Health Technology Assessment of "Portable Automated ABR" Neonatal Hearing Screening Device

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Health Technology Assessment in India (HTAIn)
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Dr. Sanghamitra Pati
Principal Investigator

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List of Abbreviations

AABR	:	Automated Auditory Brainstem Response
ANM	:	Auxiliary Nurse Midwife
AYUSH	:	Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy
BERA	:	Brainstem Evoked Audiometry Response
BOA	:	Behavioural Observation Audiometry
CEA		Cost-Effective Analysis
CHC	:	Community Health Centre
C-section	:	Caesarean Section
DALY	:	Disability -Adjusted Life Year
DEIC	:	District Early Intervention Centers
DHH	:	District Headquarter Hospital
DHR	:	Department of Health Research
ENT	:	Ear Nose Throat
FN	:	False Negative
FP	:	False Positive
GoI	:	Government of India
Ha	:	Alternative Hypothesis
HL	:	Hearing Loss
Ho	:	Null Hypothesis
HTAIn	:	Health Technology Assessment in India
ICMR	:	Indian Council of Medical Research
IDI	:	In-Depth Interview
IQI	:	Infant health-related Quality of life Instrument
JSSK	:	Janani Shishu Suraksha Karyakaram
LBW	:	Low Birth Weight
LMIC	:	Low and Middle-Income Countries
MCH	:	Medical College Hospital
MHT	:	Mobile Health Team
NHL	:	No Hearing Loss
NHM	:	National Health Mission
NPV	:	Negative Predictive Value
OAE	:	Otoacoustic Emissions
OOPE	:	Out of Pocket expenditure
PHC	:	Primary Health Centre
PICO	:	Population Intervention Comparator Outcomes
PPV	:	Positive Predictive Value
QALY	:	Quality-Adjusted Life-Years
QoL	:	Quality of Life
RBSK	:	Rashtriya Bal Swasthya Karyakram
RMRC	:	Regional Medical Research Centre
SNCU	:	Sick Newborn Care Unit
TAC	:	Technical Appraisal Committee
TN	:	True Negative
TP	:	True Positive
UNHS	:	Universal Newborn Hearing Screening
WHO	:	World Health Organisation

Executive Summary

Backgrounds: Congenital hearing impairment in infants and children has been linked with lifelong deficits in speech and language acquisition, poor academic performance, individual and social maladjustments, and emotional difficulties. Excessive emphasis is placed on the importance of early detection, reliable diagnosis, and timely intervention. Studies indicate prevalence 5 – 6 per 1000 live births in India, of neonatal Hearing Loss (HL), with highly considerable repercussion on lifelong disability and Quality of Life (QoL). However, a majority of hearing impairment remain undetected.

In India under Rashtriya Bal Swasthya Karyakram (RBSK) since 2013, neonatal HL is a part of the actions, which comprise of comprehensive hearing impairment detection during childhood. As per RBSK program, Otoacoustic Emissions (OAE) is used at the facility level, while Behavioural Observation Audiometry (BOA) is adopted at the community screening. For further confirmation, it is followed by BERA at referral facilities. Community-based screening is being carried out using a brief questionnaire and behavioural testing by a trained health-care worker during immunization. Any infant who do not pass the screening is followed up at the district hospital for OAE and AABR testing. A 2-stage screening protocol by Transient Evoked Oto-acoustic emissions (TEOAE) and automated Auditory Brainstem Response audiometry (AABR) is generally followed for the screening of newborns for HL. In hospital-based screening OAE is used as the first level of screening up to six weeks of age.

The failed neonates undergo a second screen within three weeks of the first screening. The Brainstem Evoked Audiometry Response (BERA) is used to confirm the HL if the neonates failed the second OAE screen. Some of the key issues in the implementation of the program are identified as a lack of human resources, inadequate infrastructure, equipment-related shortcomings, and low priority for deafness prevention. The BOA has low specificity which results in an increase in referral cost and Out of Pocket expenditure (OOPE). There appears to be a need for a technology with high efficacy which can detect hearing impairment through first level of screening with better or similar diagnostic accuracy and at the same time being user-friendly.

It is perceived that 'Portable Automated ABR' is clinically efficient and cost-effectiveness, which need to be assessed. The 'Portable Automated ABR' device can be used as a part of Universal Health Coverage (UHC) of hearing screening among infants in out-reach areas due to its' minimal infrastructural requirements and high diagnostic accuracy. The screening services could be

explored in out-reach areas by replacing the BOA approach of RBSK program. The 'Portable Automated ABR' may be implemented at all delivery point such as the primary health centre, community health centres, including private hospital to increase the coverage hearing screening among newborns.

Overall aim: To assess the clinical efficacy, cost-effectiveness and operational challenges in the implementation of 'Portable Automated ABR' neonatal hearing screening devices in healthcare facilities of Odisha.

Methods: This Health Technology Assessment (HTA) study is classified into three broad areas: Diagnostic validation of 'Portable Automated ABR', economic evaluation and assessment of QoL of 'Portable Automated ABR', and ethical, and social implication of 'Portable Automated ABR' implementation. This study was approved by the Technical Appraisal Committee (TAC), Health Technology Assessment, Department of Health Research (DHR), Ministry of Health and Family Welfare, Government of India. The ethical clearance was obtained from the Institutional Ethical Committee of RMRC Bhubaneswar and State Ethical Review Committee, Department of Health and Family Welfare, Govt. of Odisha.

Study	Primary data and study participants	Settings	Data analysis
Diagnostic validation	Total 367 high-risk neonates were screened using Portable Automated ABR and compared with BERA and 435 high-risk neonates were screened using OAE and compared with BERA	Maulana Azad Medical College, New Delhi	Sensitivity and Specificity analysis
Health system cost for 'Portable Automated ABR' and OAE	Data were collected from Six facilities where OAE devices are implemented (three coastal and non-coastal each)	District Early Intervention Center (DEIC)	Cost Effectiveness Analysis (CEA)
Out-of-Pocket Expenditures (OOPE) Quality of Life (QoL)	Total of 720 parents (equal number from coastal and non-coastal) of infants interviewed using the structured tool. from various level of facilities, 180 from each facility: Medical College Hospital, District and	Khurda and Koraput	

	Sub-divisional Hospitals, Community Health Centre's and Primary Health Care Centre's		
Operational feasibility of 'Portable Automated ABR' Stakeholders' perceptive	Data collected using observation checklist during hearing screening using 'Portable Automated ABR'. All types of challenges and facilitation during the test were documented. Total 26 In-depth Interviews (IDIs): ten mothers, sixteen service providers and program managers.	Community and facilities	Contents analysis

Findings: We compared the OAE hearing screening test which is commonly used in India under RBSK with 'Portable Automated ABR' the newly invented hearing screening device. The findings indicate that the sensitivity and specificity of 'Portable Automated ABR' was 100% and 97% respectively and that for OAE was 69% and 68% respectively. The sensitivity results revealed that the minimum or maximum prevalence rate of HL had not any effects on displacing the technology, and the 'Portable Automated ABR' device was associated with higher effectiveness and lower cost in comparison to OAE. The number of false positive results (i.e., the newborns who were healthy but falsely detected as cases) was far less in the 'Portable Automated ABR' method than in the OAE method, imposing less costs – direct, indirect and intangible, as well as stress and anxiety on the new-born's families.

Our primary data collection on out of pocket expenditure (OOPE) suggested that the average wage loss was highest for Medical College hospital (600 INR) or district hospital (300 INR) along with the transportation cost (441 INR). As the distance of majority of tertiary care facilities was more, followed by the DHH, where the hearing screening facilities were available, it cost significant amount to the parents of the infants. However, as the number of visits for the infants having hearing impairments were more and it cost them more as compared to the infants who do not have any hearing deficiency.

Similarly, the mean scores QoL scores among children with HL was 9.08 and children without any HL was 7.39. Having hearing difficulties significantly affects the child's growth and development. Hence, we suggest the hearing screening service provision at nearest facilities such as sub-divisional hospital, community health centers; if possible at primary health centers will reduce the indirect as well as intangible cost.

Based on the findings, the Portable Automated ABR device can detect 6240 cases and OAE can detect 9360 per annum. Per unit cost for Portable Automated ABR will be INR 97 and INR 67 for OAE. However, the universal screening by Portable Automated ABR will cost lesser if we focus on the budgetary provisions as compared to OAE as it results into ICERs 97407.69 for the system to implement Portable Automated ABR. However, initially the health system may undergo higher costs to efficiently rollout this program due to issues such as equity, access to health services, and other challenges. In this model, it was estimated that if the universal newborn hearing screening program was conducted with the 'Portable Automated ABR' at Sub-divisional Hospitals (SDHs), Community Health Centres (CHCs) and Primary Health Centres (PHCs) and Mobile Health Team (MHT), the annual health system cost would be significantly lower even after combining with diagnostic BERA at DEIC for reference newborns.

The 'Portable Automated ABR' is one of the hearing screening devices which can perform the hearing screening for the newborns just after their birth more accurately. The test was completed within 15 minutes (preparation of electrode sites, impediments set-up, placement of ear phones and swipe-counts), if the baby was calm and sleeping. However, it has certain limitations:

- It requires a silence environment, as crowd or noisy environment disturb baby's sleep and ultimately it affects the testing process.
- During the test presence of any electronic devices such as mobile charger, computer or other electric appliance etc. affect the testing process.
- It was difficult to screen above six months' infants as they are super active and they wake up with a simple touch and removed electrode.

Conclusions and policy implication: The 'Portable Automated ABR' device is a non-invasive, safe and simple technology that can be employed in existing UNHS programs under RBSK. In case of shortage of skilled and expert work force, it can be easily taught to other staffs. The high sensitivity and specificity of this device, compared to that of the OAE device, not only reduces the number of falsely referred cases, but also detects a greater number of newborns with hearing loss. Eventually, better clinical effectiveness may be achieved. Furthermore, considering the annual birth rate, the prevalence rate of HL, and the high diagnostic accuracy of this device in the long run, it can be stated that this device imposes lower costs than the OAE device. Hence, this study recommends to include the above device at SDHs, CHCs and PHCs for greater coverage of UNHS. However, there is need for small scale implementation using existing infrastructure; which will help to identify the operational feasibility of the implementation as well as prevalence of cochlear implant for furthermore budgetary implication of the treatment, and large scale implementation.

Chapter 1

1. Introduction

1.1. Statement of the Problems

Congenital hearing impairment in infants and children has been linked with lifelong deficits in speech and language acquisition, poor academic performance, individual and social maladjustments, and emotional difficulties. Excessive emphasis is placed on the importance of early detection, reliable diagnosis, and timely intervention, as it can help in developing better skills among the hearing impaired infants equivalent to their peers. Studies indicated a prevalence of 5 – 6 per 1000 live births in India (Khurmi et. al, 2015), of neonatal HL, with highly considerable repercussion on lifelong disability and Quality of Life (QoL). However, this figure only indicates a tip of the iceberg as the majority of hearing impairment cases remain undetected (WHO, 2009, and 2017).

