-stage protocol.

At specificities of 0.9425 or greater the 1-stage AABR dominates the other screening protocols. It also dominates the 1-stage AOAE at a specificity of 0.895. The AABR is not dominant at specificities between 0.80-0.895 based on the various ICER values.

Table 6: Sensitivity analysis of AABR

Sensitivity AABR	Protocol	Cost	Incremental Cost Cdn 2003 $	Effectiveness Cdn 2003 $	Incremental Effectiveness	ICER
0.84	1-stage AOAE	3494.50		0.8698		
	2-stage	3537.00	42.50	0.8866	0.0168	(Dominated)
	1-stage AABR	3539.60		0.8819		2528
0.875	1-stage AOAE	3494.50		0.8698		
	1-stage AABR	3520.00	25.60	0.8821	0.0124	2067
	2-stage	3527.80	7.80	0.8867	0.0046	1703
0.91	1-stage AOAE	3494.50		0.8698		
	1-stage AABR	3499.70	5.20	0.8823	0.0126	415
	2-stage	3518.60	18.90	0.8868	0.0044	4250
0.945	1-stage AABR	3478.60		0.8826		
	1-stage AOAE	3494.50		0.8698		(Dominated)
	2-stage	3509.40	30.80	0.8869	0.0043	7133
0.98	1-stage AABR	3456.70		0.8828		
	1-stage AOAE	3494.50		0.8698		(Dominated)
	2-stage	3500.20	43.50	0.8870	0.0042	10,399

Table 6: Sensitivity analysis of AABR (continued)

Specificity AABR	Protocol	Cost	Incremental Cost Cdn 2003 $	Effectiveness Cdn 2003 $	Incremental Effectiveness	ICER
0.80	1-stage AABR	3479.50		0.8533		
	1-stage AOAE	3494.50	15.00	0.8698	0.0165	908
	2-stage	3508.10	13.60	0.8850	0.0152	897
0.8475	1-stage AABR	3477.50		0.8693		
	1-stage AOAE	3494.50	17.00	0.8698	0.0004	40,252
	2-stage	3508.10	13.60	0.8859	0.0161	844
0.895	1-stage AABR	3475.70		0.8815		
	1-stage AOAE	3494.50		0.8698		(Dominated)
	2-stage	3508.10	32.40	0.8868	0.0053	6153
0.9425	1-stage AABR	3474.00		0.8899		
	1-stage AOAE	3494.50		0.8698		(Dominated)
	2-stage	3508.00		0.8877		(Dominated)
0.99	1-stage AABR	3472.40		0.8944		
	1-stage AOAE	3494.50		0.8698		(Dominated)
	2-stage	3508.00		0.8886		(Dominated)

Downstream costs

Downstream costs were decreased in the sensitivity analyses for infants with delayed language. The values ranged from $850,000-$900,000 (Cdn 2003 $) where the lowest level is approximately a 10% reduction in costs. Sensitivity analysis was performed to determine if lower downstream costs would be influenced by the proportion of false negatives (F-). If a screening alternative has high false negatives (F-) the proportion of these infants will have a significant impact on downstream costs. These downstream costs have a direct impact on the expected costs of the screening alternative and its incremental cost effectiveness.

The results of the sensitivity analysis for downstream costs are displayed in Table 7. With downstream costs of $850,000 (Cdn 2003 $) the 1-stage AOAE dominates the AABR. The ICER between the AOAE and 2-stage protocol is 104. At $862,500 (Cdn 2003 $) the 1-stage AOAE is the lowest cost alternative. The ICER between the 1-stage protocols is 272 and the ICER between AOAE and the 2-stage protocol is 13. Downstream costs between $875,000 and $900,000 (Cdn 2003 $) demonstrate that the 1-stage AABR dominates the AOAE alternative. The ICER between the AABR and 2-stage protocol are 1346, 2679 and 4011.

