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AUTOMATED AUDITORY BRAINSTEM RESPONSE (AABR) AND OTOACOUSTIC EMISSIONS (OAE) DEVICES IN UNIVERSAL NEWBORN HEARING SCREENING

HEALTH TECHNOLOGY ASSESSMENT SECTION
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DISCLAIMER

Technology review is a brief report, prepared on an urgent basis, which draws on restricted reviews from analysis of pertinent literature, on expert opinion and / or regulatory status where appropriate. **It has been subjected to an external review process.** While effort has been made to do so, this document may not fully reflect all scientific research available. Additionally, other relevant scientific findings may have been reported since completion of this review.

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DISCLOSURE

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EXECUTIVE SUMMARY

Background

Hearing loss is one of the most common major abnormalities that presents at birth and if undetected will impair speech, language and cognitive development. In 2009, World Health Organization (WHO) reported that around zero point five to five (0.5 to 5) in every 1000 neonates and infants have congenital hearing loss. Basically, first three years of life is a critical period for language and speech development in children.

Therefore, a neonatal hearing screening is the best mean to minimize the adverse effects of hearing loss. Universal neonatal hearing screening (UNHS) program is the current standard of practice in developed countries to detect hearing loss among children at early age.

In Ministry of Health (MOH), the high risk neonatal hearing screening program (HRNHS) has been introduced in hospitals since 2001. The 2015 Guideline for Neonatal Hearing Screening involved two stages of screening which used two different method of hearing screening which is automated auditory brainstem response (AABR) and otoacoustic emission (OAE). Based on UNHS analysis for 2014, the outcome of UNHS using OAE showed higher referral rate compared to automated auditory brainstem response. Hence this technology review was requested by the audiologist from Kuala Lumpur Hospital to review the evidence on AABR and OAE for UNHS and the protocols involved in UNHS as an input to standardize the screening protocol and devices in MOH.

Objective/aim

To assess the safety, efficacy and cost-effectiveness of automated auditory brainstem response (AABR) and otoacoustic emissions (OAE) devices in universal newborn hearing screening

Results & Conclusion

There were 12 studies included in this technology review. Three studies were using OAE, one study using AABR, one study on comparison of OAE and AABR and four studies were combination of OAE and AABR for newborn hearing screening. Three cost-effectiveness analyses on universal newborn hearing screening also included in this technology review.

In conclusion, there were studies which showed various findings based on the types of screening protocols used. In OAE alone, the pooled referral rate and false positive rate was lower when screening was done after two days of life compared to within two days of life. However, it varies according to the frequency used. Then, for AABR alone, limited evidence to suggest double screening steps

with AABR before discharge was effective to lower the referral rate. While comparing OAE and AABR, limited evidence to suggest that initial screening with AABR had significantly lower referral rate compared to initial screening with OAE for newborns younger than 48 hours. Nevertheless, the evidence showed that combination of OAAE and AABR was the best protocol compared to the single used device and was considered as cost-effective for long term practice.

Safety

No retrievable evidence on safety. Both OAE and AABR have received United State Food and Drug Administration approval.

Cost/Cost-Effectiveness

Cost of OAE ranged from RM30,000 to RM50,000 and AABR ranged from RM70,000 to RM80,000. Two cost-effectiveness studies suggest potential long-term cost saving for UNHS.

Methods

Electronic databases were searched through Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1948 to present, and Embase 1996 to 2015 June 08. Searches were also run in PubMed, Horizon Scanning databases, UM Library website, FDA website and INAHTA for published reports.

Search was limited to studies published within 1990s to 2000s. Google and Google Scholar were also used to search for additional web-based materials and information about the technology. Besides, additional articles from reviewing the references of retrieved articles also included.

AUTOMATED AUDITORY BRAINSTEM RESPONSE (AABR) AND OTOACOUSTIC EMISSIONS (OAE) DEVICES IN UNIVERSAL NEWBORN HEARING SCREENING

1. BACKGROUND

Hearing loss is one of the most common major abnormalities that presents at birth and if undetected will impair speech, language and cognitive development.[1] In over 5% of the world's population, 360 million people has disabling hearing loss. Disabling hearing loss refers to hearing loss greater than 40 decibels (dB) in the better hearing in adults and hearing loss greater than 30 dB in the better hearing ear in children.[2]

In 2009, World Health Organization (WHO) reported that around zero point five to five (0.5 to 5) in every 1000 neonates and infants have congenital hearing loss. Basically, first three years of life is a critical period for language and speech development. Thus, it is very important for any children who are identified with hearing loss as early as zero to six months of life to receive immediate interventions for improvement in their cognitive, language and social development.[1]

Therefore, a neonatal hearing screening is the best mean to minimize the adverse effects of hearing loss. Universal neonatal hearing screening (UNHS) program is the current standard of practice in developed countries to detect hearing loss among children at early age. The purpose of the UNHS is to detect hearing loss in newborn babies before three months old and to provide appropriate intervention at no later than six months of age.[1]

In the Ministry of Health (MOH) Malaysia, the high risk neonatal hearing screening program (HRNHS) has been introduced in hospitals since 2001. To date, 28 hospitals have implemented HRNHS and six hospitals have progressed to UNHS.[1] Most hospitals use otoacoustic emission (OAE) as a screening devices. However, based on UNHS analysis for 2014, the outcome of UNHS using OAE showed higher referral rate compared to automated auditory brainstem response. Hence this technology review was requested by the audiologist from Kuala Lumpur Hospital to review the evidence on AABR and OAE for UNHS and the protocols involved in UNHS as an input to standardize the screening protocol and devices in MOH.

2. OBJECTIVE/AIM

To assess the safety, efficacy and cost-effectiveness of automated auditory brainstem response (AABR) and otoacoustic emissions (OAE) devices in universal newborn hearing screening

3. TECHNICAL FEATURES

3.1 Universal Newborn Hearing Screening (UNHS)

Universal Neonatal/Newborn Hearing Screening (UNHS) is a strategy for early detection of permanent congenital hearing loss. It describes the use of objective testing methods (usually OAE testing or AABR testing) to screen the hearing of well newborns in a particular target region. There is widespread agreement that universal physiological screening using otoacoustic emissions (OAE) testing or auditory brainstem response (ABR) is the best approach.[3]

i) Otoacoustic Emissions (OAE)

Otoacoustic Emissions (OAEs) are sounds of cochlear origin, which can be recorded by microphone fitted into the ear canal. They are caused by motion of the cochlea's sensory hair cell as they energetically respond to auditory stimulation.[4] The automated hearing test with OAEs measured the sounds emitted by normal, healthy inner ear.[1] The otoacoustic Emissions provide simple, efficient and non-invasive objective indicator of healthy cochlear function. The OAE screening is widely used in universal newborn hearing screening programs.[4]

Figure 1: OAE[5]

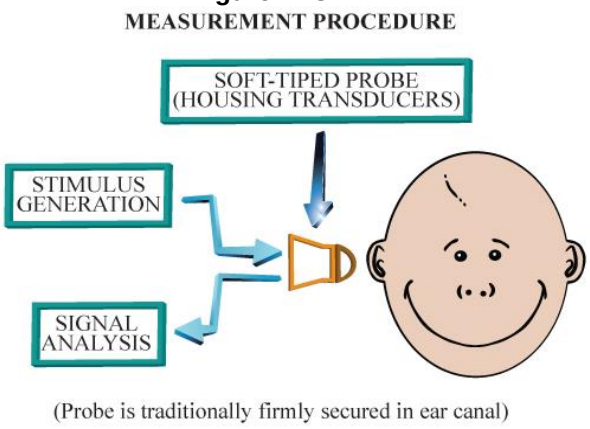


Figure 1b: Actual OAE Test[6]

The primary purpose of otoacoustic emission screening test is to determine cochlear status, specifically hair cell function. The information from the tests can be used to:[4]

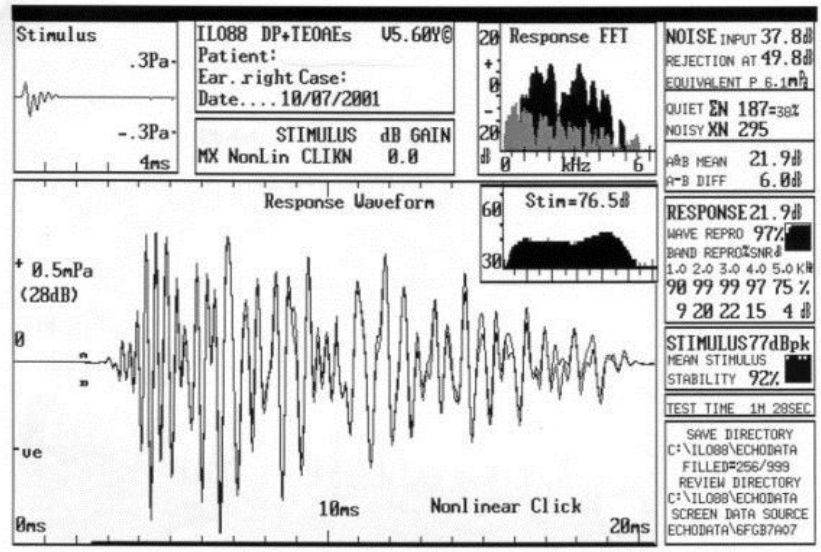
i) Screen hearing particularly in neonates, infants or individuals with developmental disabilities
ii) Partially estimate hearing sensitivity within a limited range

iii) Differentiate between the sensory and neural components of sensorineural hearing loss
iv) Test for functional hearing loss

There are four types OAEs:[4]

1) Spontaneous otoacoustic emissions (SOAEs) – sounds emitted without an acoustic stimulus
2) Transient otoacoustic emissions or transient evoked otoacoustic emissions (TEOAEs) – sounds emitted in response to an acoustic stimuli of very short duration; usually clicks but can be tone-bursts
3) Distortion product otoacoustic emissions (DPOAEs) – sounds emitted in response to two simultaneous tone of different frequencies
4) Sustained-frequency otoacoustic emissions (SFOEAs) – sounds emitted in response to a continuous tone

Figure 2: TEOAEs recorded in the right ear of a 10-year-old child[3]

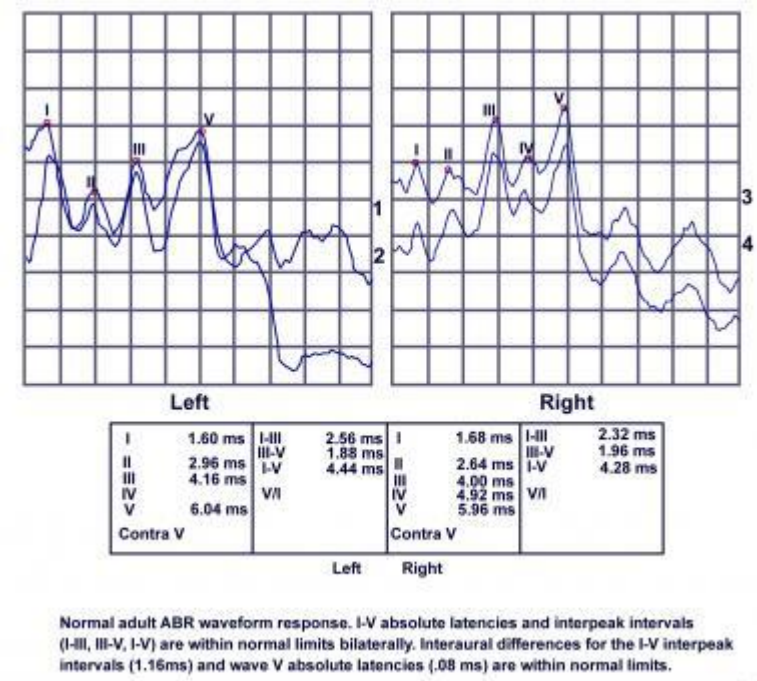


ii) Automated Auditory Brainstem Response (AABR)

Auditory brainstem response (ABR) audiometry is a neurologic test of auditory brainstem function in response to auditory (click) stimuli.[7] It is an automated test of hearing and evaluate the nervous system response to the sounds.[1] It is the most common application of auditory evoked responses. Test administration and interpretation typically performed by an audiologist. ABR audiometry refers to an evoked potential generated by a brief click or tone pip transmitted from an acoustic transducer in the form of an insert earphone or headphone. The elicited waveform response is measured by surface electrodes typically placed at the vertex of the scalp and ear lobes.[7]

Figure 3: AABR Screening

Figure 4: Waveforms of Click Stimulus[7]



Normal adult ABR waveform response. I-V absolute latencies and interpeak intervals (I-III, III-V, I-V) are within normal limits bilaterally. Interaural differences for the I-V interpeak intervals (1.16ms) and wave V absolute latencies (.08 ms) are within normal limits.