Figure 1.1: Effects of hearing impairment on child development

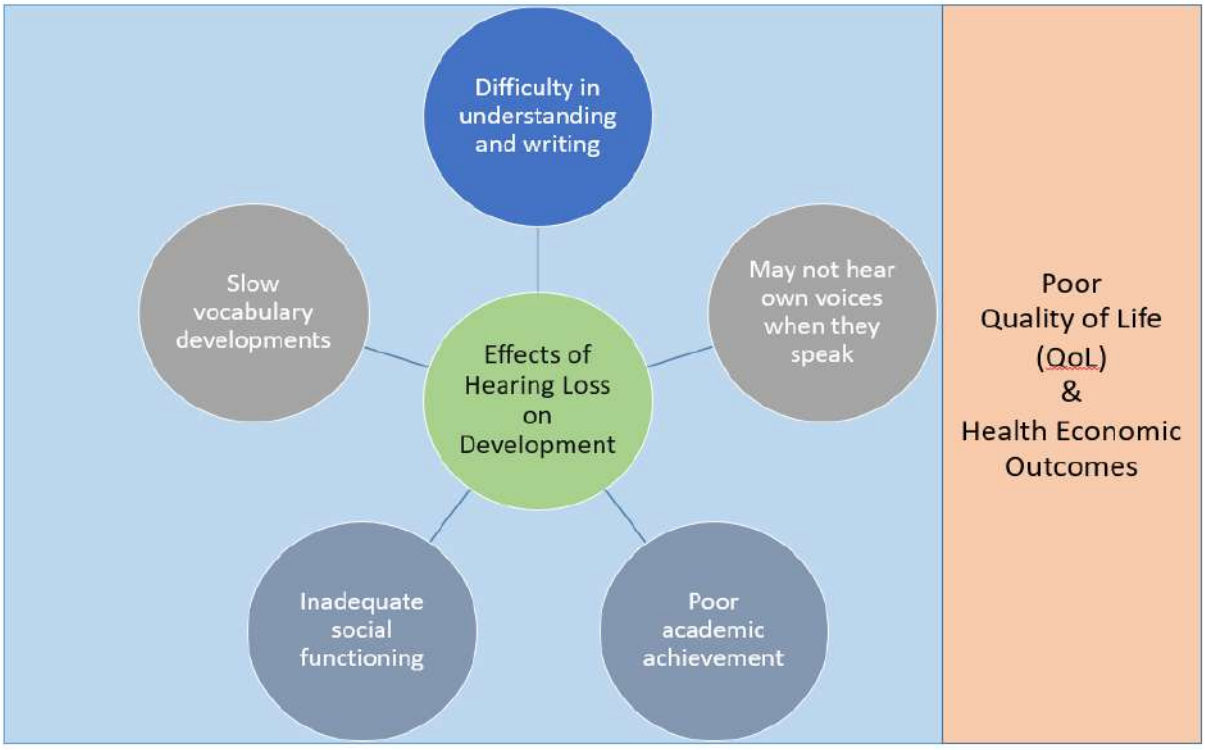
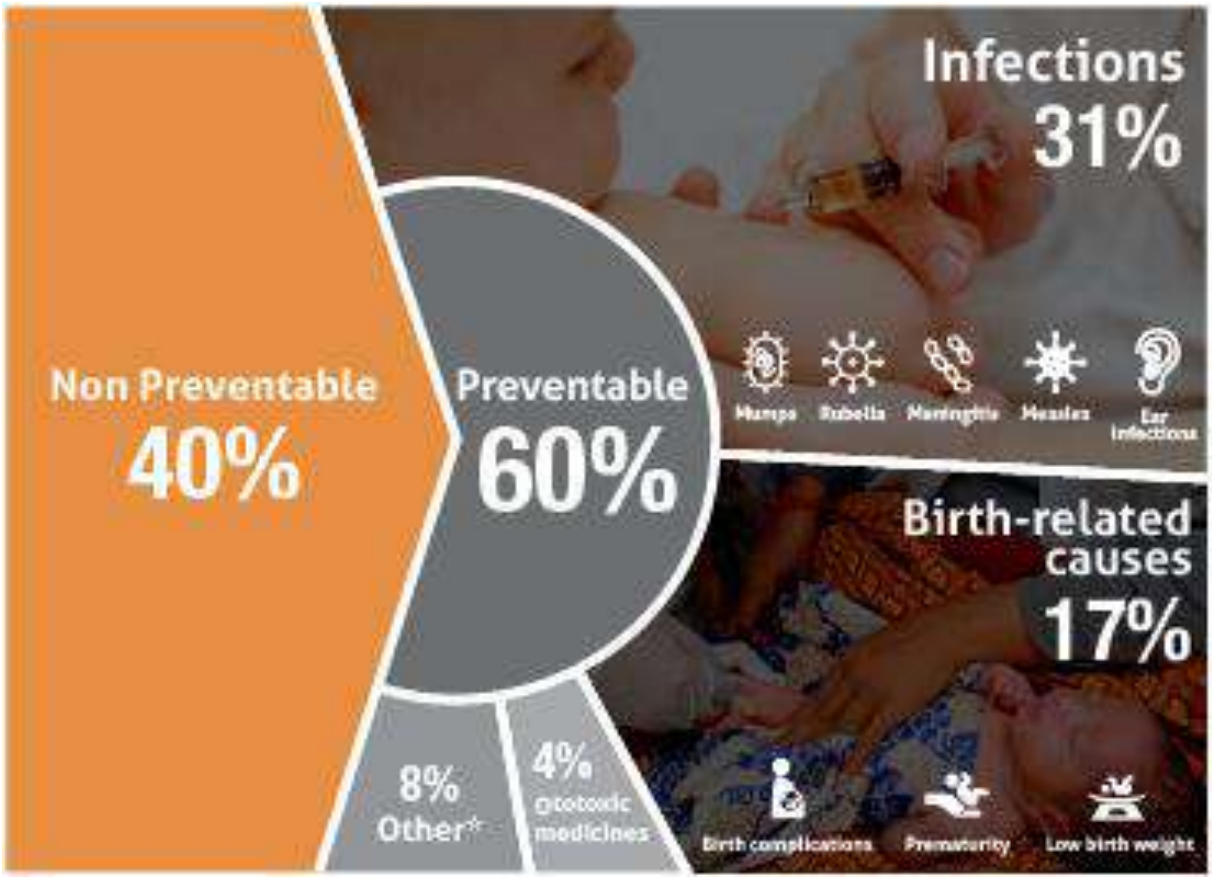


Figure 1.2: Global prevalence of preventable HL (WHO)



In India, under Rashtriya Bal Swasthya Karyakram (RBSK) since 2013, neonatal HL is a part of the actions, which comprise of comprehensive hearing detection healthcare program during childhood. As per RBSK program, an Otoacoustic Emission (OAE) is used at the facility level, while Behavioural Observation Audiometry (BOA) is adopted at the community level for hearing screening. For further confirmation, it is followed by Brainstem Evoked Audiometry Response (BERA) at referral facilities (Khurmi et. al., 2014). Community-based screening is being carried out using a brief questionnaire and behavioural testing by a trained health worker during visit of mobile health team (MHT) under RBSK. Any infant who did not pass the screening is to be followed up at the district hospital for OAE and automated Auditory Brainstem Response audiometry (AABR) testing. A 2-stage screening protocol by Transient Evoked Oto-acoustic emissions (TEOAE) and AABR is generally followed for the screening of newborns for hearing the loss in hospital-based screening OAE is used as the first level of screening up to six weeks of age (Wroblewska et al., 2017). The failed neonates undergo a second screen within three weeks of the first screening. The BERA is used to confirm the HL if the neonates failed in the second OAE screening (Yoshinaga et al., 2014).

The advantages of OAE are: cost-effective, quick performance, and minimal training required for operation, and it is portable. However, in case of OAE screening there is higher likelihood of false refers which may results in high referral follow up testing with BERA, which is costly and the child requires sedation. Furthermore, the OAE does not test beyond the cochlea.

Some of the key issues in the implementation of the program were identified as a lack of human resources, inadequate infrastructure, equipment-related shortcomings, and low priority for deafness prevention. There appears to be a need for a technology to detect hearing impairment through first level screening with better diagnostic accuracy.

The "Portable Automated ABR", a new health technology device has been designed based on the principle of BERA. The device has been developed by the School of International Bio design (SIB) startup Portable Automated ABR Innovation Labs India Pvt. Ltd by Dept. of Biotechnology (DBT) Govt. of India. The 'Portable Automated ABR' device is intended to screen neonates for hearing impairment with high sensitivity and specificity and is claimed to be specially designed for universal screening of neonates in resource-constrained settings. The portable 'Portable Automated ABR' hearing screening measures auditory brain waves via three electrodes placed on the baby's head. When stimulated, they detect electrical responses generated by the brain's auditory system. If there is no response, the child cannot hear. The battery-operated device is non-invasive, which means babies do not need to be sedated. Another key advantage over other testing systems is the patented, in-built algorithm that filters out ambient noise from the test signal. The 'Portable Automated ABR' uses BERA technology in hearing screening in an innovative way with an easy to use interface to meet the needs of the system. Every test is sent to the centralized server and results are re-evaluated by a trained audiologist. If the baby passes the test, the results are confirmed PASS. If the audiologist confirms the result as REFER, the family is directed to nearby audiology center or an ENT specialist.

The advantages of 'Portable Automated ABR' are that it can be used for testing the ears of newborns just after their birth i.e. 0-3 babies which is difficult to be tested with other hearing screening devices. However, clinically efficiency and cost-effectiveness need to be assessed. However, there is limited evidence available on cost-effectiveness of this device in the context of screening for hearing impairment among neonates. Therefore, the present Health Technology Assessment in India (HTAIn) on 'Portable Automated ABR' aims to determine the cost-effectiveness of this technology by comparing against OAE as well as BERA, and examine the potential ethical implication prior to its introduction into the universal screening program.

1.2. The Rationale of the Study

The 'Portable Automated ABR' device can be used as a part of UHC of hearing screening among infants in out-reach areas due to its portability and low infrastructural requirements. The screening services could be explored in out-reach areas by replacing the BOA approach MHTs under RBSK program. The team can provide screening services at community out-reach program and all deliver points including private hospitals for universal coverage of hearing screening.

1.3. Overall Aim

To assess the clinical efficacy, cost-effectiveness and operational challenges in the implementation of 'Portable Automated ABR' neonatal hearing screening devices in healthcare facilities of Odisha, India.

1.3.1. Specific objectives

- To determine the **efficacy** of 'Portable Automated ABR' and OAE neonatal hearing screening devices against the gold standard (BERA).
- To explore the **operational feasibility** of 'Portable Automated ABR' neonatal hearing screening device for a universal hearing screening.
- To measure the **health system cost** of implementation of 'Portable Automated ABR' and OAE neonatal hearing screening devices.
- To examine the **out-of-pocket expenditures (OOPE)** and **Quality of Life (QoL)** on neonatal hearing screening using 'Portable Automated ABR' and OAE devices.
- To explore the perspective of consumers, service providers, and program managers in terms of the **operational challenges** with respect to ethical, social and equity facets for introducing 'Portable Automated ABR' hearing screening device

1.4. Population, Intervention, Comparator, and Outcomes (PICO)

Population: All Newborns (0 to 28 days)

Intervention: 'Portable Automated ABR' neonatal hearing screening device.

Comparator: OAE neonatal hearing screening device.

Outcome measures: The sensitivity and specificity for detecting neonatal hearing screening with 'Portable Automated ABR' and OAE device each against BERA. The sensitivity of a test is the proportion of neonates having the hearing impairment and has a positive test result.

1.5. Ethical Considerations

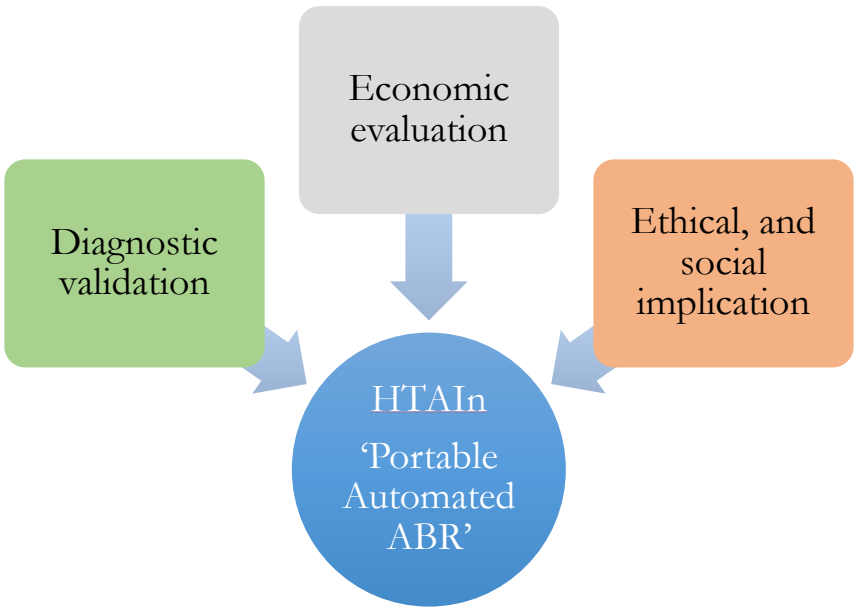
This study was approved by the Technical Appraisal Committee (TAC), Health Technology Assessment, Department of Health Research (DHR), Ministry of Health and Family Welfare, Government of India. The ethical clearance was obtained from the Institutional Ethical Committee of RMRC Bhubaneswar and State Ethical Review Committee, Department of Health and Family Welfare, Govt. of Odisha. Permission was taken from the concerned local authority in this case the head of the health facilities where neonatal hearing screening services were carried out. Consent from the study participants was obtained before the interview. They informed that the assessment would not anyway harm to them rather it would be a benefit for large scale implementation of the neonatal hearing screening program in India, and obtained information would be used for result interpretation, sharing, and policy decision.

Chapter 2

2. Methodology and Results

This Health Technology Assessment (HTA) study is classified into three broad areas: diagnostic validation of 'Portable Automated ABR', economic evaluation and assessment of QoL of 'Portable Automated ABR', and ethical and social implication of 'Portable Automated ABR' implementation (HTAIn, 2017).

Figure 2.1: Overview of Health Technology Assessment of 'Portable Automated ABR' hearing screening device



2.1. Literature Review

2.1.1. A systematic review and meta-analysis of screening, diagnostic accuracy, and risk indicators for HL among under-five children in the South Asian Region

Objectives

The objectives of the present study were twin fold: firstly, it assessed the accuracy of hearing screening procedures along with the relative diagnostic tests for various hearing impairment. Secondly, it also examined the associated risk factors with partial and permanent HL among neonatal and under-five children.

Methods

Literature search: Search strategies were designed and conducted by e-librarian (EBSCO host) using designed methods to optimize the term selection. The steps in this process conducted according to the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analysis Protocols) guidelines for meta-analysis [32, 33]. The databases such as MEDLINE, Embase, The Cochrane Library, PubMed, and ProQuest were searched along with Teacher Reference Centre (TRC) which provides indexing and abstracts for 280 periodicals. Further, the e-Book Clinical Collection, GreenFILE database searched as it offers well-researched information on various aspects of human and environmental interactions. We also used Library, Information Science & Technology Abstracts (LISTA) as it indexes more than 560 core, 50 priorities, and 125 selective journals; research reports and proceedings. Secondary references were searched and reviewed along with reference lists of the articles, using the keyword 'hearing impairment' paired with 'HL' or 'hearing screening' or 'diagnostic tests' or 'hearing examination' and 'children'. This systematic review protocol title has been registered with the International Prospective Register of Systematic Reviews (PROSPERO) database (registration number: CRD42018114817).

Selection criteria: Neonates and under-five children with partial/permanent bilateral or unilateral HL were included for the present study. The searches were carried out regardless of language and publication status. We included randomized controlled trials (RCTs), quasi-experimental studies, non-randomized comparative studies (case-control, prospective, or retrospective cohort), non-randomized studies without comparison group (e.g., prospective or retrospective cohort, cross-sectional), and pre-post studies. Studies on animal and rodents, case reports/case studies, editorials, commentaries/viewpoints/opinion, conference abstracts, rapid/scoping reviews, and studies outside from South Asia were excluded from this review.

Intervention/exposure(s): Studies must report information on risk indicators associated with partial/ permanent bilateral or unilateral HL. We included specific risk indicators such as cytomegalovirus, toxoplasmosis, neonatal intensive care, ototoxic medications, and family history of HL. Risk indicators related to temporary HL were excluded.

Comparator/control(s): For studies that include a comparison group, the comparators were either 1) healthy subjects or 2) no risk indicators or 3) a comparison between one risk indicator and other indicators (s). Due to the nature of the studies required in these trials, most of the studies were not included as a comparison group.