Table 7: Sensitivity analysis of downstream costs

Downstream costs	Protocol	Cost	Incremental Cost Cdn 2003 $	Effectiveness Cdn 2003 $	Incremental Effectiveness	ICER
850 000	1-stage AOAE	3392.30		0.8698		
	2-stage	3394.10	1.80	0.8869	0.0171	
	1-stage AABR	3399.70		0.8826		104
862 500	1-stage AOAE	3407.60		0.8698		
	1-stage AABR	3411.10	3.50	0.8826	0.0128	272
	2-stage	3411.10	0.10	0.8869	0.0043	13
875 000	1-stage AABR	3422.40		0.8826		
	1-stage AOAE	3422.90		0.8698		(Dominated)
	2-stage	3428.20	5.80	0.8869	0.0043	1346
887 500	1-stage AABR	3433.80		0.8826		
	1-stage AOAE	3438.20		0.8698		(Dominated)
	2-stage	3445.30	11.50	0.8869	0.0043	2679
900 000	1-stage AABR	3445.10		0.8826		
	1-stage AOAE	3453.50		0.8698		(Dominated)
	2-stage	3462.40	17.20	0.8869	0.0043	4011

Lost to follow up (LTFU) rates

Sensitivity analysis was performed on the first and second LTFU because both rates were relatively high. Under a universal screening program the LTFU rate would be expected to be lower. The first LTFU (LTFU1) rate ranged from 0.04 to 0.08 and the second LTFU (LTFU2) ranged from 0.01 to 0.03.

Results of the sensitivity analysis are presented in Table 8. Results of the sensitivity analysis for both LTFU rates did not change the original outcome of the cost effective alternative. The 1-stage AABR still dominates the AOAE protocol. The ICER is 7575 for each LTFU1 rate between the AABR and 2–stage protocol. In LTFU2 the 1-stage AABR dominates the AOAE. The ICER between the AABR and 2-stage protocol was different for each LTFU2 rate used and range from 5780 to 6510.

Table 8: Sensitivity analysis for LTFU rate

Lost to Follow-up 1	Protocol	Cost	Incremental Cost Cdn 2003 $	Effectiveness Cdn 2003 $	Incremental Effectiveness	ICER
0.04	1-stage AABR	3456.80		0.9464		
	1-stage AOAE	3477.20		0.9326		(Dominated)
	2-stage	3491.80	34.90	0.9510	0.0046	7575
0.05	1-stage AABR	3459.70		0.9365		
	1-stage AOAE	3479.90		0.9229		(Dominated)
	2-stage	3494.30	34.50	0.9411	0.0046	7575
0.06	1-stage AABR	3462.60		0.9267		
	1-stage AOAE	3482.50		0.9132		(Dominated)
	2-stage	3496.80	34.20	0.9312	0.0045	7575
0.07	1-stage AABR	3465.50		0.9168		
	1-stage AOAE	3485.20		0.9035		(Dominated)
	2-stage	3499.30	33.80	0.9213	0.0045	7575
0.08	1-stage AABR	3468.40		0.9070		
	1-stage AOAE	3487.90		0.8938		(Dominated)
	2-stage	3501.80	33.50	0.9114	0.0044	7575
Lost to Follow-up 2	**Protocol**	**Cost**	**Incremental Cost Cdn 2003 $**	**Effectiveness Cdn 2003 $**	**Incremental Effectiveness**	**ICER**
0.01	1-stage AABR	3466.10		0.8852		
	1-stage AOAE	3486.10		0.8734		(Dominated)
	2-stage	3500.10	34.00	0.8911	0.0059	5780
0.015	1-stage AABR	3467.60		0.8848		
	1-stage AOAE	3487.40		0.8728		(Dominated)
	2-stage	3501.40	33.70	0.8904	0.0056	6001
0.02	1-stage AABR	3469.10		0.8844		
	1-stage AOAE	3488.80		0.8722		(Dominated)
	2-stage	3502.70	33.50	0.8897	0.0054	6244
0.025	1-stage AABR	3470.70		0.8839		
	1-stage AOAE	3490.20		0.8716		(Dominated)
	2-stage	3503.90	33.30	0.8891	0.0051	6510
0.03	1-stage AABR	3472.20		0.8835		
	1-stage AOAE	3491.50		0.8711		(Dominated)
	2-stage	3505.20	33.10	0.8884	0.0049	6804

PART 3: DISCUSSION/CONCLUSION

This report has several findings on the cost effectiveness of technologies on screening for hearing in newborns/infants. It finds that the 1-stage AABR is the cost effective alternative compared to the 1-stage AOAE. It dominates AOAE because the AABR has lower expected costs and higher effectiveness.