The waveforms of click stimulus are typically plotted with the vertex site electrode in the positive or negative voltage input of amplifier resulting in I, II, III and V wave peaks.[7]

iii) Gold Standard (Auditory Brainstem Response (ABR))

Diagnostic ABR are performed in infants who are failed in one or both ears after screening protocols.[8] For example the diagnostic ABR used in one study as a reference method was using click stimuli with 35 dB, a rate repetitions of 33/s, an alternating stimulus polarity and a masking noise related to the stimulus level.[9]

4. METHODS

4.1. Searching

Electronic databases were searched through Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1948 to present, and Embase 1996 to 2015 September 29. Searches were also run in PubMed, Horizon Scanning databases, UM Library website, FDA website and INAHTA for published reports.

Search was limited to studies published within 1990s to 2000s. Google and Google Scholar were also used to search for additional web-based materials and information about the technology. Besides, additional articles were also search by reviewing the references of retrieval articles.

Appendix 1 showed the detailed search strategies.

4.2. Selection

A reviewer screened the titles and abstracts against the inclusion and exclusion criteria and then evaluated the selected full-text articles for final article selection.

The inclusion and exclusion criteria were:

Inclusion criteria

Population	Newborn
Interventions	Otoacoustic emissions (OAEs), Automated Auditory Brainstem Response (AABR), Universal Newborn Hearing Screening (UNHS)
Comparators	None
Outcomes	Positive Predictive Value (PPV), Negative Predictive Value (NPV), referral rate, detection rate, detection rate, specificity, sensitivity, prevalence of hearing loss
Study design	Cross-sectional, Cohort, Diagnostic Accuracy Study, Systematic review, cost-effectiveness analysis
	English full text article

Exclusion criteria

Study design	Animal studies and laboratory studies
	Non English full text article

Relevant articles were critically appraised using Critical Appraisal Skills Programme (CASP) and evidence graded according to the US / Canadian Preventive Services Task Force (Appendix 2). Data were extracted from included studies using a pre-designed data extraction from (evidence table as shown in Appendix 3) and presented in tabulated format with narrative summaries. No Meta-analysis was conducted for this review.

5. RESULTS AND DISCUSSION

There were 12 studies included in this technology review. Three studies were using OAE, one study using AABR, one study on comparison of OAE and AABR and four studies were combination of OAE and AABR for newborn hearing screening. Three cost-effectiveness analyses on universal newborn hearing screening also included in this technology review.

5.1. EFFICACY/ EFFECTIVENESS

5.1.1 Otoacoustic Emissions (OAE)

Akinpelu OV. et al. conducted a SR in 2014 which included 10 studies with total involvement of 119,704 newborns. The purpose of the SR was to determine the effects of different screening protocols on the referral rates and positive predictive values (PPV) of the OAE newborn screening test. Most of the studies reported OAE screening test at four frequencies, requiring a specific signal-to-noise ratio (SNR) at three or four frequencies for a pass. One study screened five frequencies, requiring three of these to have an acceptable SNR to pass. The frequency ranges tested were 1.0 – 4.0 kHz, 1.5 - 4.0 kHz and 1.0 - 6.0 kHz. SNR values reported were 3, 4, 5 or 6 dB above the noise floor. For screening age, two studies screened within the first 48 hours of life, six studies strictly screened after 48 hours, one study screened at 14 to 21 days of age and one study screened between 12 hours and four days after birth. Diagnostic ABR was used during referral or as confirmation of any hearing impairment. Data from individual studies were pooled in order to show the effects of the age at screening, the frequencies tested and the SNR pass criteria on the referral rates, PPV and FP rates. The pooled referral rate when screening was done within two days of birth was 13.8%, while the rate was reduced to 4.7% when screening was done after two days of life. The referral rate for 3 dB SBR pass criterion was 9.4% while for 6 dB the referral rate was only 3.2%. The referral rate was higher for frequencies 1.0 - 4.0 kHz

(6.1%) and 1.0 – 6.0 kHz (3.5%) than for 2.0 – 4.0 kHz and 2.0 – 5.0 kHz (1.6%). It was possible that the inclusion of 1 kHz amongst the frequencies screened was responsible for higher referral rates. This may also explain the higher referral rates with a 3 dB SNR pass criterion since all the studies with this criterion also included 1 o 1.5 kHz among the frequencies screened. The pooled FP rates showed trends similar to those for referral rates. Higher FP rates were associated with screening within two days (13.2%), with screening using an SNR of 3 dB (9.2%) and with screening involving 1.0 – 4.0 kHz and 1.0 – 6.0 kHz (5.8% and 3.1% respectively). The pooled PPV was equivocal for the two age groups. However, the PPV was higher (0.07) for screenings using SNR of 6 dB or dual SNR than for SNR of 3 (0.02), and the PPV was higher for screenings involving 2.0 – 4.0 kHz and 2.0 – 5.0 kHz (0.23) than for screenings involving 1.0 – 4.0 kHz and 1.0 – 6.0 kHz (0.04 and 0.11 respectively). The study showed that, age at screening, the frequencies screened and the SNR values accepted for a pass could be part of a strategy to ensure a better performance of OAE tests.[10, level 1]

Beier Q et al. conducted cross-sectional diagnostic accuracy study in order to design a specific UNHS protocols based on local social characteristics of internal migrants which would improve the screening rates for hearing loss in newborn babies. The device used was only OAE screening test and the confirmation device was a combination of OAE and diagnostic ABR. The study involved 10,983 babies who were born between January 2007 and December 2009. Two screening phase were conducted; phase one was inpatient screening (first stage and second stage OAE screening) and second phase was outpatient screening (first stage and second stage OAE screening). All newborn babies underwent first inpatient OAE screening within 24 to 48 hours after birth. Second inpatient screening was done if the infants stayed in the hospital beyond 48 hours after birth. Meanwhile the outpatient screenings was for newborns that were tested for first inpatient screening but not underwent the second inpatient screening, as well as for newborns that were positive in both stages of inpatient screening. The outpatient OAE test was done at one month and two months after birth. Confirmation test used for any failure result after the two stages of outpatient screening was diagnostic ABR test. The overall results found that, during first stage of inpatient screening, 72.78% (7,993) newborns passed the hearing screening meanwhile 27.22% (2,990) were referred for second inpatient screening. Out of 2,990 only 1,712 newborns underwent the second inpatient OAE screening test with 973 infants passed the test. Thus, from the phase 1 screening process, 2,017 infants were suspected to have hearing impairment but only 1,147 underwent phase two screening (outpatient OAE screening). Out of 1,147 of them 919 (80.12%) passed first stage of outpatient OAE screening and 228 were referred for second stage of outpatient OAE screening. The overall referral rate at this stage was

2.08%. Only 141 of 228 accepted the referral and 103 (73.05%) were positively tested. They were referred to final confirmatory click ABR hearing impairment test with final referral rate of 1.73% at 2 months of age; which was lower than referral rate at one month of age. Fifty four infants went to the diagnostic ABR test and 35 infants were confirmed positive for impaired hearing. Another 19 infants had normal hearing.[11, level II-2]

Xu Zm et al. conducted a cross-sectional diagnostic accuracy study to observe the sensitivity and specificity of targeted (high-risk) neonatal hearing screening for single-session DPOAE technique and combined DPOAE and AABR technique. Two stages of tests were conducted; screening stage at age less than one month old and diagnostic stage at two months old. Screening stage was performed with two types of screening procedures. The two procedures were DPOAE screening procedure and combine DPOAE and AABR screening procedure. Inclusion criteria for failed screening was failed both combine DPAE and AABR procedure, or failed AABR screening. If the infants failed DPOAE screening but passed the AABR screening, the infants were considered passed the screening stage. During screening stage, all 3,000 high risks newborn underwent both screening procedures. Failure subject was referred to newborn that failed in both procedures, and also failed the AABR test in the combination procedure. The failure underwent diagnostic test for confirmation of hearing impairment. During the study, the newborns were divided into four groups; group I was for very low weight newborn, group II was for preterm babies, group III was for babies with hyperbilirubinaemia and group IV was for babies with asphyxia. Results for DPOAE screening procedure found that higher DPOAE referral rates in group 1 (12.08%) and group II (10.22%) but lower referral rates in group III (4.46%) and group IV (3.38%). The referral rates were significant difference among group I, II, III and IV (F-test, $p < 0.01$). In combine DPOAE and AABR screening procedure, 240 newborns failed the DPOAE screening and 151 newborns failed the AABR screening. There was significant difference in referral rates (t-test, $p < 0.01$) between DPOAE screening and AABR screening. The referral rates of group III (5.29%) and group IV (5.06%) for the combined procedure were slightly higher than group I and group II. Only 151 were referred for diagnostic stage, the 151 failure also included 127 newborns who failed both combine DPOAE and AABR screening and 24 newborns that failed the AABR but passed the DPOAE screening. Eighty nine newborns that failed in DPOAE screening was excluded from referral as they passed the AABR screening. After diagnostic stage, they ruled out that 69 newborns (2.30%) who failed the DPOAE alone had abnormal hearing and 91 infants who failed combined DPOAE and AABR screening were confirmed to have hearing impairments. When considering subjects, false-positive (FP) rate of DPOAE screening alone was 4.96%, and that of combined DPOAE and

AABR screening was 2%. The false-negative (FN) rate of DPOAE screening alone was 0.8% and that of combined DPAOE and AABR screening was 0.06%. Thus, while comparing referral rate, FP and FN of two hearing screening protocols, it showed that there was a significant differences (t-test, $p < 0.05$, $p < 0.01$, $p < 0.01$). The referral rate, FN and FP of the combined DPOAE and AABR protocol were significantly lower. These data imply that combined DPOAE and AABR increases test specificity without affecting its sensitivity for hearing loss. Because of that the authors concluded that combination of DPOAE/AABR ensures high sensitivity and acceptable specificity and predict the auditory neuropathy profile in the neonatal intensive care unit (NICU) babies.[12, level II-2]