Primary outcome(s): Screening and subsequent diagnostic audiological assessment and surveillance were carried out in the hospital, community health and clinical settings. The primary

outcomes of the present study were permanent bilateral or unilateral HL. We categorized the outcomes according to the onset of HL. Congenital and early onset was defined as HL present at birth or diagnosed within the first 28 days of life. Late-onset was defined as the occurrence of HL, typically after 28 days of age, after a normal hearing confirmation or screen of normal hearing through audiological assessment. These definitions were allowed for known variations in the classification of onset of hearing the loss in the literature. We excluded trials which include only temporary HL.

Secondary outcome(s): The secondary outcomes were progressive of HL (permanent bilateral or unilateral). Any degree of progressive HL as defined by the study included. All other inclusion criteria detailed under the primary outcome will apply.

Data extraction and quality assessment: Titles and abstracts were assessed by three independent reviewers for potential relevance; the reviewers resolved the conflict (e.g., "yes" or "maybe" and selected "no") and involved a third reviewer. Prior to the title and abstract screening, a screening form were developed based on the inclusion and exclusion criteria and tested among reviewers with a subset of peer-reviewed articles. Two independent reviewers were screened all potentially relevant full-text articles (all articles tagged as "yes" or "maybe" during the previous stage). Disagreements resolved by consensus or a third member of the research team. Using study-specific data forms, pre-determined data were extracted for each study. Data extract included: 1) study characteristics, 2) study design, 3) population characteristics, 4) details of control or comparison groups (if available), 5) risk indicators, 6) onset of HL, 7) progressive loss, 8) outcome data and 9) Study year. One researcher will extract all information, which verified by a second reviewer. Findings resolved through consensus or a third reviewer. In case of information or data were missing or incomplete.

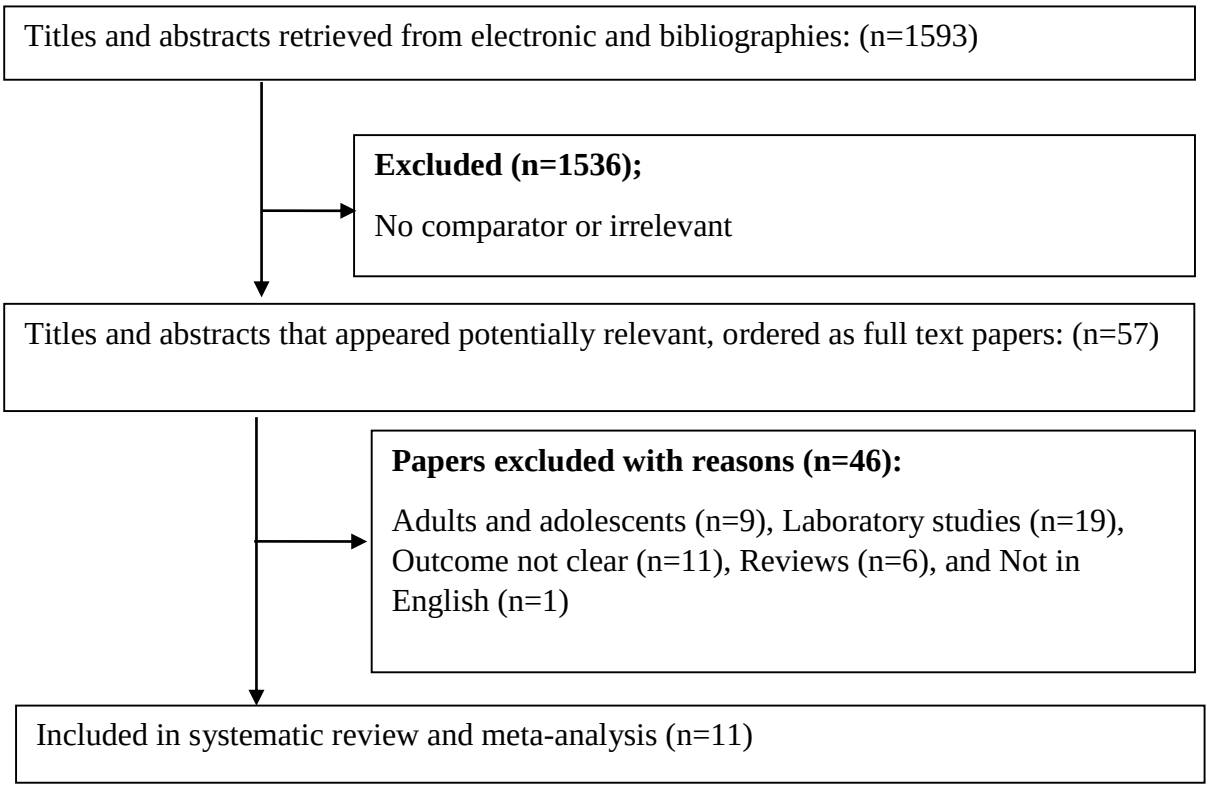
All processes ensured that bias minimized while deciding whether to include or exclude certain studies based on the application of objectives, inclusion/exclusion criteria, independent reviewers, and conflicts resolved through a third reviewer. A PRISMA-P flow chart presented the number of studies included/excluded in each stage of the selection process. Main reasons for exclusion during the full-text screening stage documented.

The risk of bias assessed using PRISMA guidelines by one reviewer and verified by second. Information collected from each included studies on selection bias, study design, confounders, blinding, data collection methods, withdrawals and dropouts, intervention integrity, and analysis. Disagreements in assessments resolved through discussion by involving a third reviewer. Study characteristics summarized in tables. We presented study outcomes in qualitative/quantitative

format in a series of summary of findings tables, organized by types of data. The neonatal, under one year, and under five year data pooled by using meta-analysis techniques.

Statistical Analysis: The outcome of the present study estimated in terms of an effect size, which is the variation between the cases and the control groups, referred to as the odds ratio (OR)/relative risk (RR) and calculated for the included trials. Once an effect size estimated for each trial, the overall effects of these results were assessed by the Q statistic, which measures the extent of inconsistency among trails. The Q test statistic follows the chi-square distribution with k-1 degrees of freedom, k being the number of trails computed under the assumption of homogeneity among the effect sizes. Another strategy for quantifying the heterogeneity in a meta-analysis consists of estimating the variance (i.e. tau square, τ^2) between studies. The overall effects size of these results assessed for sampling error (homogeneous, $\tau^2 = 0$).

Figure 2.1.1: PRISMA flow diagram for included studies



A fixed-effects meta-analysis applied to obtain the pooled effect size with 95 % confidence interval (CI) or else a random-effects meta-analysis would be performed (heterogeneous, $\tau^2 > 0$). The parameter I^2 quantifies the extent of heterogeneity from a collection of effect sizes, which interpreted as approximately the percentage of the total variation in study estimates due to heterogeneity rather than sampling error [34, 35]. The heterogeneity of results represented in the form of a forest plot. Typically, for each study, there was a blob in the middle of the 95 % CI that

represents the single central estimate of the effect size found in that study. The pooled or combined result of the effect sizes were represented by a diamond with a width of 95 % CI for the pooled data. A vertical line indicates no effect line and also differentiates between the studies which favour the intervention and comparator. The forest plot also described the chi-square test (Q-test statistic), τ^2, d.f., I^2, Z, and P-value. An I^2 value of more than 75 % was considered to indicate significant heterogeneity between the trials. Publication bias assessed by funnel plot and Egger's regression test, which was equivalent to a weighted, linear, ordinary least squares regression model with standard error as a covariate. If heterogeneity exists, a meta-regression model used to identify the heterogeneity by relating study characteristics. After identifying the confounders, a covariate meta-analysis performed to estimate the net pooled effect size [30-36]. Statistical analyses performed with Review Manager (RevMan) software version 5.3, IBM SPSS version 24, STATA 14, and Comprehensive Meta-Analysis (CMA) software.

Subgroup analysis: The results organized in tables according to the individual risk indicators. Other classifications to consider were the type of hearing and specific age, data extraction, and quality assessment.

Results

The reduction of child mortality and morbidity in a global priority. Hearing disabilities among infants and children are highly associated with increased mortality and co-morbid conditions which not only have a considerable repercussion on lifelong disability but also affects the QoL of these children.

Figure 2.1.2: Forest plot for hearing screening test for under five year children

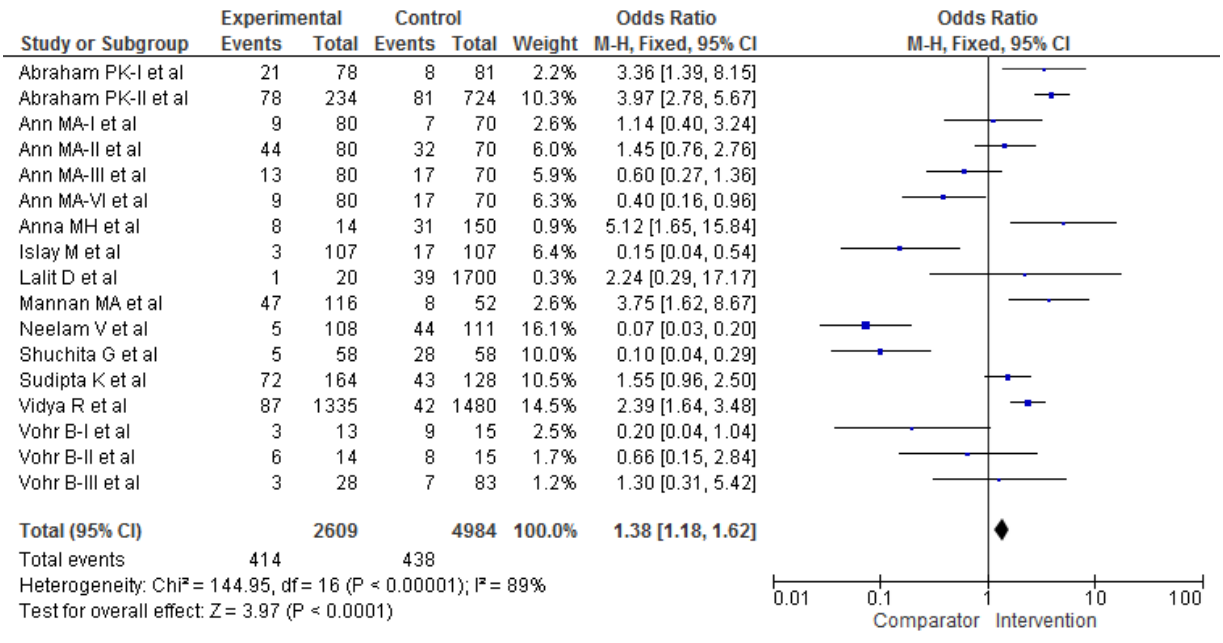
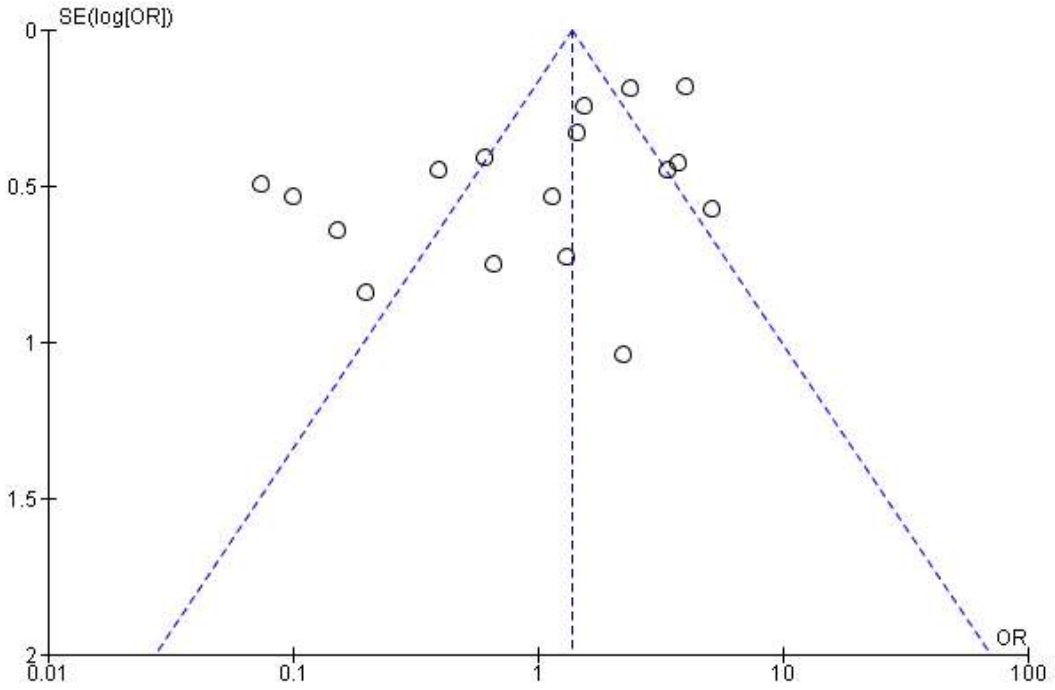


Figure 2.1.3: Funnel plot for hearing screening test for under five year children



A total of 1593 articles were identified, of which 1536 were excluded because they were no comparator or their interventions were not relevant to the purpose of the current analysis. Fifty-seven potentially relevant articles were selected for full text evaluation, out of which eleven relevant articles were submitted to meta-analysis after employing the inclusion and exclusion criteria (Fig. 1). All eleven studies evaluated the effect of various levels of screening evaluations. Three studies of multiple interventions with multiple levels of screening among the children. Of these four included studies, each one had more than one trial. The trials were either based on different levels of intervention.

The meta-analysis results indicated that the hearing screening was significantly higher in the intervention group than in the control/comparator group (n 7593; OR 1.63, 95% CI 1.18, 1.62; $p<0.00001$), as depicted on the forest plot (Fig. 2). There was significant heterogeneity for the outcome evaluation reported among the included trials. All statistical tests of heterogeneity such as the Q statistic (chi-square=144.95, df =16), which was more than df; Tau-square greater than zero ($\tau^2 >0$); and I^2 greater than 50% (I^2=89 %) were higher than the expected value, indicating heterogeneity among the studies.