This report cannot provide a clear answer on the cost-effective alternative between the 1-stage AABR and the 2-stage protocol (AOAE and AABR). The 2-stage protocol has higher expected costs but also higher effectiveness. The Incremental Cost Effective Ratio (ICER) between the 1 stage AABR protocol and 2-stage protocol is $7574.78 (Cdn 2003 $). This translates to an additional cost of $7574.78 (Cdn 2003 $) to correctly identify the hearing status of one additional infant between the two protocols. The 2-stage protocol includes a greater number of sequential screens over time. This increases the number of false negative cases, but decreases the number of false positive cases. It is a value judgment to determine whether correctly identifying one additional infant is worth the additional cost. Without knowing the budget constraints, resource restraints and opportunity costs of the provincial health care system, in particular the Health Ministry and Regional Health Authorities, it is not clear which is the cost-effective alternative.

Limitations of this report include the narrow definition of hearing loss. This report defined hearing loss as bilateral moderate to profound hearing loss tested at 40dB.[2] This definition excludes unilateral hearing loss and also hearing loss tested at different decibels. The ICER value of $7574.78 (Cdn 2003 $) is applicable only to a hearing loss cohort as defined in this report. The technologies examined in this report are for newborns/infants tested at a short time horizon. Infants who are older than 3 months require different screening tests.

Sensitivity analysis found that the 1-stage AABR dominates the AOAE alternative if the sensitivity of AOAE was 0.92 or less. At a sensitivity of 0.945 or higher the 1-stage AABR dominates the AOAE alternative. Comparisons between the 1-stage AABR and 2-stage protocols resulted in the 2-stage protocol exhibiting higher expected costs but also higher effectiveness. ICERs ranged in value depending on the test characteristics. Downstream costs between $875,000 and $900,000 (Cdn 2003 $) demonstrate that the 1-stage AABR dominates the AOAE alternative. The ICER between the AABR and 2-stage protocol vary. Results from the sensitivity analysis for both lost to follow-up dates (before the initial screen and after the first screening test) for each protocol did not change the original outcome of the cost effective alternative. The 1-stage AABR still dominates the AOAE protocol. The 2-stage protocol still had higher expected costs and effectiveness compared to the AABR.

AOAE is less sensitive than AABR, resulting in higher rates of false negatives for each screen test performed. The higher false negatives rates result in a higher proportion of infants with hearing loss who are erroneously identified as having normal hearing. This ultimately reduces the number infants who are correctly identified with hearing loss. It is the accuracy of the screening technologies and the protocol and the associated downstream costs of infants with hearing loss who are not identified that lowers the cost effectiveness of AOAE screening.

This report finds that the 1-stage AABR screening protocol is a cost-effective alternative compared to the 1-stage AOAE protocol. The 1-stage AOAE protocol is less accurate and costs more. The 2-stage protocol was found to be more effective with higher expected costs compared to the 1-stage AABR protocol. It is a value judgment to determine whether correctly identifying one additional infant is worth the additional cost. The cost of this additional accuracy is $7574.78 (Cdn 2003 $) per infant identified between the two screening protocols.

APPENDIX A: UPDATED LITERATURE SEARCH SUMMARY: NEWBORN HEARING SCREENING

General Information

The literature search was conducted by the AHFMR Research Librarian between June 14, 2006 and August 10, 2006. Major electronic databases used include: The Cochrane Library, NHS Centre for Reviews and Dissemination (CRD Databases: NHS EED, HTA, DARE), PubMed, and EMBASE. In addition relevant library collections, web sites of practice guidelines, regulatory agencies, evidence-based resources and other HTA related agency resources (AETMIS, CCOHTA, ECRI) were searched. Internet search engines were also used to locate grey literature.