5.1.2 Automated Auditory Brainstem Response (AABR)

Huang HM et al conducted another cross-sectional study to establish a hearing screening program with high coverage, low referral rate, high follow-up rate and early intervention in Taipei city. The hearing screening device used was AABR and diagnostic device was combination of OAE and AABR. Participants involved were 15,930 newborns involved but only 15,790 received the screening test. The screening conducted involved two steps; first screening step was at the age of 24 hours to 36 hours after birth. If failed, the screening was repeated at 36 hours and 60 hours of age or before discharge. A second screening step was done if the newborn failed the retested screening. The second screening step was actually initial diagnostic test and if any failure in the test, the newborns would undergo full diagnostic hearing work-up for confirmation of hearing loss which included OAE test, tympanometry, diagnostic auditory braistem response (ABR), auditory steady-state response (ASSR), auditotry observation audiometry (BOA) and visual reinforcement audiometry (VRA). Out of 15,790 newborns, almost all (15,631; 98.99%) passed the first and second screening. The other 159 newborns were referred for initial diagnostic hearing tests after discharge from the hospital. However, only 151 underwent the initial diagnostic screening test. From the 151, 74 (49.0%) passed the initial diagnostic hearing examinations with combined OAE and AABR. The rest 77 newborns failed at least one of the initial hearing tests and were referred for full diagnostic investigations for hearing tests. After the diagnostic test, 22 babies passed and 55 babies confirmed with hearing impairment either bilateral or unilateral hearing loss. These findings showed that the overall UNHS program in Taipei City was an effective program with high coverage rate (99.1%), low referral rate (1.0%) and good followed-up rate 94.4%. The strategy of double screening steps with AABR before discharge was proven to be effective to lower the referral rate.[13, level II-2]

5.1.3 Comparison of Procedures (Otoacoustic Emissions and Automated Auditory Brainstem Response Test)

Dyk MV. et al. conducted cross-sectional diagnostic study to evaluate the outcome of the newborn hearing screening within the first 48 hours using AABR without the need for costly disposables typically required and compared with transient evoked otoacoustic emissions (TEOAE). The study involved 150 (300 ears) healthy newborns. Two types of devices, used were AABR and TEOAE. The study included three stages of screening where the first screening was early screening after birth, second stage screening only conducted on ears that yielded a refer results during initial stage and the third stage screening. Initially all the newborns were screened with both devices; AABR and TEOAE. Out of 300 ears, 278 ears were successfully screened either with TEOAE or AABR. Forty one point three percent (41.3%) newborns passed bilaterally with both devices at initial screened. Over the three stages of screening, the AABR had significantly lower initial refer rate per ear compared to TEOAE; 16.7% versus 37.6%. Besides that, rescreen refer rates was also higher per ear in TEOAE (49.5%) compared to AABR (36.1%) screening. In terms of age effects of screening outcome, the overall AABR refer rate per ear for infants screened between 24 hours and 36 hours (20.2%) and between 36 hours and 48 hours (18.9%) was similar but significantly lower than for TEOAE. Mean age for pass results with AABR was 31 hours and 22 hours for refer results but for TEOAE 32 hours and 25 hours. Thus the authors finally concluded that initial screening with AABR was significantly more effective than TEOAE for newborns younger than 48 hours. Screening infants within 24 hours post birth with AABR resulted in reduced costs associated with high referral and false-positive rates.[14, level II-2]

5.1.4 Combination of Procedures (Otoacoustic Emissions and Automated Auditory Brainstem Response Test)

Firoozbakht M et al conducted eight year (2005 to 2012) cross-sectional study involving 3,350,995 infants to establish the prevalence of hearing impairment among infants, and efficacy of the program. In Iran hearing screening started since 2005 where it utilized OAE and AABR to detect any permanent bilateral or unilateral hearing loss of 30dB or worse in the range 0.5 kHz – 4.0 kHz. The infants were first tested for TEOAE (three times). Based on the results of this test, the positive cases were referred to the next stage, where they were tested for AABRs. If they also tested positive on AABRs they were referred to the diagnostic and rehabilitation stages. Results indicated an infant hearing impairment prevalence of 3 per 1000. Although the rate was as high as 5 per 1000 in the early years of the programme it decreased to 2.6 per 1000 in the last year. The absolute referral rate was 14.5% in the first stage, which decreased to 0.9% and 0.2% on the second and the third stages, respectively. The follow-up rate

was 70% in the first stage, which increased up to 73% and 85% in the second and the third stages, respectively.[15, level II-2]

Unlu I. et al. conducted a cross-sectional diagnostic accuracy study to investigate the referral rate and the time when AABR should be used for newborn hearing screening. Two stages of screening were involved where the first stage was three times of screening with TEOAE and second stage was AABR test at one month old. The study involved 3,109 infants where 2,933 were healthy full term infants and 176 infants with perinatal risk factors. Those infants who failed third screening with TEOAE underwent second stage screening with AABR along with infants who have risk factors. Out of 2,933 healthy infants who underwent stage one screening, 85 infants failed third screening with TEOAE. The 85 infants underwent stage two screening with AABR along with 176 infants with risk factors. Two AABR tests within two weeks interval were done where 14 infants with perinatal risk factors and 10 infants who failed stage one screening could not passed the AABR test. All of them were referred to higher centre for further evaluation. The final results found that, 0.34% of 2,933 healthy full-term infants were detected with newborn hearing loss and 7.9% of infants with perinatal risks factors having problems due to hereditary hearing loss, cleft palate anomaly, Down syndrome, external ear canal atresia and high bilirubin levels.[16]

Wahid SNH et al. conducted another cross-sectional study to identify the outcomes of hearing screening in the same ear of the babies in neonatal unit population. The infants selected were subjected to DPOAE with frequencies at 2, 3, 4 and 5 kHz followed by AABR screening tests at the same setting as near to discharge as possible. Seventy three stable babies and problematic infants who do not need NICU treatment involved in this study. Screening results showed that AABR had higher passing rate (82.9%) compared to DPOAE (77.4%). However, the passing rate was highest if the protocol of either passed DPOAE or AABR was used (90.4%). However, rate was lower when auditory neuropathy spectrum disorder (ANSD) has been considered (82.9%). According to the authors, combined procedure where the first screening started with AABR followed with DPOAE was recommended.[17, level II-2]

Caluraud S. et al. conducted cross-sectional study to evaluate and critically analyse the universal newborn hearing screening (UNHS) with TEOAE and AABR (protocol after 2004 or current protocol). Then the authors also compared between hearing screening protocol prior to 2004 and protocol after 2004. Screening protocol prior to 2004 was two steps of screening with TEOAE. All the newborns alive in public and private hospitals as well as clinics where hearing screening was performed in upper Normandy region of France from 1999 to end of March 2011 were included in this study. The total of the newborns were 101,916 where two

steps of screening program applied. First step was pre-discharge TEOAE screening which was performed three days after birth and second step was outpatient test with AABR which was performed three to four weeks later if the first step resulted in a 'fail' for one or both ears. Infants who failed the outpatient screening was referred for diagnostic auditory assessment (ASSR), ABR and behavioural audiometry. Out of 101,916 live births babies, 101,341 (99.4%) were screened prior to hospital discharge. Only 1,192 (1.2%) infants failed the test. The 1,192 infants were recalled for step two screening. Of the 1,098 (92.1%) tested at step two, 159 (14.5%) failed and of this 139 (87.4%) hearing impairment were confirmed by diagnostic audiologic assessment. Total of 139 babies and three untested babies from step one were diagnosed with bilateral hearing impairment; a prevalence of 1.4%. By comparing the protocol prior to 2004 and protocol after 2004, failure rate in protocol prior to 2004 was higher compared with protocol after 2004 (2.3% versus 1.0%). The difference was statistically significant ($p < 0.001$, Z test). Under protocol prior to 2004, 61.1% of newborns who remained undiagnosed after two screening steps with TEOAE were subsequently confirmed to have a hearing impairment through ABR testing which was increased to 95.1% under protocol after 2004. The difference was also significant ($p < 0.001$, Z test). The author concluded that two steps protocol adopted after 2004 appeared to be the most effective and efficient.[18, level II-2]

5.2. SAFETY

No retrievable evidence on safety issue was reported on OAE or AABR. Both OAE and AABR has received United State Food and Drugs Administration (USFDA) approval.

5.3 COST/COST-EFFECTIVENESS

Currently, the market price for the device differed based on their specification. The OAE price was around RM30,000 to RM50,000 meanwhile the AABR price was around RM70,000 to RM80,000.

Gupta A et al. in their study also evaluated the cost of AABR. Total cost for AABR was assessed based on micro costing method calculating the cost of the reference unit price (RUP). The RUP is the predetermined estimated cost for providing a unit of healthcare service, from the hospital perspective. Finally the average estimated cost of AABR per test calculated was INR 276 (for the year 2013).[19]

Huang LH et al. conducted a cost-effectiveness (CE) analysis to determine the cost-effectiveness of the UNHS program implementation in eight provinces of China, in order to support evidence-based national policy making in China. The eight provinces were grouped as developed

provinces (Beijing, Shandong, Hebei, Guangdong and Zhejiang) and developing provinces (Henan, Jiangxi and Guangxi). For the purposes of this study the authors modelled the CE models for two programs; UNHS program and targeted screening program (targeted those with one or more risk factors). The UNHS programme used combined TEOAE and AABR as the screening devices. All neonates annually born in the eight provinces from 2007 to 2009 were simulated. The population that benefited referred to the proportion of infants with disorder who finally received beneficial early hearing detection and intervention. The three variables; coverage rate, diagnosis rate and intervention rate, will determined the total number of deaf infants finally receiving early interventions and benefiting from the screening program. Based on GDP per capita in each province and baseline of transition probability parameters, UNHS strategy showed cost-effectiveness in Guangdong, Shandong and Beijing. Meanwhile the targeted screening strategy showed cost-effectiveness in Zhejiang and Hebei. On the other hand, neither strategy showed cost-effectiveness in Guangxi, Jiangxi and Henan. For the sake of economic effects on long-term cost saving, universal strategy and targeted strategy led to 214,872,740 Int$ and 104,872,740 Int$ in total respectively. This was approximately equivalent to 0.14% and 0.07% of the annual expenditure. Meanwhile at baseline both strategies achieved cost saving which were greater than implementation costs. When the proportion benefit population was expanded, the effect of these screening strategies on the long-term costs saving become more and more significant, especially those of universal strategies, exceeding the total costs of the screening program implementation, suggesting a good economic effect in the long term.[20]