Meta-regression analysis was performed to detect the source of heterogeneity and indicated that the age group(s) was positively related to the effect size (regression coefficient 0.638, 95% CI 0.005, 0.731; $p<0.05$). The significant differences in the extent of improvement in screening levels as

reported in the forest plot (Fig. 2) are perhaps due to different time periods of the conducting on various age groups to the under five children. Publication bias: The funnel plot (Fig. 3) was symmetrical, indicating the probable presence of publication bias which was confirmed using Egger's weighted regression method (Egger test, $p<0.0276$).

There was strong evidence indicating towards potential benefits of early screening diagnosis on expressive language development, reduction in intellectual disability and overall cognitive development among children as a result of universal hearing screening [327, 28]. It's documented those children who have been screened early or at birth as compared to the children with no or late screening have recorded better language acquisition and cognitive improvement. Studies point out that the systematic approach for hearing screening among new-borns not only helps in timely identification but also in intervention for infants and children with permanent unilateral and bilateral HL [30-34]. Earlier reviews were centred around effectiveness, and effects of interventions on hearing screening. However, gaps have been identified in terms of availability of literature on validation of diagnostic accuracy of the available screening tests, and various risk factors associated with hearing impairment [3]. However, there is a paucity of information on high-quality evidence on new-born hearing screening in South Asian Region [35- 36].

Studies also showed that there is limited predictive value for the risk factors associated with the sensorineural HL [6]. Regarding the accuracy of hearing screening, it is evident that the auditory brainstem response has 100% sensitivities and 97.2% specificities; whereas the Otoacoustic emissions have 50% sensitivities and 49.1% specificities [30]. Previous studies showed that increasing the age at early screening and retests reduces the number of referral cases. Similarly, screenings having higher frequencies had lowered the referral cases. Hence, the use of higher frequencies devices may be useful approaches for better screening among new-borns [33]. The results of this review will be used for implementation of a new-born hearing screening, diagnostic accuracy, and risk indicators for HL among under-five children in South Asian Region. The evidence will be helpful for strategic directions for improved hearing screening and reduction of hearing disability among under-five children.

2.1.2. The economic impact of hearing the loss in children aged under five in the South Asian region: A systematic review Protocol

Research Question

To summarize available data on all relevant costs associated with hearing impairment among children under five in the South Asian region (particularly India).

Methods

Literature search: The searches were designed and conducted using e-librarian (EBSCO host) using methods designed to optimize the term selection. The steps in this process were conducted according to the PRISMA-P (Preferred Reporting Items for Systematic reviews and Meta-Analysis Protocols) guidelines for meta-analysis. The following databases were searched: NHSEED, MIDIRS, SIGLE, MEDLINE, Embase, The Cochrane Library, PubMed, and ProQuest databases. In addition: Teacher Reference Center (TRC) provides indexing and abstracts for 280 periodicals. The e-Book Clinical Collection, GreenFILE offers well-researched information covering all aspects of human impact to the environment. Library, Information Science & Technology Abstracts (LISTA) indexes more than 560 core journals, nearly 50 priority journals, and 125 selective journals; plus, books, research reports, and proceedings. Secondary references were searched from inception on October 2018 and also reviews and the reference lists of the articles, using the keyword 'hearing impairment' paired with 'HL' or 'hearing screening' or 'diagnostic tests' or 'hearing examination', 'cost' and 'children'. This systematic review protocol title has been registered with the International Prospective Register of Systematic Reviews (PROSPERO) database (registration number: CRD42019120304).

Selection criteria: The search will be performed regardless of language and publication status. We will include the following study designs: randomized controlled trials (RCTs), quasi-experimental studies, non-randomized comparative studies (case-control, prospective, or retrospective cohort), non-randomized studies without comparison group (e.g., prospective or retrospective cohort, cross-sectional), and pre-post studies. Neonates and under-five children with partial/permanent bilateral or unilateral HL were included. Studies on the animal, rodents and etc., Case reports/case studies, editorials, viewpoints/opinion, conference abstracts, and rapid/scoping review research will be excluded from this review. Countries outside of South Asia will be excluded.

Intervention/exposure(s): This review is looking at the economic impact of hearing the loss in children aged under five in the South Asian region. Studies must report available cost data on various devices and procedures used for detection of risk indicators (present at birth or later)

associated with partial/permanent bilateral or unilateral HL. Examples of specific risk indicators are cytomegalovirus, toxoplasmosis, neonatal intensive care, ototoxic medications, and family history of HL. Risk indicators related to temporary HL will be excluded.

Comparator/control(s): For studies that include a comparison group, the comparison will be either: 1) Healthy subjects; 2) Subjects with no risk indicators; 3) Comparisons between one risk indicator and another.

Primary outcome(s): The health system costs of the implementation of neonatal hearing screening devices along with OOPE attributed to households for the screening of hearing impairment (including both direct as well as indirect expenditure). OOPE includes payments made by individuals or households to the healthcare providers for availing health care facilities.

Secondary outcome(s): The cost-effectiveness of hearing treatments when the benefits were measured with quality-adjusted life-years (QALY) gained.

Data extraction and quality assessment: The titles and abstracts or the references retrieved during the searches will be assessed by three independent reviewers for potential relevance and marked as "yes", "no", or "maybe" for further assessment. Any conflicts between the reviewers over article selection will be resolved through discussion and will involve a third reviewer if required. Prior to the title and abstract screening, a screening form will be developed based on the inclusion and exclusion criteria and will be tested among reviewers with a subset of peer-reviewed articles. Two independent reviewers will then screen all potentially relevant full-text articles (all articles tagged as "yes" or "maybe" during the previous stage). Disagreements will again be resolved by consensus, or consultation with a third member of the research team. Using study-specific data forms, pre-determined data will then be extracted from each study selected for inclusion. The data to be extracted will include: 1) study characteristics, 2) study design, 3) population characteristics, 4) details of control or comparison groups (if available), 5) results, 6) onset of HL, 7) progressive loss, 8) outcome data and 9) study year (Athe et al., 2014).

All processes will ensure that bias is minimized when deciding whether to include or exclude certain studies, based on the application of objective inclusion/exclusion criteria, independent reviewers, and conflicts resolved through a third reviewer. A PRISMA-P flow chart will present the number of studies included/excluded in each stage of the selection process. Main reasons for exclusion during the full-text screening stage will be documented (Athe et al., 2015).

The risk of bias assessment will be conducted by one researcher and verified by a second by using PRISMA-P guidelines. The cost assessment will be conducted by one researcher and verified by a

second. Selection bias, study design, confounders, blinding, data collection methods, withdrawals and dropouts, intervention integrity, and analysis. Disagreements in assessments will be resolved through discussion or by involving a third researcher if required. We anticipate that the results will be organized in tables according to individual health expenditure. Other classifications to be considered are the type of cost on the treatment of hearing impairment and specific age.

Statistical Analysis: The estimate may break down by country and by age groups; including children aged less than five years, and took account of differences in the severity of HL. Cost strategies should address prevention, screening and early intervention of HL. Country-specific data on the cost of unaddressed HL and cost-effectiveness of interventions should be gathered to strengthen available evidence (Athe et al., 2015).

The outcome is estimated in terms of an effect size, which is the variation between the cases and the control groups and is calculated for the included trials. Once an effect size is estimated for each trial, the overall effect of these results is assessed by the Q statistic, which measures the extent of inconsistency among trails. The Q test is computed under the assumption of homogeneity among the effect sizes and the statistic follows the chi-square distribution with k-1 degrees of freedom, k is the number of trails. Another strategy for quantifying the heterogeneity in a meta-analysis consists of estimating the variance (i.e. tau square, τ^2) between studies. The overall effects size of these results is assessed for sampling error (homogeneous, $\tau^2 = 0$). A fixed-effects meta-analysis is applied to obtain the pooled effect size with 95 % confidence interval or else a random-effects meta-analysis is conducted (heterogeneous, $\tau^2 > 0$). The parameter I^2 quantifies the extent of heterogeneity from a collection of effect sizes, which is interpreted as approximately the percentage of the total variation in study estimates due to heterogeneity rather than sampling error (Athe et al., 2015).

The heterogeneity of results is representing in the form of a forest plot. Typically, for each study, there is a blob in the middle of the 95 % confidence interval that represents the single central estimate of the effect size found in that study. The pooled or combined result of the effect sizes is represented by a diamond, the width of which is the 95 % confidence interval for the pooled data. A vertical line is displayed to indicate no effect and to differentiate between the studies that favor the case and control group. The forest plot also describes the chi-square test (Q-test statistic), τ^2, d.f., I^2, Z, and p-value. An I^2 value of more than 50 % is considered to indicate significant heterogeneity between the trials (Athe et al., 2014).

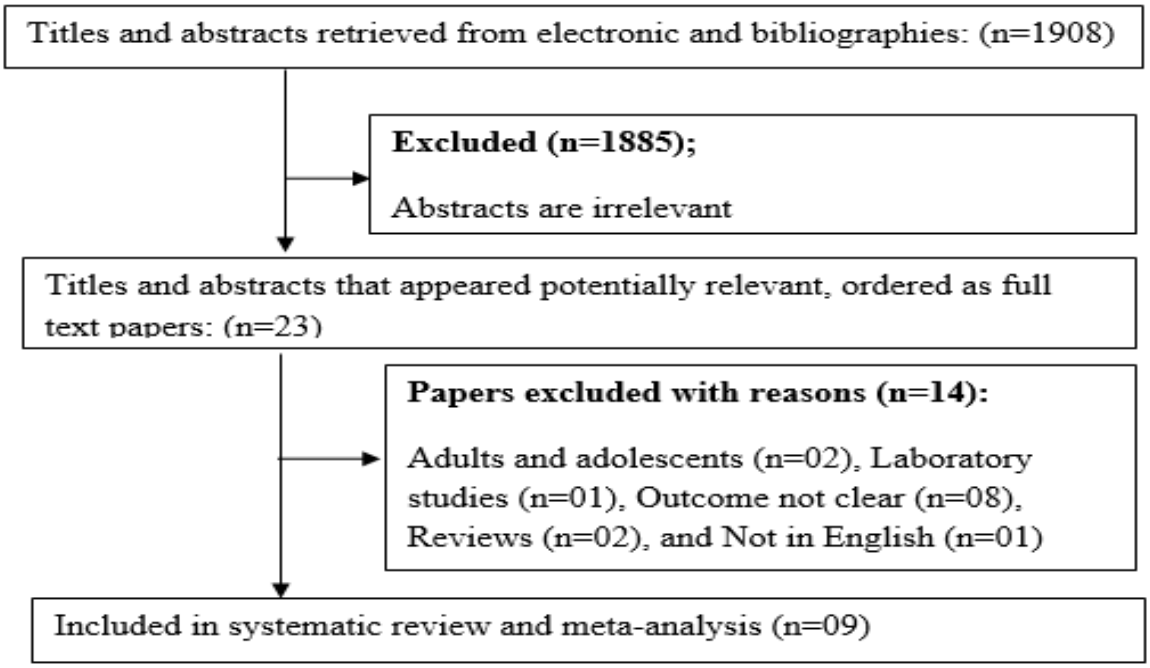
Publication bias is performed with the funnel plot and Egger's regression test. This is equivalent to a weighted, linear, ordinary least squares regression model with standard error as a covariate. If

heterogeneity existed (I^2 >50 %), a meta-regression approach is used to test the study heterogeneity by relating study characteristics. The confounders were identified and a covariate meta-analysis is performed to estimate the net pooled effect size, after removing the effect of covariates/confounders/moderators. Statistical analyses were performed with Review Manager (RevMan) software version 5.1, IBM SPSS version 24, STATA 14, and Comprehensive Meta-Analysis (CMA) software.

Analysis of subgroups or subsets: We anticipate that results may be organized in tables according to referral cost, QALY, and OOPE based on the levels of HL. Other classifications to be considered are the type of hearing and specific age data extraction and quality assessment.

Results

Figure 2.1.4: PRISMA flow diagram for included studies



Around 360 million people are living with hearing impairment worldwide (Graydon et al. 2019; WHO 2017). According to the World Health Organisation (WHO) 32 million children are living with hearing impairment; and most of them are from Asia and Africa (WHO 2017; Colgan et al. 2012). It is a common condition that occurs among the newborn, about 0.5 to 5% suffering HL (WHO 2017; Hjalte et al. 2012). In low-income countries, it occurs largely due to higher rates of infection, poor preventative measures, and inadequate healthcare services (Störbeck 2012). Hearing impairment has significant consequences among children including mental and physical wellbeing, and educational as well as employment opportunities (Graydon et al. 2019). Hearing

impairment influence the social welfare system and wellbeing along with the medical care system (Hjalte et al. 2012). The consequences of HL among children directly associated with the out-of-pocket expenditure of households, health system cost and quality of life of individuals. The economic costs include healthcare, educational support, loss of productivity, and social costs in relation to the stigma due to HL and poor quality of life (WHO 2017; Chiou et al. 2017; Looi et al 2016; Baltussen et al. 2009; Feher-Prout et al. 1996).

The indirect costs account for the major part of the total costs of hearing disorders. The largest cost of HL is linked with loss of wellbeing (Grosse and Ross 2006; Kemper and Downs 2000). The loss of productivity contributes significantly to the global financial burden (WHO 2017). The indirect costs include lost working hours and changes in the fields of education and income. Lost working hours were calculated as – four hours per visit and average income were calculated based on the nature of work and sex of the individual. Three working days of leave were considered at the time of the intervention. The cost beyond the health system is the educational expenditure of hearing disorders children (WHO 2017; Boss et al. 2011). Moreover, the changes in the costs of education are based on differences in educational placements before and after receiving the implant (Cheng et al 2000). There is little information on the social cost of HL (Hjalte et al. 2012; Feher-Prout et al. 1996). Hence, this review will intend to explore the societal costs for all degrees of hearing disorders.

Globally, HL is estimated to cost 750 billion dollars per year (WHO 2017). The financial components incurred by the society include medical expenses (medical appointments, hearing aids and accessories) and non-medical costs (special education and rehabilitation) (Mohr et al. 2000; Huang et al. 2012, Vlastarakos et al. 2015). A conventional annual loss of productivity has been estimated to be $100 billion; most of these losses are in LIMCs (WHO 2017; Baltussen et al. 2009; Olusanya and Akinyemi 2009). A study in Australia showed that in HL the total financial costs of $15.9 billion per year – $648 per head of population (Foteff et al. 2016; Austirial 2017); and their little information for LMICs. The lifetime cost for a HL individual will be reduced if the HL will be diagnosed during childhood (Mohr et al. 2000); which compel to generate robust evidence.