Medical Subject Headings (MeSH) terms relevant to this topic are: mass screening; infant, newborn; infant; hearing; evoked potentials, auditory, brain stem;

Table A1: Updated Literature Search Summary: Newborn Hearing Screening See below for limits[†]

Database	Edition or date searched	Search Terms [††]
Databases		
The Cochrane Library http://www.thecochranelibrary.com	Issue 2, 2006 June 16, 2006	(infan* OR newborn*) AND ((hearing AND screening) OR OAE OR DPOAE OR TEOAE OR AABR OR ABR OR otoacoustic emission* OR auditory brainstem response) in **Title, Abstract or Keywords**
PubMed http://www.pubmed.gov	June 16, 2006	#1: (Infan* OR newborn* OR neonat*) AND (OAE OR DPOAE OR TEOAE OR AABR OR ABR OR otoacoustic emission* OR auditory brainstem response OR hearing screening) Limits: English, Publication Date from 2001 #2: #1 Limits: Animals #3: #1 NOT #2 #4: #3 Limits: Editorial, Letter, Meta-Analysis, Practice Guideline, Review, Consensus Development Conference, "Consensus Development Conference, NIH", Evaluation Studies, Government Publications, Guideline #5: in process[sb] OR publisher[sb] #6: #3 AND #5 #7: #4 OR #6
CRD Databases (DARE, HTA & NHS EED)	June 16, 2006	(infant OR newborn OR neonat) AND ((hearing AND screening) OR OAE OR DPOAE OR TEOAE OR AABR OR ABR |OR otoacoustic emission* OR auditory brainstem response)

Table A1: Updated Literature Search Summary: Newborn Hearing Screening (continued)

Database	Edition or date searched	Search Terms ††
Databases (continued)		
EMBASE –Ovid platform (Licenced resource)	(2006 Week 23) June 16, 2006	1. (Newborn/ or Infant/) and ((hearing and screening).mp. or exp Otoacoustic Emission/ or auditory brainstem response.mp. or (OAE or DPOAE or TEOAE or AABR or ABR).mp.) 2. limit 1 to (human and english language and yr="2001 - 2006") 3. (meta-anal$ or metaanal$).mp. or review.pt. or (review$ or overview$).mp. or (hta$ or health technology assessment$ or biomedical technology assessment$).mp. or exp CONSENSUS DEVELOPMENT/ or exp CONSENSUS/ or exp Practice Guideline/ 4. 2 and 3
Web of Science – ISI platform (Licensed resource)	June 16, 2006	1. TS=(newborn* or infan* or neonat*) AND TS=(OAE OR DPOAE OR TEOAE OR AABR OR ABR OR otoacoustic emission* OR auditory brainstem response OR (hearing AND screening)) Language=English; Databases=SCI-EXPANDED, SSCI, A&HCI; Timespan=2001-2006 2. #1 DocType=Review; 3. #1 AND TS=(review* OR overview* OR guideline* OR clinical pathway OR consensus OR meta analysis OR meta-analysis OR HTA OR technology assessment) 4. #2 OR #3
Library Catalogue		
NEOS (Cenral Alberta Library Consortium)	June 16, 2006	(newborn$ or infant$ or neonat$) and hearing and screening; otoacoustic emission$ or auditory brainstem response
Guidelines		
AMA Clinical Practice Guidelines http://www.topalbertadoctors.org/TOP/CPG/	June 14, 2006	Browsed list of guidelines
CMA Infobase http://mdm.ca/cpgsnew/cpgs/index.asp	June 16, 2006	Hearing; otoacoustic; auditory brainstem
National Guideline Clearinghouse http://www.ngc.gov	June 14, 2006	(newborn* OR infant*) AND hearing AND screening

Table A1: Updated Literature Search Summary: Newborn Hearing Screening (continued)