Keren R. et al. conducted cost-effectiveness study to evaluate the UNHS and selective screening in terms of both short and long-terms benefit, harms, and financial costs and to identify steps in the screening process that could be improved to increase cost-effectiveness. The cost-effectiveness analysis were conducted from the societal perspective compared the projected outcomes of no NHS, selective NHS and UNHS for hypothetical state birth cohort of 80,000 infants. The selective screening identified 62 of the 128 deaf infants in birth cohort, referred 0.18% of all infants for diagnostic evaluation and had a PPV of 43%. Meanwhile the UNHS identified 116 of the 128 deaf infants. Referred 1.6% of all infants and had a PPV of 8.8%. The authors models simulated real-world conditions in which some infants whose deafness was identified at screening do not receive a definitive diagnosis of being deaf before 6 months; and a portion of deaf and hard-of-hearing infants who have FP screening test results, were not screened or fail the hearing screen but were not immediately followed up with diagnostic evaluation nonetheless received a diagnosis by 6 months of age. In the absence of NHS, approximately 30 deaf infants were identified by 6 months of age by passive detection alone at a cost of $69, 000. The selective screening

protocol, when compared with no NHS, resulted in an additional 36 infants whose deafness was diagnosed by 6 months at an additional cost of approximately US$600,000, yielding an incremental cost-effectiveness of approximately US$16,000 per additional infant whose deafness was diagnosed by 6 months. Then compared with selective screening, the UNHS protocol resulted in 33 additional infants whose deafness was diagnosed by 6 months of age at an additional cost of approximately US$1.5 million, yielding an incremental cost-effectiveness of approximately US$44,000 per additional infants whose diagnose by 6 months of age. Increasing the rate of follow-up to diagnostic evaluation from the base-case estimate of 77% to 100% decreased the incremental cost of UNHS to US$38,000 per additional infant whose deafness was diagnosed by 6 months. Under the base-case assumptions about lifetime savings that results from normal language with early intervention, UNHS resulted in normal language achievement for more deaf children and was cost saving in the long-term compared with both selective screening and no screening. Thus to conclude, the short-term cost-effectiveness of UNHS was comparable to the cost per case diagnosed of other newborn screening programs and could be improved by increasing the rate of follow-up to diagnostic evaluation after positive screening test results. However, if early identification results in improved language abilities, lower educational and vocational costs and increased lifetime productivity then UNHS has the potential for long-term cost savings compared with selective hearing screening and no screening.[21]

Kemper AR. et al. conducted a cost analysis to compare the expected costs and benefits of targeted screening with universal screening for the detection of significant bilateral congenital hearing loss. The analysis was from the health care system perspective, including costs directly related to screening and initial follow-up evaluation. The results showed that for every 100,000 newborns screened, universal screening detects 86 of 110 cases of congenital hearing loss, at a cost of US$11,652 per case identified. Targeted screening identifies 51 of 110 cases, at US$3,120 per case identified. Universal screening produces 320 FP results, 304 more than targeted screening. Switching to universal screening from targeted screening would cost an additional US$23,930 for each extra case detected.[22]

5.4 LIMITATIONS

This technology review has several limitations. The selection of studies was done by one reviewer. Although there was no restriction in language during the search but only English articles were included in this report. Only studies published in 2010 to 2015 were included in this technology review report. There was also five full text articles from relevant titles/abstracts could not be retrieved from available database.

6. CONCLUSION

In conclusion, there were studies which showed various findings based on the types of screening protocols used. In OAE alone, the pooled referral rate and false positive rate was lower when screening was done after two days of life compared to within two days of life. However, it varies according to the frequency used. Then, for AABR alone, limited evidence to suggest double screening steps with AABR before discharge was effective to lower the referral rate. While comparing OAE and AABR, limited evidence to suggest that initial screening with AABR had significantly lower referral rate compared to initial screening with OAE for newborns younger than 48 hours. Nevertheless, the evidence showed that combination of OAAE and AABR was the best protocol compared to the single used device and was considered as cost-effective for long term practice.

Safety

No retrievable evidence on safety. Both OAE and AABR have received USFDA approval.

Cost/Cost-Effectiveness

Cost of OAE ranged from RM30,000 to RM50,000 and AABR ranged from RM70,000 to RM80,000. Two cost-effectiveness studies suggest potential long-term cost saving for UNHS.

8. REFERENCES

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9. APPENDIX

9.1. Appendix 1: LITERATURE SEARCH STRATEGY

Ovid MEDLINE® In-process & other Non-Indexed citations and OvidMEDLINE® 1948 to present

1. Infant, Newborn/
2. newborn.tw.
3. Infant.tw.
4. Evoked Potentials, Auditory, Brain Stem/ or Hearing Tests/ or Audiometry, Evoked Response/
5. AABR.tw.
6. automated auditor$ brainstem respon$.tw.
7. evoked potential$ auditor$ brainstem.tw.
8. evoked respon$ auditor$ brainstem.tw.
9. auditor$ brainstem evoked respon$.tw.
10. brainstem auditor$ evoked potential$.tw.
11. acoustic evoked brainstem potential$.tw.
12. brainstem respon$ auditor$.tw.
13. (respon$ adj auditor$ brainstem).tw.
14. (hearing adj1 test$).tw.
15. audiometer$ evoked respon$.tw.
16. (evoked adj1 respon$ audiometer$).tw.
17. (electroencephalic adj1 respon$ audiometer$).tw.
18. audiometer$ electroencephalic respon$.tw.
19. electrocochleograph$.tw.
20. Otoacoustic Emissions, Spontaneous/
21. (spontan$ adj1 otoacoustic emission).tw.
22. 1 or 2 or 3
23. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
24. 20 or 21
25. 22 and 23
26. 22 and 24

Embase 1996 to 2015 September 29

1. Infant, Newborn/
2. newborn.tw.
3. Infant.tw.
4. Evoked Potentials, Auditory, Brain Stem/ or Hearing Tests/ or Audiometry,Evoked Response/
5. AABR.tw.
6. automated auditor$ brainstem respon$.tw.
7. evoked potential$ auditor$ brainstem.tw.
8. evoked respon$ auditor$ brainstem.tw.
9. auditor$ brainstem evoked respon$.tw.
10. brainstem auditor$ evoked potential$.tw.
11. acoustic evoked brainstem potential$.tw.
12. brainstem respon$ auditor$.tw.
13. (respon$ adj auditor$ brainstem).tw.
14. (hearing adj1 test$).tw.
15. audiometer$ evoked respon$.tw.
16. (evoked adj1 respon$ audiometer$).tw.
17. (electroencephalic adj1 respon$ audiometer$).tw.
18. audiometer$ electroencephalic respon$.tw.
19. electrocochleograph$.tw.
20. Otoacoustic Emissions, Spontaneous/
21. (spontan$ adj1 otoacoustic emission).tw.
22. 1 or 2 or 3
23. 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
24. 20 or 21
25. 22 and 23
26. 22 and 24

OTHER DATABASES	
EBM Reviews - Cochrane database of systematic reviews	Otoacoustic emissions (OAEs), Automated Auditory Brainstem Response (AABR), Universal Newborn Hearing Screening (UNHS)
EBM Reviews - Health Technology Assessment	Otoacoustic emissions (OAEs), Automated Auditory Brainstem Response (AABR), Universal Newborn Hearing Screening (UNHS)
PubMed	Otoacoustic emissions (OAEs), Automated Auditory Brainstem Response (AABR), Universal Newborn Hearing Screening (UNHS)
NHS economic evaluation database	Otoacoustic emissions (OAEs), Automated Auditory Brainstem Response (AABR), Universal Newborn Hearing Screening (UNHS)
INAHTA	Otoacoustic emissions (OAEs), Automated Auditory Brainstem Response (AABR), Universal Newborn Hearing Screening (UNHS)
FDA	Otoacoustic emissions (OAEs), Automated Auditory Brainstem Response (AABR), Universal Newborn Hearing Screening (UNHS)
Others (Google Scholar, Google)	Otoacoustic emissions (OAEs), Automated Auditory Brainstem Response (AABR), Universal Newborn Hearing Screening (UNHS)
UM Library	(Find full text only from relevant abstract)

9.2. Appendix 2

HIERARCHY OF EVIDENCE FOR EFFECTIVENESS STUDIES

DESIGNATION OF LEVELS OF EVIDENCE

I Evidence obtained from at least one properly designed randomised controlled trial.

II-I Evidence obtained from well-designed controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III Opinions or respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

SOURCE: US/CANADIAN PREVENTIVE SERVICES TASK FORCE (Harris 2001)

9.3. Appendix 2

HIERARCHY OF EVIDENCE FOR TEST ACCURACY STUDIES

Level	Description	
1.	A blind comparison with reference standard among an appropriate sample of consecutive patients	
2.	Any one of the following	Narrow population spectrum
3.	Any two of the following	Differential use of reference standard
4.	Any three or more of the following	Reference standard not blind Case control study
5.	Expert opinion with no explicit critical appraisal, based on physiology, bench research or first principles.	

SOURCE: NHS Centre for Reviews and Dissemination (CRD) University of York, Report Number 4 (2nd Edition)

9.4. Appendix 3 EVIDENCE TABLE

Evidence Table: Efficacy/Effectiveness (OAE)
Question: Is

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
1. Akinpelu OV, Peleva E, Funnell WB, & Daniel SJ. Otoacoustic Emissions in Newborn Hearing Screening: A Systematic Review of the Effects of Different Protocols on Test Outcomes. International Journal of Paediatric Otorhinolaryngology. 2014; 78: 711-717	Systematic Review (10 included studies) Obj: To determine the effects of different screening protocols on the referral rates and positive predictive values (PPV) of the OAE newborn screening test	1	119,714 newborn participants	OAE			- Most of the studies reported OAE screening tests at 4 frequencies, requiring a specific signal-to-noise ratio (SNR) at 3 or frequencies for a pass - 1 study screened 5 frequencies (ranges tested 1-4, 1.5-4,1.4-4 and 1-6kHz) – SNR values reported were 3, 4, 5 of 6dB above the noise floor - 2 studies included newborns screened within the 1st 48h of life, 6 studies strictly screened after 48h, 1 study screened at 14-21 days of age and 1 study screened between 12h and 4 days after birth Referral rates - Based on the 1st OAE tests were between 1.3% and 9% for the 8 of the 10 included studies - Higher rates of 13% and 21% in 2 other studies Age at 1st test -0.5 days to 21 days False Positive (FP) rates = 1.2% to 19.5% Positive predictive value (PPV) = 0.02 and 0.4 Wide ranges of value probably due to: - Differences in the expertise of the operators - Prevalence of hearing loss in different	

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
							populations Measured prevalence of permanent congenital hearing lost (PCHL) based on diagnostic ABR at 3 months (not included false negatives) = 0.08 and 1.5% - referral rates higher for studies that had higher prevalence of PCHL (study in India was the highest; 1.5%) Proportion lost to follow up (expressed as percentage of the total number of newborns screened) = 0% to 11% Pooled Results 1) Referral rates when: - Screening was done within 2 days of birth = 13.8% - Screening was done after 2 days of life = referral rate reduce to 4.7% - 3 dB SNR pass criterion = 9.4% - 6 dB SNR pass criterion = 3.2% - Frequencies 1-4 kHz = 6.1% - Frequencies 1-6 kHz =3.5% - Frequencies 2-4 kHz and 2-5 kHz = 1.6% (inclusion of 1 kHz amongst the frequencies screened was responsible for higher referral rates) (higher referral rate with 3 dB SNR pass criterion since all of the studies with the criterion also included 1 or 1.5 kHz among the frequencies screened) 2) FP rates; Higher FP rates associated with: - Screening within 2 days = 13.2% - Screening using an SNR of 3 dN = 9.2%	

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
							- Screening involved frequencies 1-4 kHz (5.8%) and 1-6 kHz (3.1%) 3) PPV - Equivocal for the 2 age groups - Higher for screening using 6 dB SNR screening (0.07) or dual SNR than for 3 dB SNR (0.02) - Higher for screening involving 2-4 and 2-5 kHz (0.23) than for screening at 1-4 (0.04) and 1-6 kHz (0.11) Conclusion - Use of more sophisticated OAE algorithms with high frequency resolution and more robust artifact rejection and noise-floor estimation may be useful approaches to improve DPOAE measurements	