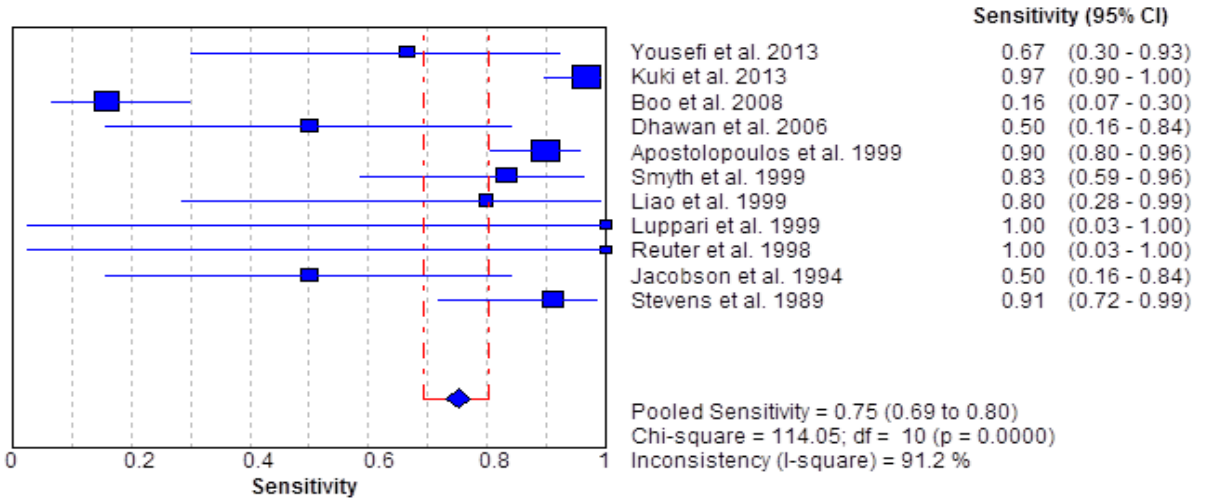
The largest economic cost is related to lost work productivity – 67% of the total loss (Mohr et al. 2000; Kotby et al. 2008) because of poor quality of life (Tafforeau and Demarest 2001). The major adverse impact of hearing impairment during childhood is poor cognitive development, which worsts the quality of life (Wroblewska-Seniuk et al. 2017). Furthermore, among adults it unemployed, delay in the job seeking, and require extra support due to stresses related to their hearing impairment (Looi et al 2016). The above factors significantly reduced the earnings over

their lifetime in comparison with a non-hearing-impaired population (Garg et al. 2012; Olusanya 2009). The diagnosis and treatment of HL cause huge financial distress to the households and poor quality of life among the affected children and it also increases the societal costs (Wroblewska-Seniuk et al. 2017). However, there is little information on the economic impact of HL among children in the South Asian region, where the burden is high. The country-specific information is crucial for the development and implementation of a context-specific intervention for universal coverage of hearing screening among children.

2.1.3. Diagnostic validation of OAE screening device

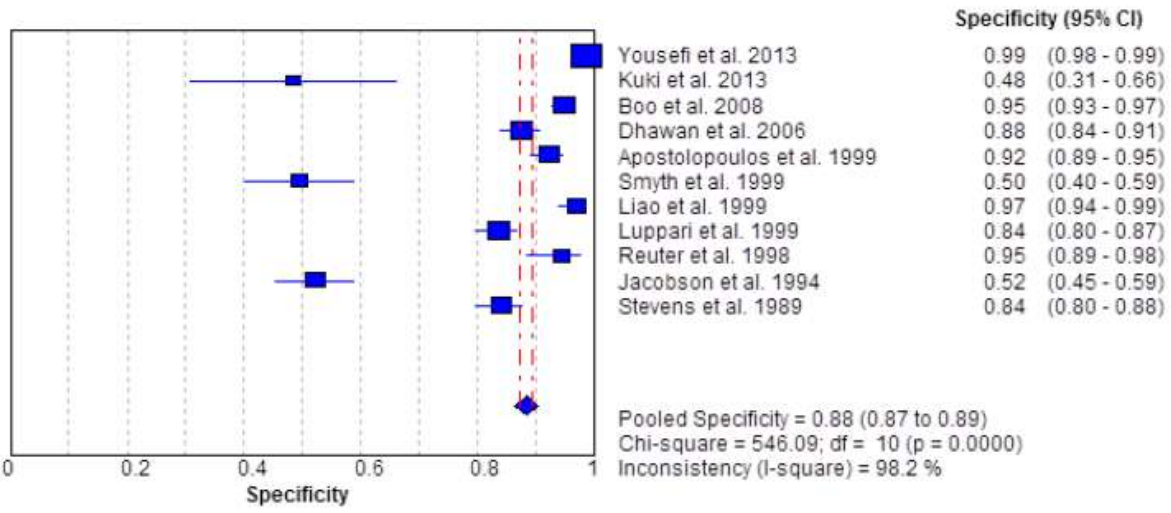
A systematic review and meta-analysis study showed the sensitivity and specificity of the OAE. The pooled sensitivity of OAE was estimated at 0.75 and the pooled specificity of OAE device was 0.88 (Heidari et al. 2015).

Figure 2.1.5: Pooled sensitivity of OAE vs ABR as the gold standard (Heidari et al. 2015).



The sensitivity of the OAE was compared to that of the ABR (as the gold standard) using the Mantel-Haenszel method in a sample of 3914 newborns with and without risk factors. Based on the meta-analysis, the pooled sensitivity of the OAE device was estimated at 0.75 (95% CI: 0.694 to 0.804; figure 2.1.5).

Figure 2.1.6: Pooled specificity of OAE vs ABR as the gold standard (Heidari et al. 2015).



The specificity of the OAE was compared to that of the ABR (as the gold standard) using the Mantel-Haenszel method in a sample of 3914 newborns with and without risk factors. Based on the meta-analysis, the pooled specificity of the OAE device was estimated at 0.88 (95% CI: 0.873 to 0.894; figure 2.1.6). From the pooled sensitivity and specificity values positive predicted value (PPV) and negative predicted value (NPV) of OAE screening device was calculated with the prevalence of 5 per 1000 hearing impairment using following formula:

2.1.4. Utility values for HL

Figure 2.1.7: Utility values assigned for HL vs NHL (Abrams et al. 2005)

Level	Description	Utility Value
1	Able to hear what is said in a group conversation with at least three other people, without a hearing aid	1.0
2	Able to hear what is said in a conversation with one other person in a quiet room without a hearing aid, but requires a hearing aid to hear what is said in a group conversation with at least three other people.	.95
3	Able to hear what is said in a conversation with one other person in a quiet room with a hearing aid, and able to hear what is said in a group conversation with at least three other people, with a hearing aid.	.89
4	Able to hear what is said in a conversation with one other person in a quiet room, without a hearing aid, but unable to hear what is said in a group conversation with at least three other people even with a hearing aid.	.80
5	Able to hear what is said in a conversation with one other person in a quiet room with a hearing aid, but unable to hear what is said in a group conversation with at least three other people even with a hearing aid.	.74
6	Unable to hear at all.	.61

*Adapted from the Multi-Attribute Health Status Classification System: Health Utilities Index Mark 3 (HUI3) (http://www.fhs.mcmaster.ca/hug/).

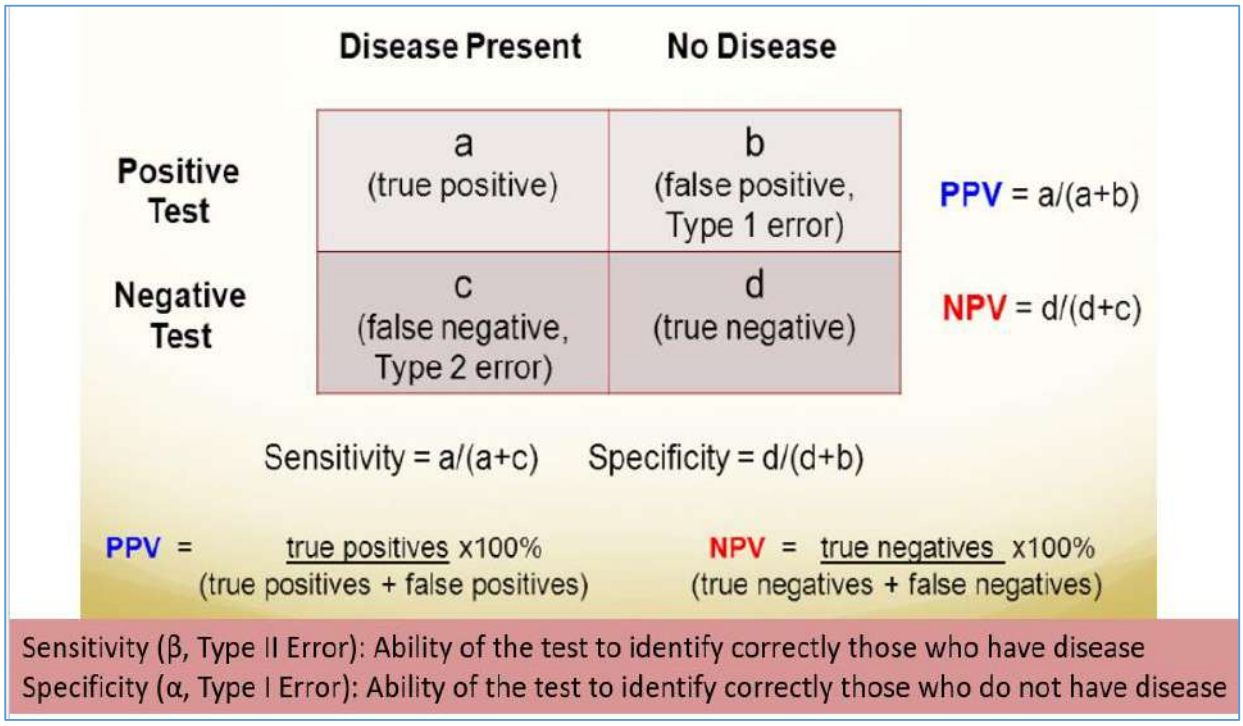
2.2. Primary Data Collection

2.2.1. Diagnostic Validation of 'Portable Automated ABR' Hearing Screening Device

Objective: To determine the efficacy of 'Portable Automated ABR' hearing screening devices against the gold standard (BERA).

Methods: A prospective clinical validation study was carried out at Maulana Azad Medical College, Delhi among the relatively at risk neonates (weight <2kg / admitted in NICU for >24 hrs/ Needing PT). Even though, BERA is the gold Standard, whenever there is doubt in the results, the test was repeated with same and only taking the BERA that were definitely conclusive / else were repeating the same and then only considering. Hence, even though we have done 600 ears, this data is of lesser ears, as the inconclusive BERA tracings are not included. Same is true for the Portable Automated ABR. Total 367 Ears for Portable Automated ABR, where both the Portable Automated ABR and the BERA were conclusive.

Figure 2.2.1: Diagnostic validation formula



Results: In this study, it was found that the sensitivity of 'Portable Automated ABR' was 100% and specificity was 97%. The Positive Predictive Value (PPV) was 52% and Negative Predictive Value (NPV) was 100% (fig 2.2.2). The sensitivity of OAE was 69% and specificity was 68%. The Positive Predictive Value (PPV) was 7% and Negative Predictive Value (NPV) was 98% (fig 2.2.3).

Figure 2.2.2: Diagnostic validation of 'Portable Automated ABR' hearing device with gold standard ABR (BERA)

		BERA Test Result (n=367)		
		Positive (+)	**Negative (-)**	
Portable Automated ABR Screening Result (n=367)	**Refer (+)**	True Positive (TP)=11	False Positive (FP)=10	Positive Predictive Value PPV=TP/(TP+FP) =11/ (11+10) =0.52 =52%
	Pass (-)	False Negative (FN)=0	True Negative (TN)=346	Negative Predictive Value NPV=TN/(TN+FN) =346/ (346+0) =1.00 =100%
		Sensitivity =TP/(TP+FN) =11/(11+0) =1.00 =100%	**Specificity =TN/(FP+TN) =346/(10+346) =0.97 =97%**	

Figure 2.2.3: Diagnostic validation of 'OAE' hearing device with gold standard ABR (BERA)

		BERA Test Result (n=435)		
		Positive (+)	**Negative (-)**	
OAE Screening Result (n=435)	**Refer (+)**	True Positive (TP)=11	False Positive (FP)=135	Positive Predictive Value PPV=TP/(TP+FP) =11/(11+135) =0.07 =7%
	Pass (-)	False Negative (FN)=5	True Negative (TN)=284	Negative Predictive Value NPV=TN/(TN+FN) =284/(284+5) =0.98 =98%
		Sensitivity =TP/(TP+FN) =11/(11+5) =0.69 =69%	**Specificity =TN/(FP+TN) =284/(135+284) =0.68 =68%**	

2.2.2. Health System Cost Data Collection (Screening, Diagnosis and Treatment)

Specific objective: To measure the health system cost of implementation of 'Portable Automated ABR' and OAE neonatal hearing screening devices.

Methods: A cross-sectional study was conducted in six facilities – three coastal and three non-coastal facilities which were randomly selected where OAE devices were implemented at DEIC under RBSK in Odisha. All the health system-related expenditure information on the implementation of OAE was collected using a pre-designed questionnaire. We applied a decision tree model with a time horizon of one year to economically evaluate the 'Portable Automated ABR' and OAE devices for newborn hearing screening. The perspective was health system and societal. The health system cost on the implementation of 'Portable Automated ABR' was also collected. The followings costs were included:

Human Resource: Salaries of the personnel (medical/non-medical) involved in screening.