Database	Edition or date searched	Search Terms ††
Coverage/Regulatory/Licensing Agencies		
Alberta Health and Wellness http://www.health.gov.ab.ca	June 14, 2006	Infant +hearing +screening; newborn +hearing +screening
Medical Devices Active Licence Listing http://www.mdall.ca/	June 16, 2006	**Device name:** otoacoustic **Device name:** auditory brainstem
Health Canada http://www.hc-sc.gc.ca	June 16, 2006	"newborn hearing screening"; "infant hearing screening"; "otoacoustic emissions"; "auditory brainstem"
US Food and Drug Administration Databases http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/search/search.cfm	June 16, 2006	otoacoustic; auditory brainstem response
Aetna Clinical Policy Bulletins http://www.aetna.com/about/cov_det_policies.html	June 14, 2006	"otoacoustic emissions"; "auditory brainstem response"
HTA resources		
AETMIS http://www.aetmis.gouv.qc.ca	June 14, 2006	otoacoustic; "auditory brainsterm"; "hearing screening"
CADTH http://www.cadth.ca/index.php/en/hta/reports-publications/search	June 14, 2006	otoacoustic; auditory brainstem; hearing
Institue for Clinical and Evaluative Sciences (ICES), Ontario http://www.ices.on.ca/	June 15, 2006	otoacoustic; auditory brainstem; hearing
Health Technology Assessment Unit At McGill http://www.mcgill.ca/tau/	June 15, 2006	Browsed list of topics

Table A1: Updated Literature Search Summary: Newborn Hearing Screening (continued)

Database	Edition or date searched	Search Terms [††]
HTA resources (continued)		
Medical Advisory Secretariat http://www.health.gov.on.ca/english/providers/program/mas/mas_mn.html	June 15, 2006	Browsed list of reviews
CCE http://www.med.monash.edu.au/healthservices/cce/	June 15, 2006	Browsed list of reviews
ECRI http://www.ecri.org (Licenced Resource)	June 15, 2006	(infant* OR newborn*) AND hearing AND screening; otoacoustic; auditory brainstem
Health Quality Council, Saskatchewan http://www.hqc.sk.ca/	June 15, 2006	"auditory brainstem response"; otoacoustic
BlueCrossBlue Shield http://www.bluecares.com/tec/index.html	June 14, 2006	Browsed list of assessments
MHRA (UK) http://www.mhra.gov.uk	June 15, 2006	Browsed list of assessments
NZHTA http://nzhta.chmeds.ac.nz/publications.htm	June 15, 2006	Browsed list of publications
NICE (UK) http://www.nice.org.uk/	June 15, 2006	otoacoustic; auditory brainstem response
Search Engines		
Google http://www.google.com	August 10, 2006	1. Newborn hearing screening auditory-brainstem-response OR otoacoustic-emission –pubmed; 2. Newborn hearing screening auditory-brainstem-response OR otoacoustic-emission –pubmed Technology assessment (first 50 results of each)

Note:

[†] **Limits:** Searches were limited to **publication dates** 2001-2006; **language:** English only; **studies:** human studies only. These limits are applied in databases where such functions are available.

[††] "*", "# ", and "?" are truncation characters that retrieve all possible suffix variations of the root word e.g. surg* retrieves surgery, surgical, surgeon, etc.

; are used to separate search terms that were searched separately

Inclusion criteria were English language studies on the economic evaluation, economic costing and cost effectiveness of AOAE, AABR 1-stage protocol and 2-stage protocol. Inclusion criteria focused on the economic evaluation of the technologies. Exclusion criteria excluded articles that examined screening programs and did not incorporate the technologies.

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Notes

Notes

IHE Publications

- Cost-effectiveness in the detection of syphilis
- The use and benefit of teleoncology services
- Screening newborns for hearing
- Screening newborns for cystic fibrosis
- The use of nitric oxide in acute respiratory distress syndrome
- Rountine pre-operative testing – is it necessary?
- Consensus Statement on Self-monitoring in Diabetes
- Consensus Statement on How to Prevent Low Birth Weight

Permanent congenital hearing impairment/loss (PCHI) is one of the most common congenital anomalies found at birth which can be expected to lead to delays and deficits in the development of speech, language, cognition and learning, as well as secondary effects on the child and family. Limited scientific evidence suggests that early identification and subsequent appropriate intervention (within the first 6 months) in infants with PCHI can minimize these effects. As a result, there has been a growing interest for universal newborn hearing screening (UNHS) in attempts to diagnose PCHI as early as possible. This report reviews the evidence in the field.

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