Evidence Table: Efficacy/Effectiveness (OAE)
Question: Is

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
2. Qi Beier, Cheng X, En H, Liu B, Peng S, Zhen Y, Cai Z, Huang L, Zhang L, & Han D. Assessment of the Feasibility and Coverage of a Modified Universal Hearing Screening Protocol for Use with Newborn Babies of Migrant Workers in Beijing. BMC Paediatrics. 2013;13:116	Cross-sectional study Aim: To design a specific UNHS protocols based on local social characteristics of internal migrants – would improve the screening rates for hearing loss in newborn babies 1st screening: All newborn babies underwent inpatients OAE test 24-48 hours after birth 2nd screening: baby tested positive and could stay in hospital beyond 48 hrs Outpatient test: positive at 1st test, not underwent 2nd test / positive 1st and 2nd tests as an inpatient – referred for an outpatient OAE test at 1 month after birth Positive after 1 month: they were referred to an additional OAE test at 2 months after birth For confirmation of	II-2	10,983 babies (6048 males and 4935 females) born between Jan 2007 and December 2009 at Beijing's Shangdi Hospital	OAE : nonlinear clicks at 75dBpeak equivalent sound pressure level (SPL) AABR used in diagnostic assessment for impaired hearing		Inpatient = OAE test 24-48 hours after birth Outpatient = OAE test at 2 months after birth	OAE Positive detection rate (inpatient) • 98.91% (10,983/11,104) of newborn (≤ 48hours) babies were tested at 1st inpatient screening • 72.78% (7993/10,983) - passed the screening • 27.22% (2990/10,983) - referred for a 2nd inpatient hearing test 48-72 hours of birth • 57.25% (1712/2990) parents agreed to take 2nd OAE test inpatient • 56.83% (972/1712) passed the test – significantly decreased the overall positive rate from 27.22% (2990/10,983) to 18.36% ([2990-973/10,983)]; $X^2 = 244.906$, p = 0) Referral rate for hearing screening test • 2017 (2990-973) infants suspected to have hearing impairment (48-72 hrs after birth) • Only 1147 (56.87%) underwent OAE test after 1 months (outpatient) • Of these, 919 (80.12%) passed the test • 228 (19.88%) tested positive again and were referred for an additional OAE test at same hospital at 2 months old (overall referral rate 2.08% (228/10,983)) • 141/228 accepted the referral – 103/141 (73.05%) tested positive again with OAE test and were referred to a final confirmatory click ABR hearing impairment test (final referral rate 1.73% ([228-38/10,983] at 2 months age; $X^2 = 4.013$, p = 0.045<0.05) vs referral rate of 2.08%	

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
	diagnosis hearing impairment: all infants with positive results after 1 months were referred for ABR Abnormal ABR: further audiology test (OAE + ABR), 1kHz tympanometry and CT (if necessary) – performed before 6 months old)						at 1 month of age) • Off 190 infants referred, 84 parents agreed for their babies to undergo final ABR test at 2 months after birth • Only 54 attended the test and 35 were confirmed positive for impaired hearing • Of these 35 infants SNHL, 12 had bilateral hearing loss ranging from mild to profound and 23 had unilateral hearing loss • Prevalence of hearing loss in newborns of migrants in Beijing based on this findings was 0.32% (35/10,983)	

Evidence Table: Efficacy/Effectiveness (DPOAE vs DPOAE+AABR)
Question: Is

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
3. Xu Zm, Cheng Wx & Yang Xl. Performance of Two Hearing Screening Protocols in NICU Shanghai. International Journal of Otorhinolaryngology. 2011;75:1225-1229	Cross-Sectional Aim: To study the sensitivity and specificity of targeted neonatal hearing screening for the single-session DPOAE technique and combined DPOAE/AABR technique To investigate the referral rate, and false positive and false negative rates for single and combination Methods Stage 1 – screening at age less than 1 months -all babies underwent both screening procedures - if subjects failed the screening in both procedures they were referred to diagnostic stage Inclusion criteria in subject that failed in combination procedure: 1.failed both DPOAE and AABR	II-2	3000 high-risk newborns at Children's Fudan University Hospital (1680 males, 1320 females within range 3 and 24 days) Divided into 4 groups i. 670 very low weight newborn (1340 ears) ii. 890 preterm babies (1780 ears) iii. 850 babies with hyperbilirubinaemia (1700 ears) iv. 790 babies with asphyxia (1580 ears) Inclusion criteria: -Birth wt ≤1500g for VLBW -Gestational age under 32-37 weeks for preterm -Hyperbilirubinaemia jaundice index of 280-83ml/DL	DPOAE – considered pass when at least 3 of the 5 frequencies were passed 5 frequencies (1500, 2000, 2500, 3000, 3500 and 4000Hz)	DPOAE + AABR For AABR click stimulation was used to elicit the responses Diagnostic test: 1. Classic click-evoked ABR measuring 4 ABR threshold to categorized the hearing loss: Mild (36-50dBnHL) Moderate (51-70 dBnHL) Severe (71-90 dBnHL) Profound (>90dBnHL) 23. coustic Impedence measuring 1000 Hz pure-tone		DPOAE Screening alone - Screened 6000 ears of 3000 NICU babies - 240/3000 (8% babies) failed -40/240 had unilateral refer -200/240 had bilateral refer -Results by group a) Higher DPOAE referral rates in groups I (12.08%) and group II (10.22%) b) Lower DPOAE referral rates in group III (4.46%) and group IV (3.38%) -The referral rates was significant difference among group I, II, III and IV (F-test, p<0.01) DPOAE/AABR Screening - Screened all the same 6000 ears of the 3000 NICU babies -240/3000 newborns failed DPOAE screening -151/3000 babies failed the AABR screening -There was significant difference in referral rates (t-test, p<0.01) between DPOAE screening and AABR screening -Based on combined DPOAE/AABR criteria, 151/3000 babies (5.03%) were referred based on the combined screening DPOAE/AABR -127/151 babies (4.23%) failed both DPOAE and AABR tests -24/151 babies (0.8%) who were referred from AABR screening passes the DPOAE screening -89/240 babies who failed the DPOAE screening, passed the AABR test	

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
	2.failed AABR and passes DPOAE -if failed DPOAE but passed AABR the result of the combination procedure was considered as 'pass' Stage 2 – diagnostic stage at 2 months Subjects underwent an otologic examination (measure the classic click-evoked ABR and acoustic impedence of the middle ear) Subjects were tested under sedation in supine position in sound proof room		-Lack of oxygenation within 2-3 mins for nb with asphyxia		stimulation		-Referral rates: 5.29% and 5.06% for the combined DPOAE/AABR screening of group III (hyperbilirubinaemia) and IV (asphyxia) were slightly higher than group I (VLBW) and II (preterm) Diagnostic procedure -At age of 2 months -69/3000(2.30%) had abnormal hearing -64/69 had bilateral hearing loss -5/69 had unilateral hearing loss -91/3000 (3.03%) were confirmed to have hearing impairment -84/91 had bilateral hearing loss -7/91 had unilateral hearing loss -When considering subjects: • False-Positive rate of DPOAE screening alone = 4.96% • False-Positive rate of combined DPOAE/AABR screening = 2% • 24 babies failed DPOAE screening but passed the AABR screening • False-Negative rate of DPOAE alone = 0.8% • False –Negative rate of DPOAE/AABR = 0.06% • 22 babies who passed DPOAE screening but failed AABR screening had hearing loss based on classic ABR -Comparisons of the referral rate, FP and FN rate of 2 hearing screening protocols revealed significant differences (t-test, $p<0.05$, $p<0.01$, $p<0.01$) -Referral rate, FP and FN of combined screening protocol were significant	

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
							lower – the combined protocol increases test specificity without affecting its sensitivity for hearing loss - 22 babies with severe to profound hearing loss in group III and IV, who passed DPOAE but failed the AABR, had abnormal AABR and absent middle-ear muscle reflexes (MMR) when tested with 500 and 1000Hz - Abnormal ABRs consist of absent ABR (36%) and atypical ABR (64%) - 24% babies with hearing losses were diagnosed with auditory neuropathy and from groups III and IV Conclusion The use of combination of DPOAE and AABR screening testing ensures high sensitivity and acceptable specificity and predict the AN profile in NICU babies.	

Evidence Table: Efficacy/Effectiveness (AABR)
Question: Is

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
4. Huang HM, Chiang SH, Shiau YS, Yeh WY, Ho HC, Chen SC, Lin HC, Chen KC, Chiang H, Yang MC, Yu LH,, Lin HL, Chiu AWH, Hsiao KJ. The Universal Newborn Hearing Screening Program of Taipei City. International Journal of Paediatric Otorhinolaryngology 77. 2013; 77: 1734-1737	Cross-Sectional Aim: To establish a hearing screening program with high coverage, low referral rate, high follow-up rate and early intervention in Taipei city Methods The screening program was divided into 2 stages: 1st stage: From Sept 2009 to May 2010 10 hospitals and 13 obstetric clinic involved 2nd stage: From May 2010 to December 2010 85% of delivery units in Taipei City (20 hospitals and 14 obstetric clinic involved included all facilities from 1st stage Steps of Screening 1st screening performed at 24 – 36hr after birth If failed, retested	II-2	15,930 newborn participated	AABR			- 15,790/15,930 (99.1%) received the hearing screening test and 96.0% was done within 7 days of birth - 15,164/15,790 (96.0%) passed the 1st screening test - 467/15,790 (3.0%) passed the 2nd test - So 99.0% newborn passed the screening phases (1st n 2nd screening) - 160/15790 (1.0%) newborns were referred for initial diagnostic hearing tests after discharge from hospital - 140/15930 (0.9%) newborns did not received the screening test - 44/140 (0.3%) newborns did not take the screening test due to parental refusal - 42/140 (0.3%) newborns missed the screening test - 54/140 (0.3%) newborns did not log in into database - The rest 0.9% who did not receive hearing screening were under regular followed-up by public health nursing staff Referral Phase - 151/160 referrals babies, (94.4%) underwent the initial diagnostic hearing test - 9/160 (5.6%) did not receive further hearing test (1 dead, 8 refused) - All 7 babies did not received initial diagnostic hearing test were under close followed-up by public health nursing staff - 74 (49.0%) passed the initial diagnostic hearing examinations (OAE and AABR) - 77 (51.0%) failed at least 1 of the	

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
	repeated at 36 and 60 hr of age or before discharge If still failed the 2nd retested screening, babies were referred immediately to receive initial diagnostic hearing test in OPD which involved OAE and AABR testing at 1 month age If failed any of the initial diagnostic test would undergo full diagnostic hearing work-up for confirmation of hearing loss included OAE, tympanometry, ABR, ASSP and auditory observation audiometry (BOA) or visual reinforcement audiometry (VRA) -Congenital hearing loss was defined as hearing thresholds of 35 dB or greater in one of both ears -Hearing loss in ABR defined on the basis presence and persistence of V wave for acoustic stimuli ≥ 35 dB nHL						initial hearing test – underwent full diagnostic investigations for hearing tests -24/77 (31.2%) passed the hearing diagnostic test -22/77 (28.6%) had bilateral hearing impairment -24/77 (31.2%) had unilateral hearing loss -Incidence of unilateral and bilateral hearing loss was 1.5 per 1000 (24/15790) and 1.4 per 1000 (22/15790) respectively Management -22 babies with bilateral hearing loss were referred to 1 of the 3 rehabilitation centres in Taipei -11/22 received early rehabilitation program and 5 of them wear hearing aids fitted -9/22 were under evaluation in medical centres -2/22 refused further followed-up and intervention Conclusion UNHS program in Taipei City is effective program with high coverage rate (99.1%), low referral rate (1.0%) and good followed-up rate 94.4% Strategy of double screening steps with AABR before discharge was proven to be effective to lower the referral rate	