Medical Equipment/Consumables: These would include the medical equipment used for screening – primarily focusing on the costs associated with the OAE and 'Portable Automated ABR' devices being used in the screening protocol. Consumables included both medical (drugs, reagents, etc.) and non-medical (stationary, etc.) consumables being used, and data regarding their number and price collected.

Non Consumables: These include materials like furniture and technical equipment like computers at the screening centres.

Maintenance: Maintenance costs were listed as a percentage of annual costs.

Utilities: The amounts of utility items allocated to the program which includes electricity, and water.

Results:

In this study, the cost of the new-born's screening and the cost of definite diagnosis of new-born's hearing ability were calculated based on the sources of cost used in hearing screening and definite diagnosis in government facilities, and not based on the costs in private clinics. To determine the costs, the sources of costs were identified first, and then the amount of each source was quantified and evaluated. Both direct as well as indirect costs were considered to identify the sources.

The unit cost was determined in two steps: In the first step, the unit cost of each of the devices was outlined for screening; and in the second step, the unit cost of the gold standard was outlined. In these two steps, first we have collected information on the direct cost to the health care system

which include employees' salaries and wages, human resources training, consumables (both medical and non-medical), overhead costs, and treatment costs.

Through contacting six districts i.e. three costal and three non-coastal districts of the state of Odisha along with the Government of Odisha RBSK head office, we have obtained information about OAE and BERA device's cost, lifespan, and salvage value across the country. For Portable Automated ABR, the manufacturers have been contacted for the detailed information on various cost heads.

Table 2.2.1: Human resources cost for implementation of OAE, Portable Automated ABR and BERA

Human Resource								Annual cost		
Screening and diagnosis	Monthly Salary	Number of working days (Monthly)	Time spend exclusively for screening (in hour per day)	Time on screening in hours (Monthly)	overall working hours (Yearly)	Apportioning statistic	Cost to system (Monthly)	OAE	Portable Automated ABR	BERA
Staff nurse	15000	22	8	176	2080	1	15000	180000	180000	180000
Technician	18000	22	8	176	2080	1	18000	216000	216000	216000
Audiologist	50000	22	8	176	2080	1	50000	0	0	600000
Paediatrician or Anaesthesiologist	90000	22	2	44	2080	0.25	22500	0	0	270000
Post Service training per person (staff nurse, technician and audiologist)								25000	25000	25000
Total (Screening and diagnosis cost)								**421000**	**421000**	**1291000**

Table 2.2.1 indicates the human resources cost for implementation of OAE, Portable Automated ABR and BERA which indicates that the OAE and portable Automated ABR cost around INR 421000, and BERA cost around INR 1291000 for Manpower. Further in table 2.2.2, we have shown medical non-consumables and consumables cost for implementation of OAE (per child). Table 2.2.3 indicates the annual non-consumables and consumables (medical and non-medical) cost for implementation of OAE.

Table 2.2.2: Medical non-consumables and consumables cost for implementation of OAE (per child)

Cost associated with OAE					
Items	**Cost (INR)**	**Description**	**Per unit**	**Per baby**	**Per 1000 babies**
OAE Device cost	260000				
Annual maintenance cost for device	26000				
OAE Probe	72000	life would be 1-1.5			
Disposable ear trips	15		15	15	15000
Total cost of testing with disposable probe			**15**	**15**	**15000**

Table 2.2.3: Annual non-consumables and consumables (medical and non-medical) cost for implementation of OAE

Heads	Expected Life	Units	Unit Price	Total cost	Discount factor (DF)	Annual maintenance rate (AMR)	Annualization Factor (F)	EUAC Capital	Annual Maintenance cost(AMC)	Present worth maintenance	Total annual cost
Medical (Device cost)											
OAE	**6**	**1**	**320000**		0.03	0.05	0.1846	59071.20	16000	13399.75	***72470.95***
Total (A)											***72470.95***
Non-medical											
not applicable											
Consumables											
Medical											
Disposable ear trips and others	One time	**1**	**15**		**single use for per baby**						**140400**
Total (B)											140400
Non-medical											
not applicable											
Total (A+B)											212871

Table 2.2.4, we have shown medical non-consumables and consumables cost for implementation of Portable Automated ABR (per child). Table 2.2.5 indicates the annual non-consumables and consumables (medical and non-medical) cost for implementation of Portable Automated ABR. Table 2.2.6 shows the annual non-consumables and consumables (medical and non-medical) cost for implementation of BERA.

Table 2.2.4: Total medical non-consumables and consumables cost for implementation of Portable Automated ABR

Cost associated with Portable Automated ABR					
Items	**Cost (INR)**	**Description**	**Per unit**	**Per baby**	**Per 1000 babies**
Portable Automated ABR Device	330000	per unit		na	na
Annual maintenance cost for device	9000	per device		na	na
one ear tip	5	used for 20 after cleaning	0.25	0.25	250
Total cost for testing with non-disposable electrodes				9	9017
Disposable electrode	5	3 for 1 baby	15	15	15000
Disposable electrode lead	3600	set of 3	1	1	1000
one ear tip	5	can be used for 20 after cleaning	0.25	0.25	250
Earphones	1	15000	0.5	0.5	500
Total cost for testing with disposable electrodes				**16.75**	**16750**

Table 2.2.5: Annual non-consumables and consumables (medical and non-medical) cost for implementation of Portable Automated ABR

	Non-consumables										
	Expected Life	**Units**	**Unit Price**	**Total cost**	**Discount factor(DF)**	**Annual maintenance rate (AMR)**	**Annualization Factor (F)**	**EUAC Capital**	**Annual Maintenance cost(AMC)**	**Present worth maintenance**	**Total annual cost**
						Medical (Device cost)					
Portable Automated ABR	**6**	**1**	**330000**		0.03	0.05	0.1846	60917.18	16500	13818.49	***74735.67***
Total (A)											74736
						Non-medical					
						not applicable					
						Consumables					
						Medical					
Disposable electrode, lead, ear trips	**One time**	**1**	**16.75**			**single use for per baby**					**104520**
Total (B)											104520
						Non-medical					
						not applicable					
Total (A+B)											179256

Table 2.2.6: Annual non-consumables and consumables (medical and non-medical) cost for implementation of BERA

Non-consumables											
	Expected Life	Units	Unit Price	Total cost	Discount factor(DF)	Annual maintenance rate (AMR)	Annualization Factor (F)	EUAC Capital	Annual Maintenance cost(AMC)	Present worth maintenance	Total annual cost
Medical (Device cost)											
BERA (A)	**6**	**1**	**826184**		0.03	0.05	0.1846	152511.50	41309.2	34595.80	***187107.31***
Non-medical											
Computer	5	1	20000	20000	0.03	0.05	0.218	4367.09	1000	862.61	5229.70
Air conditioner	10	2	36000	72000	0.03	0.05	0.117	8440.60	3600	2678.74	11119.33
Printer	5	3	3000	9000	0.03	0.05	0.218	1965.19	450	388.17	2353.37
Table	5	2	9000	18000	0.03	0.05	0.218	3930.38	900	776.35	4706.73
Chair	5	3	3000	9000	0.03	0.05	0.218	1965.19	450	388.17	2353.37
Stool	5	2	1000	2000	0.03	0.05	0.218	436.71	100	86.26	522.97
Bed	5	1	8000	8000	0.03	0.05	0.218	1746.84	400	345.04	2091.88
Almirah	7	1	10000	10000	0.03	0.05	0.161	1605.06	500	406.55	2011.61
Tube lights and others	2	2	2000	4000	0.03	0.05	0.523	2090.44	200	188.52	2278.96
Soundproof room	5	**1**	**408000**	408000	0.03	0.05	0.2184	89088.67	20400	17597.22	106685.88
Total (B)											**139353.80**
Total (A+B)											**326461.11**
Consumables Medical											
Testing and general supplies (Cotton, gel, conductive and cleaning, sanitizers etc.)											11440
If disposable electrodes use											18720
Sedatives(Triclofos)											156000
Total (C)											**186160**
Non-medical											
Including ink and paper and other stationary items											4000
Total (D)											**4000**
Total (C+D)											**190160**
Grand Total (A+B+C+D)											**516621.11**

Table 2.2.7 indicates the human resources cost for treatment of hearing impairment while table 2.2.8 indicates the procedural cost for the treatment of hearing screening.

Table 2.2.7: Human resources cost for treatment of hearing impairment

Treatment and rehabilitation								
	Human resource							
HR	Monthly Salary	Number of working days (Monthly)	Time spend exclusively for screening(in hour per day)	Time on screening in hours(Monthly)	overall working hours (in a year)	Apportioning statistic	Monthly cost to system	Treatment cost (for only positive cases)
ENT Specialist	90000	22	2	44	2080	0.25	22500	**270000**
Counsellor	18000	22	8	176	2080	1	18000	**216000**
Therapist	32000	22	3	66	2080	0.375	12000	**144000**
Total (A)								**630000**

Table 2.2.8: Procedural cost for treatment of hearing impairment

Procedural cost (Per Child)											
	Cost	Expected Life	Units	Unit Price	Discount factor(DF)	Annual maintenance rate (AMR)	Annualization Factor (F)	EUAC Capital	Annual Maintenance cost(AMC)	Present worth maintenance	Total cost (Yearly)
Hearing Aid	**20000**	5	1	As mentioned	0.03	0.05	0.22	4367	1000	863	5230
Cochlea Implant	**550000**	Life time	1	As mentioned	0.03	0.05	0.03	18967	27500	3577	22545
Therapy cost (Lump sum)	**50000**	1		0	0	0	0	0	0	0	50000
Total (PC) (B)											**77774**
Total (A+B)											**707774**

2.2.3. Out-of-pocket expenditures

Objective: To measure the out-of-pocket expenditures on neonatal hearing screening using 'Portable Automated ABR' and OAE devices.

Methods: A cross-sectional study was conducted among the caretakers (parent) of sick infants to estimate their direct and indirect cost and QoL when they seek care at a different level of healthcare facilities such as tertiary, secondary, and primary. This study conducted at two districts i.e. Khurda and Koraput of Odisha.

Sample size: The sample size was calculated as per the given criteria using Open Epi software. The population size for finite population correction factor of 1000000, hypothesized % frequency of outcome factor in the population 10% (expected 10% only had OOP as infant healthcare service is free under JSSK Scheme), power 80%, Confidence limits 95% and design effect for cluster surveys is 5. The required sample size was 692.

Sampling: About 180 samples were collected from each level of healthcare facilities. The facilities were selected using stratified random sampling methods. Three Medical College Hospitals (n=180, 60 samples from each facility), four District Hospital/Sub-division Hospitals (n=180, 45 samples from each facility), Twelve Community Health Centres (n=180, 15 samples from each facility), and the Primary Health Centre under the selected Community Health Centres (n=180).

Study variables: Patient costs refer to all costs at the point of service delivery such as inpatient and outpatient visits; bed days, laboratory tests (if any), user fees for the screening, travel costs, costs for food and lodging. Here we have included cost under two heads i.e. direct and indirect costs. Direct cost includes doctor's/surgeon's fee, hospital staff/other specialists, medicines, diagnostic tests, bed charges, other medical expenses (attendant charges, physiotherapy, personal medical appliances, blood, and oxygen). On the other hand, indirect cost includes cost on transport for patient, other non-medical expenses incurred by the household such as food, transport for others, expenditure on escort, lodging charges if any, person-times, productivity losses and loss of wages. The approach to measure OOPE for healthcare payments has been adopted from the World Bank document. Therefore, the outcome variable in the study is OOPE for the hearing screening among the infants in India. The focus is to get direct costs being paid in terms of OOPE by the family members for the treatment of the infant. Along with OOPE the socio-demographic profile of the participants was collected. The parents of the infants were interviewed regarding the expenses they incurred for getting their child screened.

Results:

The information on patient perspective in terms of OOPE were collected. As majority of the things are covered under the JSSK and RBSK program, and provided by other government funded schemes for the maternal and child healthcare, it was mentioned that there was zero OOPE for the patients. However, as patients have to travel sometimes in case of emergency, so until they are referred through proper channel it may cost them some travel cost along with wage loss in case of absence from work or lesser working hours. We have taken into consideration the wage loss as indirectly the measure of OOPE (Table 2.2.9).

Table 2.2.9: Out-of-Pocket Expenditure for hearing screening at various levels of healthcare facilities

Direct cost of parent for test Average transport cost per visit				
Medical college hospital		440.65	Estimated	440.65
District or Sub-divisional Hospital		300.08	Estimated	300.08
Community Health Centre		206.83	Estimated	206.83
Primary Health Centre		99.5	Estimated	99.5
Indirect cost (wage loss of parent for test)				
Medical college hospital		600	Estimated	600
District or Sub-divisional Hospital		300	Estimated	300
Community Health Centre		225	Estimated	225
Primary Health Centre		150	Estimated	150
Centre	**Av. No. of Visits (NH)**	**Av. No. of Visits (HL)**	**Total per facility (NH)**	**Total per facility (HL)**
Medical college hospital	1	3	1481	4444
District or Sub-divisional Hospital	1	3	900	2700
Community Health Centre	1	3	639	1916
Primary Health Centre	1	3	349	1047
Centre	**Av. No. of Visits (R)**			**Total per facility (R)**
Medical college hospital	2			2963
District or Sub-divisional Hospital	2			1800
Community Health Centre	2			1277
Primary Health Centre	2			698
% weightage of pts.	**Weighted Cost per facility (NH)**			**Weighted Cost per facility (HL)**
0.2	296			889
0.2	180			540
0.4	255			766
0.2	70			209
Total OOPE per pt.	***802***			***2405***
% weightage of pts.	**Weighted Cost per facility (R)**			
0.2	593			
0.2	360			
0.4	511			
0.2	140			
Total OOPE per pt.	***1603***			

As the distance of majority of tertiary care facilities was more, followed by the DHH, where the hearing screening facilities were available, it cost significant amount to the parents of the infants. However, as the number of visits for the infants having hearing impairments was more it cost them more as compared to the infants who do not have any hearing deficiency.