Evidence Table: Efficacy/Effectiveness (OAE + AABR)
Question:

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
5. Dyk MV, Swanepoel DW, & Hall JW. Outcomes with OAE and AABR Screening in the First 48H Implications for Newborn Hearing Screening in Developing Countries. International Journal of Paediatric Otorhinolaryngology. 2015; 79:1034-1040	Cross-Sectional Obj. To evaluate the outcome of the NHS within the 1st 48h using AABR without the need for costly disposables typically required and transient evoked Otoacoustic emissions (TEOE)	II-2	- 150 healthy newborns (300 ears) with no documented medical difficulties - 75 boys and 75 girls - Median gestational age 39 weeks with mean birth wt of 3208g - 74.2% were born via caesarean section Pilot study with TEAOE and AABR was conducted on 60 healthy newborn in order to refine the screening techniques, test procedures and data collection before commencing the study	TEOE AABR Screening Protocol: Infants were screened at several points in time as early as possible after births Re-screened if screening techniques initially yielded a refer outcome All the screening performed by the same audiologist 3-stage screening protocol 2nd stage screen only conducted on ears that yielded a refer results during initial stage 3rd stage screening			**Screening Outcomes** - 278 ears successfully screened either with TEOE or AABR - 41.3% subjects passed bilaterally with both devices at initial screen - Over 3 stages screening: TEOE had significantly higher referral rate of 37.9% (55/145 subjects) than AABR 16.7% (24/144 subjects) - Overall AABR had significantly ($p<0.001$; chi-square) lower initial refer rate per ear compared to TEOE - Right ears had significantly ($p<0.05$; chi-square) lower rate for both devices compared to left ears - Rescreen refer rates were also higher per ear for TEOE (49.5) compared to AABR (36.1%) screening - TEOE presented with a higher false-positive rate (39/103; 37.9%) than AABR (3/61; 4.9%) - Mean screen duration for a pass result was 31s (SD 26) for TEOE and 53s (SD 40) for the AABR - Mean duration for a refer result was 109s (SD 18)with TEOE and always 180s for AABR due to the test protocol – if the pass criterion was not reached after 180s of the test time, the result 'refer' was displayed - No significant difference ($p>0.05$;Wilcoxon) in time between the left and right ears when both passes or both referred with TEOAE - Half the TEOAE pass results (48.5%) were obtained within the first 20s of screening and half AABR was pass results (50.0%) were obtained between 11 and 40s	

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
				The ear specific time segments were measured with a stopwatch for TEOAE and read from MB 11 software for the AABR screening			**Age Effect of Screening Outcome** - Screening refer rate per ear showed progressive decrease with increasing age - AABR refer rate per ear was significantly lower ($p<0.001$; chi-square) than TEOAE refer rate when an infant was screened before 12h after birth - Overall TEOAE refer rate per ear was similar for infants screened between 24 and 36h (40.7%) and 36 and 48h (41.9%) - Overall AABR refer rate per ear for infants screened between 24h and 36h (20.2%) and between 36 and 48h (18.9%) was also similar but significantly lower than for the TEOAE - Lowest initial refer rates per ear and per subject (TEOAE 35.3%, AABR 5.6%) were obtained after 48h post birth (average age for TEOAE 61h post birth, average age for AABR 57h post birth) - Refer rate for ears screened after 24h was significantly ($p<0.001$; chi square) less than those screened before 24h for both AABR and TEOAE - Majority of infants were screened between 24 and 48h (TEOAE 47.8%, AABR 47.2%) - Percentage of infants screened before 24h post birth was 41.5% with TEOAE and 42.1% with AABR - Few numbers of infants were screened 48h post birth for both screening techniques (TEOAE 10.7%; AABR 10.7%) - Mean age for a pass results with TEOAE during the first screen was	

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
							32h (SD 15) and 25h (SD 14) for a refer result - Mean age for an AABR pass result was 31h (SD 15) and 22h (SD 13) for a refer result - Mean age at screen was significantly greater for those with a pass result compared to those with a refer result with either the AABR or TEOAE ($p<0.05$; Mann-Whitney test) **Conclusion** - Initial screening with AABR is significantly more effective than TEOAE for newborns younger than 48h - Screening infants within 24h post birth with AABR results in reduced costs associated with high referral and false-positive rates - AABR screening using technology without disposable-related costs may be the most appropriate choice for sustainable and cost-effective programs - AABR may be not entirely efficient option for birthing centres where infants are discharged within 24h after birth due to high referral rates which influence factors such as costs, logistics, infrastructural considerations, case definition, targeted referral rates and follow-up default - UNHS protocols for South African may require: AABR for public health care sector (hospital-based setting) and OAE reserved for screening older infants at health care visits such as community –based immunization clinics or midwife obstetric units	

Evidence Table: Efficacy/Effectiveness (OAE+AABR)
Question: I

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
6. Firoozbakht M, Mahmoudian S, Alaeddini F, Esmaeilzadeh M, Rafiei M, Firouzbakht A, Rahimi F & Farhadi M. Community-based Newborn Hearing Screening Programme for Early Detection of Permanent Hearing Loss in Iran: An Eight-Year Cross-Sectional Study from 2005 to 2012. J.Med.Screen.2014; 2(1):10-17	Cross-sectional Study Aim: to establish the prevalence of hearing impairment among infants, and efficacy of the programme Hearing programme in Iran started in 2005 – utilizes OAEs/AABR to detect permanent bilateral or unilateral hearing loss of 30dB or worse in the range 0.5-4Khz Healthy baby – screening is recommended by 3rd day of life and before discharge from maternity ward in hospital and must do before 14th day of life Severely ill babies – if failed to complete the procedures, screening is performed as soon as is practical considering the baby's medical condition and before the end of the 1st month of life	II-2	3,350,995 infants All infants screened with OAE 3 times and categorized into 3 major groups based on the results: 1. Infants with pass response, divided in to 2 sub-groups a- Low-risk infants: educational brochures containing information on hearing, speech, language and cognitive skills developmental miles stones were given to the parents – parents were informed if re-screening was necessary after discharge b- High-risk infants: the infants were tested for AABRs within 2 month of the TEOAEs test. Infants with at least 1 risk factor also fell under this sub-groups	OAE + AABR 2. Infants with referral response: all the infants were tested for AABRs as soon as possible before age of 1 month. Then were re-categorized under 2 sub-groups based: a- Infants with pass response: further categorized into 2 groups a1) low-risk infant: educational brochures (as above) were given to the parents before discharge a2) high-risk infants: although passed the AABRs test, they were followed up regularly (twice before age of 6 months and once before age of 9 months in the 1st year, once before	none	8 years (2005 to 2012)	Overall screening rates increased since 2005 to 2012 (10% to 65%) Referral and Testing Stage: 1) Infants referred to 2nd Stage : 14% to 16% 2) Infants tested in the 2nd stage : 43% to 83% 3) Infants referred to the 3rd stage: 23% to 8% 4) Infants tested in 3rd stages: 51% to 81% 5) Intervention stage: with referral decreasing from 63% to 31% 6) Intervention increase from 71% to 92% 7) Prevalence decreased from 4.7% (1st year of study) to 2.6% (8th year of study) Cost of the series method was higher than single-step methods Series of TEOAEs/AABRs method was efficient in Iran	

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
				age of 18 months in 2nd year and once before age of 30 months in the 3rd year) b- infants with referral response: the infants had some level of hearing impairment and were referred to the closet diagnostic centre, where the type and level of hearing impairment was diagnosed before age of 3 months 3.Infants with incomplete response: In some infants, TEOAE s test was not possible to run 3 times due to existence of any mass in ears, environmental noise, un-calibrated instruments, parent's refusal or unsatisfactory conditions of the infants – was tested again after 1 week – if response not complete they were tested with AABRs				

Evidence Table: Efficacy/Effectiveness (OAE + AABR)
Question: Is

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
7. Unlu I, Guclu E & Yaman H. When Should Automatic Auditory Brainstem Response Test be Used for Newborn Hearing Screening? Auris Nasus Larynx. 2015; 199-202	Cross-Sectional Study Aim: To investigate the referral rate and when automatic aABR should be used for newborn hearing screening To detect the incidence of permanent childhood hearing loss in population with and without perinatal risk factors in Duzce, Turkey Methods TEOAE screening done by same audiometrist (noise level <30dB in quite room) at age of 5 days Infants who passed the 35dB hearing screen continued to the regular aABR test Infants whom emission response was obtained bilaterally were considered passed the screening process *Screening Stages*	II-2	3109 infants (2933 healthy full-term infants and 176 infants with perinatal risk factors) Born between January 2009 and December 2013 2933 healthy infants were screened by 3 stages protocol include TEOAE 176 with ≥1 risk factors were tested with aABR	TEOAE (DP-Echoport ILO-292 (UK) aABR (Maico Mb-11 (DE)			Stage 1 (TEOAE) 284/2933 (9.6%) infants not passed 1st screening with TEOAE 5/284 (1.7%) had otitis media (OM) with effusion – retest with TEOAE at 15 days old – passed the second screening 255/284 (8.6%) underwent 2nd TEOAE screening at age of 15 day (included 5 infants with OM before) – 29 (9.5%) not come to the 2nd screening 97/255 (3.3%) infants failed 2nd screening – 90 (3%) underwent 3rd TEOAE screening at 30 days old – 7 (0.2%) not came to the 3rd retest 85/90 (2.9%) – failed 3rd TEOAE screening 85/284 infants who were failed at stage 1 screening underwent 2nd stage screening with aABR – along with 176/3109 infants with perinatal risk factors Stage 2 (aABR) 2 aABR tests made with a 2-weeks interval 14/176 (7.9%) infants with perinatal risk factors and 10/85 (11.7%) infants who failed at stage 1 screening could not pass the aABR test All of them referred to higher centre for further evaluation	

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
	Stage 1 (TEOAE) 1st screening with TEOAE Failed 1st TEOAE screening – repeated TEOAE at 15th day of birth Failed 2nd TEOAE screening – repeated TEOAE at 30th day of birth Failed 3rd TEOAE screening – referred 2nd stage screening with aABR Stage 2 (aABR) Infants who failed 3rd screening with TEOAE Infants with risk factors were tested with aABR at 1st months of birth						Final result - 0.34% of 2933 healthy full-term infants (without perinatal risk factors) were detected with newborn hearing loss - 7.9% (14) of 176 infants with perinatal risk factors having a problem • 2 suspicions of hereditary hearing loss • 1 cleft palate anomaly • 1 Down syndrome • 1 external ear canal atresia • 9 undergo treatment in NICU (5 for low birth wt, 3 for high bilirubin levels and 1 for various reasons) - None of the infants had any history of feverish disease during pregnancy and marriage between relatives Conclusions TEOAE as screening test with best results after 30 days of life More suitable to carry out TEOAE screening in healthy newborn and aABR in newborn with risk factors Healthy newborns who cannot passed at least 2 retest with TEOAE may decrease the need for aABR significantly	

Evidence Table: Efficacy/Effectiveness (DPOAE + AABR)
Question: Is

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
8. Wahid SNH, Daud MK, Sidek D, Rahman NA, Mansor S & Zakaria MN. The Performance of Distortion Product Otoacoustic Emissions and Automated Auditory Brainstem Response in the Same Ear of the Babies in Neonatal Unit. International Journal of Pediatric Otorhinolaryngology.2012: 76:1366-1369	Cross-Sectional Study Aim: to identify the outcomes of hearing screening using different protocols of both DPOAE and AABR tests in the same ear of the babies in neonatal unit population Methods Neonatal unit of HUSM – stable babies and problematic infants who do not need NICU treatment such as mild to moderate neonatal jaundice Screening All subjects will underwent both screening with DPOAE (2, 3, 4 and 5 KHz) followed by AABR At the same setting as near to discharge as possible Test will be repeated 2 times in cases with 'refer' results Descriptive statistics such as frequency and percentages were	II-2	73 newborns involved (61.6% male and 38.4% female) – total ears screened 146 ears Risk Factors of hearing problems: Ototoxic medication Hyperbilirubinaemia Low birth weight Sample size = calculated using single proportion formula based on prevalence of babies who were at risk for hearing loss at 44% - the calculation indicated that minimum sample size of 95 subjects would be sufficient to obtain 0.1 precision to calculate the prevalence of babies who were at risk for hearing loss with 95% CI – with	DPOAE AABR	None		41% of the infants had at least 1 risk factor 12% had 2 risk factors 1% had 3, 4 and 5 risk factors Screening Results -AABR had higher passing rate (82.9%) -DPOAE passing rate lower (77.4%) -The highest passing rate was achieved if the protocol of either passed DPOAE or AABR was used (90.4%) -Rate was lower when auditory neuropathy spectrum disorder (ANSD) has been considered (82.9%) Conclusion AABR had higher passing rate as compared to DPOAE Use of both instruments in the screening process especially NICU babies will be very useful to determine ANSD problem Protocol in which newborns are tested with AABR first followed by DPOAE on those who fail AABR is recommended	

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
	calculated for all the categorical variables		anticipation of 20% non-response rate, it was decided to take 114 subjects All infants in neonatal unit were included in the study – used by systematic random sampling – conditions of ears were assessed using an otoscope (impacted ear wax, middle ear effusion and persistent mesenchyme in the external ear were excluded)					

Evidence Table: Efficacy/Effectiveness (TEOAE+AABR)
Question: Is

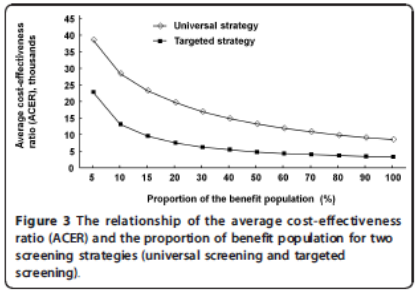
Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
9. Caluraud S, Marcolla-Bouchetemble A, Barros Ad, Moreau-Lenoir F, Sevin Ed, Rerolle S, Charriere E, Lecler-Scarcella V, Billet F, Obstoy MF, Amstutz-Montadert I, Marie JP,& Lerosey Y. Newborn Hearing Screening: Analysis and Outcomes After 100,000 Births in Upper-Normandy French Region. International Journal of Paediatric Otorhinolaryngology. 2015; 79:829-833	Cross-Sectional Study Aim: to evaluate and critically analyse the universal newborn hearing screening with TEOAE/AABR Method: 2 steps programme applies: 1) Pre-discharge screen was performed 3 days after birth 2) Outpatients test was performed 3 to 4 weeks later, if the 1st pre-discharge screen resulted in a 'fail' for one or both ears Healthy Newborn No hearing impairment risk factors Admitted to a WIN, TEOAE was performed on both ears If both ears fail, immediate retested with AABR was conducted If fail the retest, outpatient AABR was scheduled 3 to 4 weeks later in an ENT dedicated department (7 centres)	II-2	100,000 newborns (All newborns alive in public and private hospitals and clinics where hearing screening was performed in Upper Normandy region of France from 1999 to end of March 2011) Data collector still ongoing 2015 onwards Extend to all 14 birth centres in the region	TEOAE AABR	Confirmation test Diagnostic audiologic assessment	1999-March 2011	Global Population Results -From the funding program 1999-March 2011 (101,916 live births -99.4% (101,341) were screened prior to hospital discharge -99.6% (95,457) newborns admitted to well-infants nurseries (WINs) and 97.1% (5884) newborns from NICU were tested at the 1st step -1.2% of 101,341 (1192) infants screened positive and 0.6% (575) were not tested -1.7% (1767) children were recalled for outpatient screening one month later -89.1% (1575) recalled outpatients presented at second step and were tested, resulting in total of 101,724 (99.8%) infants screened -170/1575 (10.8%) or 0.2% out of the global population failed at the 2nd step and recalled for diagnostic assessment; 203 (0.2%) infants were lost to follow up Positive Screening Population Result -Only positive screenings at 1st step (not the missed or unscreened cases) were analysed -1192 (1.2%) failed both ears were referred to second step -Of the 1098 (92.1%) tested at step 2, 159 (14.5%) failed and 139 (87.4%) hearing impairment were confirmed by diagnostic audiologic assessment -139+3 untested at step 1 children were diagnosed with bilateral hearing impairment, a prevalence of 1.4% -94 (7.9%) lost to follow up between 1st and second step but none between	

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
	Infants admitted to NICU or who present with hearing impairment risk factors 1st test was AABR If failed, the infants will be referred (at age of 3 to 4 weeks) back with AABR Infants who failed the outpatient screening was referred for diagnostic auditory assessment (ASSR), ABR and behavioural audiometry Costs Considered material cost (purchase, maintenance, and disposable accessories) and human resource cost (testers, secretaries, coordinating physician) The 1st protocol (TEOAE/ABR) was estimated at 15€ per newborn while the current protocol (TEOAE/AABR) was estimated at 15€ per newborn						the second step and the subsequent diagnostic appointment Separate Analysis of Nurseries Outcomes from NICUs Outcomes - Data from 1st step screening in WINs and NICUs were compared - 6060 newborns were transferred to NICU or hospitals out of the region (5.9%) Comparing the 2 protocols - During 1st protocol (prior 2004) was applied, 2.3% of newborn screened positive (a fail) at the first step, with the current protocol (after 2004), a 1% fail rate was obtained – the difference was statistically significant ($p < 0.001$, Z test) - Under initial protocol (prior to 2004) 61.1% of newborns who remained undiagnosed after 2 screening steps were subsequently confirmed to have a hearing impairment through ABR testing – increased to 95.1% under second protocol (after 2004) – significant difference ($p < 0.001$, Z test) Lost to Follow Up - 203 cases (0.2% of the total test group) were lost to follow-up; 192 after step 1 and 11 after step 2 - Among untested. 109 (18.9%) lost to followed-up - 87 (7%) of newborns screening positive at step 1 and 11 (6.3%) screening positive at step 2 were lost to followed-up - The difference between loo to followed-up rate for untested and for	

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
							tested one or both steps was statistically significant ($p < 0.001$, Z test) - Difference between the infants lost to followed-up admitted to WIN and NICU was statistically significant ($p < 0.001$, Z test) Conclusion UNHS program in Upper-Normandy, France, screens 99.8% of the overall newborn population 2 steps protocol adopted after 2004 appears to be the most effective and efficient Median age for hearing aids in this region for severe to profound hearing loss was 7 and 6 months respectively and 11.5 months for moderate loss	

Evidence Table: Cost-Effectiveness Analysis
Question: Is

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
10. Huang LH, Zhang L, Gai Tobe RY,, Qi FH, Sun L, Teng Y, Ke QL, Mai F, Zhang XF, Zhang M, Yang RL, Tu L, Li HH, Gu YQ, Xu SN, Yue XY, Li XD, Qi BE, Cheng XH, Tang W,, Xu LZ & Han DM. Cost-Effectiveness Analysis of Neonatal Hearing Screening Program in China: Should Universal Screening be Prioritized? BMC Health Services Research. 2012; 12:97	Cost-Effectiveness Analysis Aim: to determine cost-effectiveness of the NHS program implementation, in case of 8 provinces of China, in order to support evidence-based national policy making in china Methods *Cost-effectiveness* model Modelled the CE models for 2 screening programs: a.UNHS b. Targeted screening 8 provinces of China Developed Provinces (Beijing, Shandong, Hebei, Guangdong and Zhejiang) Developing Provinces (Henan, Jiangxi, and Guangxi) *Probability Parameters* i. Drop out from diagnosis centre and inaccessibility of interventions, referred		All neonates annually born in the 8 provinces from 2007 to 2009 were simulated	UNHS screening used OAE or OAE+ AABR Universal Screening (UNHS) (covers all live births) – detects infants with disorder who have no known risk factors associated with permanent congenital and early-onset hearing impairment (PCEHI) – 50% PCHEI cases	Targeted screening which targeted those with ≥1 risk factors – one alternative to UNHS		**Results** *Benefit Population of the Current Neonatal Hearing Screening Program* • Benefit Population = proportion of infants with disorder who finally received beneficial early hearing detection and intervention • 3 variables (coverage rate, diagnosis rate and intervention rate) determined the total number of deaf infants finally receiving early interventions and benefiting from the screening program *Cost-Effectiveness of Different Strategies in 8 Provinces* • Based on GDP per capita in each province and baseline of transition probability parameters, ✓ UNHS strategy showed cost-effectiveness in Guangdong, Shandong, and Beijing ✓ Targeted screening strategy showed cost-effectiveness in Zhejiang and Hebei ✓ Neither of strategies showed cost-effectiveness in Guangxi, Jiangxi and Henan • Multivariate sensitivity analyses were performed for transitions probability parameters to determine the robustness of the model ✓ Range of uncertainty of 3 variables (Program coverage, diagnosis rate and intervention rate) has a great impact on cost-	

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
	neonates might not be either diagnosed of received interventions ii. Probability parameters potentially affecting cost-effectiveness are the proportion of infants with ≥ 1 high risks, the prevalence of PCEHI in the general population and high-risk population, the sensitivity, specificity and coverage of the screening program which shows neonates screened among those targeted by the screening program, diagnosis rate which shows those diagnosed before 6 months among those referred after the screening and intervention rate which shows infants fitted with hearing aids or cochlear implants and have started the rehabilitation course before 12 months of age among those with disorder as detected during diagnosis *Costs for the Program Implementation* Capital costs (office,						effectiveness of the screening strategies  **Figure 3** The relationship of the average cost-effectiveness ratio (ACER) and the proportion of benefit population for two screening strategies (universal screening and targeted screening). ✓ Increase proportion of benefit population (estimated by multiplying 3 variables) – reduced ACER of different strategies and gradually helped both strategies reach better cost-effectiveness ✓ Targeted strategy trended to be cost-effectives in Guangxi (9%), Jiangxi (9%), Henan (8%), Guangdong (4%), Zhejiang (3%), Hebei (7%), Shandong (5%) and Beijing (2%) ✓ Universal strategy trended to be cost-effective in Guangxi (70%), Jiangxi (70%), Henan (48%), Guangdong (10%), Zhejiang (8%), Hebei (28%), Shandong (15%) and Beijing (4%) *Economic Effects on Long-Term Cost Saving* • Cost would be saved if early detection and intervention was give • In the model universal strategy and targeted strategy led to 214,024,820 Int$ and 104,872,740 int$ of long term cost-saving in total –	