2.2.4. Quality of Life

A descriptive system for the Infant health-related Quality of life Instrument (IQI) – measuring health with a mobile app was used for assessment of QoL among infants. Total seven health attributes included in the IQI consisted of sleeping, feeding, breathing, stooling/poo, mood, skin, and interaction. The users' experiences with mobile application were generally positive (White et al., 2010).

Table 2.2.10: Quality of Life among Infants using Infant health-related Quality of life Instrument (IQI)

HL	N=198 n (%)	Mean	S.D	Probability of QoL
Normal Hearing (may have other health problems)	172 (87)	7.39		0.95
HL (Unilateral + Bilateral)	26 (13)	9.08		0.77
Unilateral HL	15 (7.6)	8.27		0.85
Bilateral HL	11 (5.4)	10.18		0.69

Table 2.2.10 shows the mean QoL scores for NHL and with HL. These mean scores were calculated on the basis of our primary data which has been collected from the field. As our QoL tool which was adapted from a recently published research work which was not validated yet, we have only calculated the mean scores along with mean differentials in QoL scores with and without HL. For the calculation purpose, we have adapted the values from Health Utilities Index Mark 3 (HUI3), which has assigned various health states for the attribute of hearing and hearing aid. Figure 2.1.7 is already given for the reference values derived for QoL estimates (Abram's et al. 2005).

2.2.5. Feasibility of 'Portable Automated ABR' Device for Universal Hearing Screening

Objective: To assess the operational feasibility of 'Portable Automated ABR' neonatal hearing screening device at the community level.

Methods: A qualitative observational study was conducted to observe the operational challenge for using 'Portable Automated ABR' hearing screening device in Odisha, India. Total 60 observations were recorded using standard check-list during hearing screening using 'Portable Automated ABR'; twenty at community setting and forty at healthcare facilities. In the case of hospital settings, eight observations were conducted at paediatric, four at gynaecology and four at sick-newborn care unit. A standard observation check-list was developed using 'Portable Automated ABR infant hearing testing protocol' information of diagnosis process – the time is taken in each step, operational and ethical challenge. The observers were from both technical (bachelor degree in audiology and diploma in audiology) and non-technical – medical and non-medical backgrounds with public health experience.

Findings

Device manufacturing issue and recommendation: Although, 'Portable Automated ABR' is one of the hearing screening devices which come with portable features; however, the research team had experienced some issues during screening and handling of the device. In case some devices the battery drained faster than the usual, which can be improved by the manufacturer. Entering of the required information using the existing keypad which is time-consuming, the manufacturer can replace it into a touch pad and stylus. Software problems like device got hanged and automatically come back to the home screen in between the test, which is resulted in increase of testing time and resources. The manufacturer can upgrade the software which can solve this technical glitch.

Operational challenges and recommendation

Motivation and counselling of care-takers: Motivating care-takers or parents is a major challenge. As community members are generally less aware of the importance of hearing screening, many times they were unwilling for hearing screening of their child at first interaction. So it is suggested that there is a huge need for massive awareness program regarding hearing screening both in media and at a community level. With this service provider should be motivated at the individual level so that he/she can motivate parents for the screening of child and should be sensitized about the importance of the development of a child depends on hearing ability.

Testing place: Place of performing test is another challenge experienced by the study team. Although 'Portable Automated ABR' requires a silent environment, as crowd or noisy environment disturbs baby's sleep and ultimately it affects the testing process. The 'Portable Automated ABR' device also requires the baby to be pacified or sleeping as slight movement in any body part interfere with the test result. This might pose as a challenging factor for use of the device in community in mobile health van.

It was observed that during the test, presence of any electronic devices such as mobile charger, computer or other electric appliance etc. affects the testing process. Screening of baby in SNCU is difficult due to the presence of different sources of magnetic and electronic sources. Hence, it is recommended for user to make distance from the above devices during screening or manufacture may modify the design of the device in order to reduce the effect electrical appliances during the test.

Ideal testing time: Generally, newborns sleep a total of about 8 to 9 hours in the daytime and a total of about eight hours at night and each baby have a different sleeping pattern. Though 'Portable Automated ABR' suggests baby should be calm and sleeping during the test, it was challenging for the research team to wait for a baby to sleep and be calm. Many parents said that baby sleep for a shorter period in day time e.g., between 8-12 a.m.

Testing procedure: To start with the screening procedure newborn should be calm and asleep. When preparing baby for screening is a major challenge for our research team, though in most cases baby wakes up when the staffs touched the baby. It is recommended that each service provider should be trained on how to handle a new born baby for ensuring a better result. Sometimes research team struggled to remove the disposal electrode as it is too sticky and it gets a stick on baby's hair if that disposal electrode can be small and less sticky it could be better. The research team found it very difficult to screen the baby for more than 6 months as they are super active and they wake up with a simple touch of someone, they also remove electrode by themselves.

Possible service providers and pre-requisite skill: Preferred service providers are Staff Nurses, AYUSH doctors, and Audiologist for conducting the test. Each service provider should have the basic skill of handling baby, infection control practice and smartphone operating skill.

Training and supportive supervisions: For appropriate screening each service provider should be trained properly with hands-on practice. It is suggested that each team should have at least two members preferably staff nurse. For supervision of service provider, one supportive supervisor should monitor for initial 1-2 months to ensure the quality of service.

Follow-up procedure: Many times our research team failed to conduct the test due to various issues like baby got wake up during testing or due to some technical issues. At the time our research team keep a record of those children and followed up them. The same procedure can be adopted by the service provider to screen all babies. It is also recommended that referred cases should be tracked and motivated for further screening at tertiary facilities.

Table 2.2.11: Suggested Training Module for 'Portable Automated ABR' Training

<table>
<tr><th colspan="8">Training modules</th></tr>
<tr><td>Target Service Provider</td><td colspan="3">Period of training</td><td>Trainer</td><td>Group size</td><td>Machine required</td><td>Training venue</td><td>Training material</td></tr>
<tr><td rowspan="2">Staff nurse/ Ayush doctors (working under MCH unit)and Mobile health unit</td><td>Day-1</td><td>Day-2 to 3</td><td>Day- 4</td><td rowspan="2">Training for the trainer for 2 days</td><td rowspan="2">16 members</td><td rowspan="2">4 machine for 16 members</td><td rowspan="2">District level</td><td rowspan="2">Test protocol Portable Automated ABR booklet</td></tr>
<tr><td>Orientation</td><td>Hands-on, Practice</td><td>Doubt clearing</td></tr>
<tr><td colspan="8">*Trainer: Audiologist working under DEIC, they need two days ToT.</td></tr>
</table>

Although 'Portable Automated ABR' requires a silence environment, as crowd or noisy environment disturb baby's sleep and ultimately it affects the testing process. It was also observed that during the test presence of any electronic devices such as mobile charger, computer or other electric appliance etc. affect the testing process. It was difficult to screen above six months' infants as they are super active and they wake up with a simple touch and removed electrode. The test was completed within 30 minutes (preparation of electrode sites, impediments set-up, placement of ear phones and swipe-counts), if the baby was calm and sleeping.

The hearing screening can be performed by any healthcare staffs with basic skill based training (3–4 days); however, each service provider should have the basic skill of handling baby, infection control practice and smartphone operating skill. The interpretation of the graphical wave more intensive so training is essential or there is a need of an audiologist. For appropriate screening, each service provider should be trained properly and should be provided hands-on practice. It is suggested that each team should have at least two members preferably staff nurse. For supervision of service provider, one supportive supervisor should monitor for initial 1-2 months to ensure the quality of service.

2.2.6. Perspective of Parents, Service Providers and Program Managers on Hearing Screening

Objective: To explore the perspective of consumers, service providers, and program managers on the operational challenges with respect to ethical, social and equity facets for introducing 'Portable Automated ABR' hearing screening device.

Methods: The qualitative explanatory study was conducted among stakeholders. Out of 32 DEIC in Odisha six were purposively selected (three coastal and three non-coastal) for the study. These DEICs were Kalahandi, Koraput, Kandhamal, Capital Hospital, Nayagarh, and Balasore. Total 26 In-depth Interviews (IDIs) were conducted among ten mothers, five service providers (audiologists), five district-level RBSK managers, five District Program Managers (DPM) and State RBSK Managers. The IDIs were carried out using IDI guide. The IDI data were analyzed using content analysis methods.

Findings:

Program managers perceptive: According to the program managers, there were a lot of issues like availability of proper mobile health team (doctors, nurse, pharmacist, and ANM) staffs and less number of a vehicle dedicated for MHT. For ensuring a positive HL case one individual needs to go through three tiers of diagnosis. At first the MHT's staffs do screening at Anganwadi center and schools in the community; secondly if positive case found, they referred to DEIC, for diagnostic BERA that particular individual needs to visit another facility where BERA is done. Because of this lengthy process many people especially people coming from a low economic background fail to follow all these processes. The program managers suggested if sufficient manpower will be provided, it will be easier for them for hearing screening at community and facility level. They also suggested that BERA and OAE should be available in the field level so that no child should be left behind.

> *"Sufficient skilled manpower, portable device, and awareness among people regarding the hearing screening can help us overcome deafness among children which is ultimately affecting the overall development of a child."*

Whereas in some districts like Nayagarh, they were screening of each child mainly in SNCU and in Delivery point. If some positive cases are found, they are providing a hearing device and if needed some sessions at DEIC center also recommended. They have also reported that due to noise sometimes they are getting false-positive cases. There is a suggestion from the audiologist that if our staff nurse can be trained then that would be much better, at least no child would be

missed out for screening. With this, if AYUSH doctors can be trained they could refer us after screening. It would be better if there will be some review-cum-orientation about screening for all the doctors, audiologist. They suggested that if a machine which can work in noise and which can be handled by any health care provider then that can save a child being deaf. Moreover, it would be better if they made the screening center in all the Districts because now it is only available in 13 districts of Odisha.

Audiologist perceptive: Similarly, an audiologist from different facilities explained that there is a lack of awareness among people regarding early hearing screening and the importance of hearing in a newborn baby. With existing technology for hearing screening audiologist are depended on OAE to perform the test which sometimes is unable to test the 0-3 babies or is not that accurate. They have reported that while Mobile Health Team screening in a field with BOA (Behavioral Observation Audiometry) they are getting many false-positive cases, for which many a time child with no impairment also getting referred to DEIC. They have also reported that they are not able to attain every child at the hospital because they are performing many responsibilities like community visit, session for impaired children at DEIC, etc.

> *"Already we are having so many responsibilities and screening individual at village level is an additional burden for us. If other health workers like ASHA can be trained to perform these screening it would be much easier for us to screen at ground level."*

Few audiologists shared some challenges which they are facing like lack of proper infrastructures and manpower; silent environment and assistant. Noise has a great impact on the result of screening which ultimately affecting the actual prevalence of HL. Due to insufficient manpower, they are performing all tests by themselves only and which results in less coverage. Similarly, another big issue is that people were not bringing their children to the DEIC after getting a referral from the field staff even after we are arranging vehicle because if they will come for screening they would lose their daily wages. They have suggested to the increase the number of manpower, assistant for the audiologist and a portable and reliable device which can be used in noisy condition and which can be operated by any health worker.

State Level Managers Perceptive

Human resource challenges: From the 29 District Early Intervention Center (DEIC) of 29 RBSK functional districts, three districts (Malkanagiri, Deogarh, Nabarangpur) were not functional yet. There were total vacancies of eight RBSK managers, four audiologists, and 19 staff nurses. The data entry operator (DEO) post was the completely outsourcing basis with a varied salary starting from a minimum of 8000 INR per month. The State Government had not given priority

to the staff nurse post as the newborn screening had not been strengthened and if the staff nurses will be appointed, then they will be utilized to do other official works. In some places staff nurses were appointed through RBSK; but though the planning was there to strengthen them with newborn screening, the orientation was not started. In Shishubhawan there was staff nurse appointed through RBSK.

> *"DEIC is a new concept and newborn screening is added to it. Within all these conceptual gaps is there. It will take time to understand the authorities. If we will appoint staff nurses now, the authorities will place them in the labour room."*

The focus of Government was not the recruitment of staff nurse and DEO. The main focus was on how to start the core work like screening on a priority basis. The RBSK is not at that level where all aspects are strengthened. As like as DEIC, the audiologist was a new post in our health system and it took almost three years to accept and function the responsibilities of that post.

Technical and operational challenges: The DEIC was started in an intention to work for cleft disease with support from the Smile trend. Total 38 diseases were supposed to be treated at first and newborn screening was not added then. At inception, there was no room to seat and focusing on one disease now the treatment is going on beyond 38 diseases. If the project would have been focused on a specific health condition, then the project might have closed like other states.

> *"As we built the trust of Government towards us, now we are managing so many health conditions."*

BERA machine has already given to 13 districts on a regional basis, as it is not necessary to keep BERA in every hospital. Before RBSK, BERA machine was in two hospitals of Odisha through All India Institute of speech and hearing impairment. Soundproof room was already prepared in 17 DIECs. But still, there were some barrier regarding the sitting arrangement, staffing as well as the soundproof room.

The hearing impairment children are screened through the mobile health team (MHT) with the support of a head to toe screening checklist. The referred children of MHT screened in a fully equipped set up with trained audiologist and with the support of ENT specialist if required; which is DEIC.

> *"After one year, there will be soundproof room in every DEIC and as DEIC is equipped as an assessment centre, there will not be any role for 'Portable Automated ABR'."*

Community challenges: All cases referred by MHT are not coming to DEIC for confirmation screening after the follow up by RBSK staffs also which is a major barrier for post follow. We need a robust monitoring mechanism to track the baby. Parent need to be aware of the significance of screening.

Innovation and suggestion: The planning is to train the staff nurse regarding screening to reduce the work burden of an audiologist. RBSK has given BOA at CHC level to screen newborn. As 'Portable Automated ABR' is effective for newborn starting from zero-days, you should give this machine to the health set up where staff nurse will be there to operate. RBSK is referring to the high-risk child to DEIC from secondary health care centre's through the provision is to refer all. So if the Portable Automated ABR machine will be in the secondary health set up, then all children can be screened for hearing impairment. Otherwise, it can be provided to MHT to screen though they actually do not need because they screen through the symptom checklist.