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
	equipment etc) Recurrent costs (salaries, utilities etc) Patient-level costs (registration fee, screening test, diagnosis test etc) *Data Collection* 2 components 1.Cost related to the screening program 2. transition probability parameters *Estimates of Health Effects* Population health is expressed as number of Disability-Adjusted Life Years (DALYs) averted as a results of the screening program DALYs lost due to PCEHI were calculated as the sum of Year Lost due to Disability (YLDs) averted Disability weights for adult-onset hearing impairment were adopted in estimation 0.216for untreated disorders and 0.168 for treated disorders *Cost-Effectiveness Analysis*						approximately equivalent to 0.14% and 0.07% of the annual health expenditure • At baseline both strategies achieve cost savings which were greater than implementation costs • When the proportion of benefit population expanded, the effect of these screening strategies on the long-term costs saving become more and more significant, especially those of universal strategies, exceeding the total costs of the screening program implementation, suggesting a good economic effect in the long term **Conclusion** - Universal strategy can be considered as ultimate implementation goal as it provided the best health and economic effects – feasible in provinces where screening, diagnosis and interventions services are good enough to benefit sufficient proportion of deaf children - In other regions, targeted strategy is temporarily more realistic than a universal strategy – require related services to cover the targeted population as much as possible	

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
	ACER is calculated for each screening strategy by determining the cost for program's implementation Total health effects in terms of DALYs ICER calculated to determine the priority of purchasing the services at different budgetary levels Monte Carlo simulation to determine uncertainty in health effect estimates and cost-effectiveness ratios							

Evidence Table: COST-EFFECTIVENESS ANALYSIS
Question: Is

Bibliographic citation	Study Type / Methods	LE	Number of patients and patient characteristics	Intervention	Comparison	Length of follow up (if applicable)	Outcome measures/ Effect size	General comments
11. Kemper AR & Downs SM. A Cost-Effectiveness Analysis of Newborn Hearing Screening Strategies. Arch Pediatr Adolesc Med. 2000; 14:484-488	Cost-Effectiveness Analysis Obj: To compare the expected costs and benefits of targeted screening with universal screening for the detection of significant bilateral congenital hearing loss Methods -To evaluate NHS, a comparison was made between the costs and benefits for both UHS and targeted, risk-based screening -Cost analysis was conducted from health care system perspective Short-Term Costs -Cost of screening and follow-up screening Long-Term Costs -Costs of treatment -any potential saving from early initiation of treatment were not included Indirect Costs		- 100,000	TEOAE followed with AABR Confirmation Test: Diagnostic AABR			Universal Screening Detection - Detect 86 cases of congenital deafness out of 110 for every 100,000 children screened, representing a 40% improvement over targeted screening - Associated with : 300 FP referrals, 19-fold increase over targeted screening - 21% for universal screening and 76% for targeted screening - Compared with targeted screening, universal screening was associated with 530% increase in total costs and a 273% increase in cost per case detected - Assumed that: there were approximately 4 million births per year in US; targeted screening would cost US$ 6.40 million compared with US$ 40 million for universal screening - However with 1,400 more cases of congenital hearing loss would be detected Incremental Cost-Effectiveness - Moving from risk-based to universal screening would cost an additional US$23,930 for each extra case detected Sensitivity Analysis - Sensitivity analysis identified important areas of uncertainty - Univariate analyses on all variables - Bivariate Sensitivity Analyses on sensitivity and specificity for each screening test were performed Probabilities	

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	-parental wages lost -Transportation cost -Child-care costs incurred because of the screening process were not included Benefits for the screening programs were addressed by the number of cases properly identified Universal Screening Assumed that: -All newborns will be screened with an automated TEOAE device -infants with positive results would then be screened with AABR device -Infants with positive results on the second screen would then referred for diagnostic ABR -In targeted screening, only newborns at high risk for hearing impairment would receive the 2-stage screening process Assumptions -All newborns would be screened and receive all necessary follow-up testing						-Over all ranges of possibility estimated, universal hearing screening detects more cases than targeted screening at greater cost Costs -Only the cost of risk-screening assessment affects the relationship between universal and targeted screening -If the cost of screening infants for high-risk factors were more than US$5.34 per infant, the cost per case detected by universal screening will be less than by targeted screening -At the extreme limit of the analysis at which the cost of risk screening was US$15 per infant, the cost per case identified by targeted screening would be US$18,990 more than the cost per case identified by universal screening	

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	Probabilities and costs were estimated based on literature Specificity of risk-based screening for congenital hearing loss was not available – applied Bayes Theorem to calculate the specificity from prevalence of hearing loss and PPV of risk assessment							

Evidence Table: COST-EFFECTIVENESS ANALYSIS
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12. Keren R, Helfand M, Homer C, McPhillips H, & Lieu T. Projected Cost-Effectiveness of Statewide Universal Newborn Hearing Screening. Paediatrics. 2002; 110(5): 855-864	Projected Cost-Effectiveness Obj: To evaluate UNHS and selective screening in terms of both short- and long-term benefits, harms and financial costs To identify steps in screening process that could be improved to increase cost-effectiveness Conducted from societal perspective for hypothetical birth cohort of 80,000 infants in 1 state – statewide cohort Methods All the screening protocols used 2-step screening before discharge (to prevents the loss to follow-up and reduce the number of FP results seen with single-step pre-discharge screening For each screening strategy the authors modelled the		-	*Selective NHS* Only infants with risk factors for congenital deafness were screened Used AABR test with repeat AABR testing for non-passes *UNHS* (TEOAE followed with AABR) All infants were screened	No NHS		Deaf term refer to wide spectrum of hearing loss – moderate to profound bilateral hearing loss (≥ 40 dB) Main Outcome 1) The incremental cost per infant whose deafness was diagnosed by 6 months which included only the cost of screening and diagnostic evaluation 2) The incremental cost per deaf child with normal language which also included the costs of medical care, education and assistive devices as well as lost productivity over the lifetime of the deaf individual Intermediate Outcome - Test results, the percentage of infants who failed the screening protocol and were referred for diagnostic evaluation (refer rate), the percentage of newborns referred who actually followed up with diagnostic evaluation and the PPV of the test **Results** ***Base-Case Results*** <u>Screening Test Results and Referral Rates</u> Sensitivity Analyses (based on authors' model) - In selective screening • Identified 62 of the 128 deaf infants in birth cohort • Referred 0.18% of all infants for diagnostic evaluation (145 of	

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	proportion of infants whose deafness was diagnosed by 6 months of age and of those the proportion who began early intervention (amplification and/or enrolment in an early intervention program) by 12 months of age Assumptions Deaf children with normal language abilities at entry to grade school would have normal language as adults Probabilities -Epidemiology and Screening Test Properties -Age diagnosis and intervention -Language outcomes Cost -Screening and Diagnostic Evaluation Costs -Societal Costs						80,000) • PPV of 43% (62 of 145) • 112 of 145 infants with positive screening tests were followed up with a diagnostic evaluation and of those, 49 received a diagnosis of being deaf - In UNHS • Identified 116 of the 128 deaf infants • Referred 1.6% of all infants (1314 of 80,000) • PPV of 8.8% (116 of 1314) 1015 of 1314 infants with positive screening tests were followed up with a diagnostic evaluation and 97 received a diagnosis of being deaf <u>Diagnosis by 6 Months, Intervention by 12 Months and Normal Language Outcomes at Entry to Grade School</u> The model was simulating real-world conditions in which a portion of deaf infants who 1) Have FN screening test results 2) Not screened under selective screening 3) Fail the hearing screen but do not have immediate follow-up with diagnostic evaluation nonetheless have their deafness diagnosed by 6 months of age • Although 49 infants under selective screening and 97 infants under UNHS received a diagnosis of being death through screening and prompt diagnostic evaluation, a total of 66 infants under selective screening and 99 infants under UNHS received a diagnosis as being deaf by 6	

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							months of age The model also simulated that not all infants who deafness is diagnosed by 6 months receive intervention before 12 moths and that some infants whose deafness was diagnosed after 6 months receive intervention before 12 months • Although 66 infants under selective screening and 99 infants under UNHS had their deafness diagnosed by 6 months, 75 infants under selective screening and 97 infants under UNHS received intervention by 12 months – of these infants, 59 under selective screening and 65 under UNHS had normal language quotients at entry to grade school <u>Incremental Cost Per Infant Whose Deafness was Diagnosed by 6 Months of Age</u> In the absence of NHS, 30 deaf infants, were identified by 6 months of age by passive detection alone • Total cost of detection of hearing loss for these infants was $69,000 Compared with no NHS, the selective screening protocol resulted in an additional 36 infants whose was diagnosed by 6 months at an additional cost of approximately $600,000, yielding an incremental cost-effectiveness of approximately $16,000 per additional infants whose deafness was diagnosed by 6 months Compared with selective screening,	

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							the UNHS protocol resulted in 33 additional infants whose deafness was diagnosed by 6 months of age at an additional cost of approximately $1.5 million, yielding an incremental cost effectiveness of $44,000 per additional infants whose deafness was diagnosed by 6 months of age <u>Incremental Cost per Deaf Child with Normal Language</u> • When lifetime savings from normal language with early intervention were incorporated, both selective screening and UNHS resulted in normal language achievement for more deaf children and total cost reduction compared with no screening UNHS was the dominant screening strategy in this analysis because it resulted in better outcomes and reduce costs compared with both selective screening and no screening ***Sensitivity Analyses*** - Base-case estimate of marginal cost per infant whose deafness was diagnosed by 6 months of age was robust to changes in most of the key probabilities and costs - 2 variables : i) The screening success rate (the proportion of infants with risk factors actually screened) under selective screening ii) The rate of follow-up with diagnostic evaluation after referral for a positive screening test - As the screening success rate under selective screening was varied from	

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							40% to 100%, the incremental cost of UNHS changed from %33,000 to $55,000 per additional infants whose deafness was diagnosed by 6 months - Increasing the rate of follow-up with diagnostic evaluation from 50% to 100% decreased the incremental cost of UNHS from $56,000 to $38,000 per additional infants whose deafness was diagnosed by 6 months - Varying the probability of diagnosis by 6 months without NHS had a smaller effect on the marginal cost per infant whose deafness was diagnosed by 6 months under selective screening and UNHS - In high risk infants proportion whose deafness was diagnosed by 6 months in the absence of NHS was decreasing from the base-case estimate of 25% to 10% the incremental cost per additional infant whose deafness was diagnosed by 6 months decreased from $16,000 to $13,000 for selective screening and $44,000 to $41,000 for UNHS - In low risk infants proportion whose deafness was diagnosed by 6 months in the absence of NHS was decreased from the base-case estimate of 20% to 10%, the incremental cost per additional infant whose deafness was diagnosed by 6 months was unchanged for selective screening and decreased from $44,000 to $39,000 for UNHS - The cost-effectiveness of UNHS was very sensitive to changes in the estimates for these variables	

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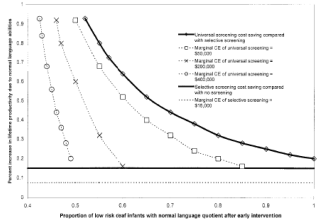
							- 2-way sensitivity analyses showed that when the percentage increased in productivity given normal language and the proportion of low risk infants with normal language after early intervention were both high, UNHS resulted in net savings - Under less favourable estimates of these probabilities, UNHS was not cost saving and the incremental cost (per additional child with normal language) increased significantly as indicated by the isocontour curves to the left of and below the above-mentioned curve - In the range of estimates modelled, selective screening was cost saving compared with no screening as long as the percentage increase in lifetime productivity given normal language was > 15% ●  Fig. 2. Two-way sensitivity analysis illustrating incremental cost per additional deaf child with normal language outcomes under a range of estimates of the percentage of low-risk deaf infants with normal language after early intervention and the percentage increase in lifetime productivity as a result of normal language.	