> *"The lost to follow up cases by RBSK in the community can be helpful by this device if you can get in touch."*

After checking the sign and symptoms, MHT can refer to the nearest CHC by which the workload of MHT can be reduced and as it is nearby CHC it will be convenient for the community.

Experience of the mother whose child has a hearing impairment

"Hearing is the sense that connects the individual with the world of sound".

The stress of a mother: A number of parents commented on the powerful emotions they experienced when they came to know about the hearing impairment of the child. Most of them reported a late detection of HL as they were not aware of early screening of hearing at the hospital. One mother expressed some ambivalent feelings about very early diagnosis resulting from ABR screening. As the mother is attached to the baby both physically and emotionally, she is the one who went through stress and depression if something happens to the baby.

> *"Everything was alright with my baby till age of seven months when one day a glass felt down I saw that my baby is not reacting anything, then I realize something strange is there with my baby. From that day I am in worried about how my child will be normal like other children"*

Financial burdens: Some parents described that financial burden is a major challenge for attending the regular session at DEIC. Those who are having hearing impairment it is recommended by DEIC that they need to attain at least one session in a week at DEIC for different exercises. For which parents need to bear travel expenses and also those who are working they need to take leave from work. Which is ultimately resulting in an increase in financial burden?

> *"When we came to know about impairment of my baby we told by Audiologist to visit DEIC at least once in a week for some activities, though we are from Ganjam and it cost a lot to travel from their every week so we took a rented house in Bhubaneswar. We are spending 40% of our income to bear all expenses including travel, food, and house rent."*

Family support: For children growing up with HL who use hearing aids, they might feel different in school and among peer, it is the family who supports them to grow good communication. Some parents mentioned the critical need for support at that time, with one parent commenting that good support had empowered her to feel she could provide well for her child despite his disability. While some parents faced challenging to bear a child with a disability in a family, especially family with the low income they consider an impaired child as an extra burden to the family.

> *"My child is everything for me she can't listen but she can feel me, but my family doesn't understand it they think like a girl child it will be very difficult for her to survive and how she will get married? While I need their support they even don't listen to me. Today also I came alone to hospital for DEIC session."*

Perception of screening

Delay in diagnosis: Following the screening process, many parents experienced lengthy delays before a diagnosis of HL because of the unavailability of screening at the health facility as well as unawareness and ignorance of early hearing screening. Delays were thought by parents to be due to difficulties with testing individual children, difficulty with interpretation of test results obtained, the need for multiple repeat tests over prolonged periods of time, and resource limitations resulting in appointment delays. This was a time of great frustration for many parents, who described feelings of helplessness and anxiety. Many parents also expressed that early screening at the facility should be mandatory like other post-natal care so that each child suffering from hearing impairment can be diagnosed from the early days of her/his life. Some parents also said that only tertiary hospital is having a screening facility, what about those who are delivering at PHCs and CHCs.

> *"When my baby born I was not aware of hearing screening and nobody in the hospital also told me about this. When my baby was 6 months then only I realize that he is having some hearing problem, it is already late and my child already lost his six months of learning."*

Treatment challenges: Parents gave numerous examples of communication difficulties and misunderstandings with providers which negatively impacted their child's care. Parents often felt that providers had not explained findings clearly enough to them. Where parents had good experiences, they often mentioned personal qualities of the providers as being "helpful" and "positive". Misleading or incorrect advice called into question the provider's knowledge.

Neonates had added challenges during the screening and diagnostic processes. Some parents commented that initially concern about HL took at other medical and developmental difficulties and was not acted on until much later. Additional problems were also experienced in obtaining

accurate audiological evaluations when the child had developmental delay. Some parents commented on the lack of rapport between child and audiologist, particularly where children exhibited challenging behaviors like not sleeping or were not calm during the test. With this parents also faced the problem of getting a hearing aid, though the required number of hearing aid is not available at the hospital they need to rush so many times to get the device.

The anxiety of mother during hearing screening: Mother is the one who feels more anxiety when something happens with the baby. When hearing screening is performed it is the mother who asks so many questions to the audiologist. After listening to all her query when she gets convinced that it is much needed for her baby then only she allowed. Many of them were concerned about the gel applied before conducting test whether it is safe, and it will not harm baby soft skin. Then they were more concerned about the electrode that is used for screening because it is attached to a device with wire and they thought current will pass to the baby through the wire. One of the major anxieties of all mothers was the result of the device. The increment of anxiety was even more if only the group of mothers whom their babies passed the second screening has been considered because the increase of alertness of the mothers towards their child responds to sound. They would feel calm and their anxieties were reduced after getting a pass result for both the ears.

> *"I will not allow my baby for the test, I am getting afraid of the test; you will pass current in my newborn baby, it may harm, may have a side effect in future"* (Mother of a newborn child).

The study explored some key issues in the implementation of the program such as human resources, inadequate infrastructure, equipment-related shortcomings, and little wakefulness among mothers on hearing screening.

Most of the mothers expressed a desire to have their children ear screened at birth and agreed that the hearing screening should be routine after childbirth before hospital discharge. However, most of the mother was unaware of the hearing screening program. Health education during antenatal services will provide adequate information to mothers and caregivers on hearing screening in order to increase demand for services.

2.3. Economic Evaluation (EE) and Cost-effective Analysis

2.3.1. Aim of EE, Description of Scenarios, PICO, Time horizon, and Perspective

Aim of economic evaluations: Ultimately, the value of a new approach to health care must be judged on the degree to which additional benefits that might arise match the amount of additional

resource that would be required to bring about the new approach (Colgan et al., 2012). This is equally required in hearing screening of neonates/infants and children in the forerunner to this HTA report. Health economic modelling was employed to this end by using a decision-analytic model after finding that there was little relevant health economic literature and reported outcomes.

Description of the scenarios: The other major change from the original health economic model was to be more specific about the methods of screening in the current report. The OAE and Portable Automated ABR tests were the two methods evaluated.

Hearing impairment in infants is a particularly serious obstacle to their optimal development and education, including language acquisition. According to a range of studies and surveys conducted in different countries, around 0.5 - 5 in every 1,000 neonates and infants have congenital or early childhood onset sensorineural deafness or severe-to-profound hearing impairment (Bu X et al., 2019). In India, the prevalence of HL is 5 in 1,000 live births on average (RBSK, 2013, WHO, 2017). Deaf and hearing-impaired children often experience delayed development of speech, language and cognitive skills, which may result in slow learning and difficulty progressing in school (DeAntonio et al., 2016). There is scientific evidence to suggest that early identification (three-six months) and administration of appropriate intervention at or before six months of age provides children with impaired hearing with the opportunity to develop normal speech and language (El-Naggar et al., 2005).

As a result, many countries have implemented neonatal hearing screening programs (Feher-Prout, 1996; Foteff et al., 2016)). The rationale for implementing a universal neonatal hearing screening programs is that it can detect more deaf infants, providing a greater opportunity for them to experience normal language development, while providing overall benefits in terms of reducing the disability and improving the health and well-being of the children (FitzZaland and Zink, 1984; Geal-Dore et al., 2010).

PICO: There are two main screening interventions generally available to a number of healthcare systems worldwide. These interventions are based on electrophysiological methods: Otoacoustic emissions (OAE), and automated auditory brainstem response (AABR) (1). Both AABR and OAE are non-invasive, rapid screening tests. OAE measures sounds that are produced by the cochlea to response to acoustic stimulation, and AABR measures electroencephalographic waveforms in response to clicks (Gloria-Cruz et al., 2013).

We have analysed the cost effectiveness of OAE and Portable Automated ABR neonatal hearing screening device which is based on the ABR system. The main objective of their study was to compare the two screening strategies: Universal screening, and targeted screening. In this two-

stage procedure, OEA and Portable Automated ABR were the applied devices, respectively and were referred to the gold standard here in our case was Brainstem Evoked Response Audiometry (BERA). However, here, our main objective was to compare Portable Automated ABR and OAE devices for implementing universal newborn hearing screening under a one-stage procedure.

Settings, Perceptive and Time horizon: In India, hearing screening is conducted by implementing universal strategy, and OAE is the most applied device (Kurmi et al., 2014). Hence, this study aimed to compare the cost-effectiveness of this device and that of Portable Automated ABR in performing universal newborn hearing screening. We aimed to find why OAE is still the most applied device in conducting universal neonatal hearing screening (UNHS) when Portable Automated ABR is apparently more accurate and cost-effective in the long run. During the last decade, the rapid expansion of UNHS programs has brought into focus questions about the most appropriate screening technology for this indication. The high prevalence of HL, its subsequent burden on the health system, and the ethical issues surrounding its delayed diagnosis has necessitated the implementation of UNHS programs (Kotby et al., 2008; Korver et al., 2017). However, due to the limited resources of the health system, and the possible associated outcomes and costs that these devices may have, we sought to perform a cost-effectiveness analysis (CEA), as each of these devices may have extra benefits for the UNHS program.

Eventually, it may be used as a tool for evidence-informed policymaking in the field of UNHS in India, and for optimizing resources to control HL and its resultant burden. The main objective of this chapter is to examine the cost-effectiveness of 'Portable Automated ABR' and OAE in UNHS programs. Furthermore, it may be used as a tool for evidence-informed policy-making in the field of UNHS in India, and for optimizing resources to control HL and its subsequent burden.

Our perspective was the health care system, and we have taken into consideration all the cost which is associated with the hearing screening (including both direct as well as indirect costs). We defined effectiveness as the number of neonates with HL, whose hearing status has been correctly detected upon using either of the devices. In general, the cost-effectiveness of these two devices was analyzed based on the annual birth rate statistics.

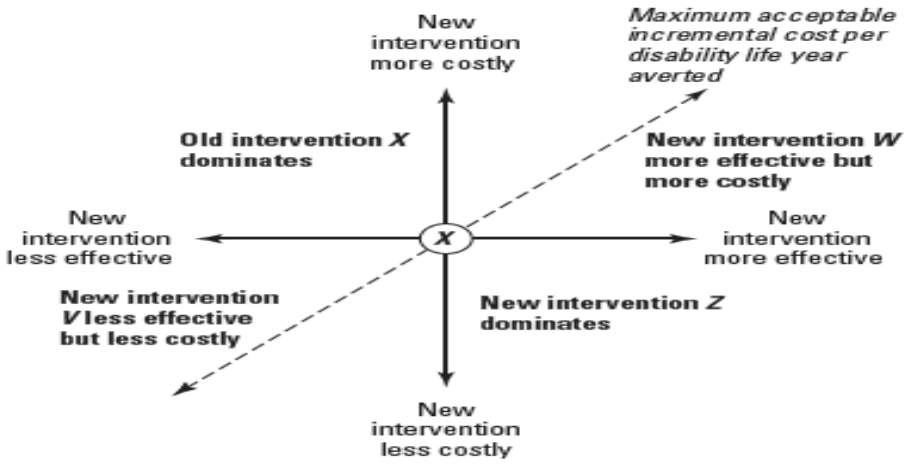
2.3.2. Model Concept

Cost-effectiveness analysis (CEA) is an economic analysis which compares the relative costs and outcomes (effects) of different courses of action. CEA is often used in the field of health services, where it may be inappropriate to monetize health effect. Typically, the CEA is expressed in terms of a ratio where the denominator is a gain in health from a measure (years of life, premature births

averted, and sight-years gained) and the numerator is the cost associated with the health gain. The most commonly used outcome measure is quality-adjusted life years (QALY) (CDC, 2019).

Figure 2.3.1: Cost-effective analysis flow diagram

Figure 2.3.2: Cost-Effectiveness plane



The most commonly used CERs are Average cost effectiveness ratio (ACER):

$$\text{ACERs} = \frac{\text{Cost B}}{\text{EffectivnessB}}$$

Cost-effectiveness analyses (CEA) are often visualized on a plane consisting of four-quadrants, the cost represented on one axis and the effectiveness on the other axis. CEA focuses on maximising the average level of an outcome, distributional cost-effectiveness analysis extends the core methods of CEA to incorporate concerns for the distribution of outcomes as well as their average level and make trade-offs between equity and efficiency, these more sophisticated methods are of particular interest when analysing interventions to tackle health inequality (WHO, 2017).

Incremental Cost Effectiveness Ratios (ICERs) are calculated as under:

$$CE = \frac{Cost_{New} - Cost_{Old}}{Effect_{New} - Effect_{Old}}$$

2.3.3. List of Assumptions

We defined effectiveness as the number of neonates with HL, whose hearing status has been correctly detected upon using either of the devices. The cost-effectiveness of these two devices was analyzed based on the annual birth rate statistics. The diagnostic accuracy of the two devices was derived from primary study. In this model, the newborns detected as positive (whether true or false) by the BERA as the gold standard-are considered to be definitely diagnosed. An audiologist performs this test, and the model presumes that its accuracy is 100%. The remaining newborns, whose results are negative (whether true or false) are discharged and not followed up (terminal node). Each device has four branches and end nodes, and their expected cost is determined as follows:

- Branch A/A': The cost of screening and definite diagnosis of newborns, reflecting with true positive HL, is included under this branch.
- Branch B/B': The cost of screening for newborns, showing false negative HL, is included under this branch.
- Branch C/C': The cost of screening and definite diagnosis of newborns, showing false positive normal hearing, is included under this branch.
- Branch D/D': The cost of screening for newborns, showing true negative normal hearing, is included under this branch.

The total costs of these four branches indicate the total cost of each device. Our expected effectiveness for each device was calculated by multiplying the number of newborns entering the model by prevalence, and by device sensitivity. The main inputs of this model include the prevalence of HL in India, device sensitivity and specificity, the cost of screening, and definite diagnosis of each newborn.

We applied decision tree models with a time horizon of one year for the prevalent population (Targeted), and another with the universal population to economically evaluate the 'Portable Automated ABR' and OAE devices used in UNHS. The diagnostic accuracy of the two devices was derived from the primary diagnostic validation study. Newborn screening and definite diagnosis costs were derived from various facilities and hearing screening centre in Odisha, India.

Figure 2.3.3: Pathway for the screening of hearing impairment

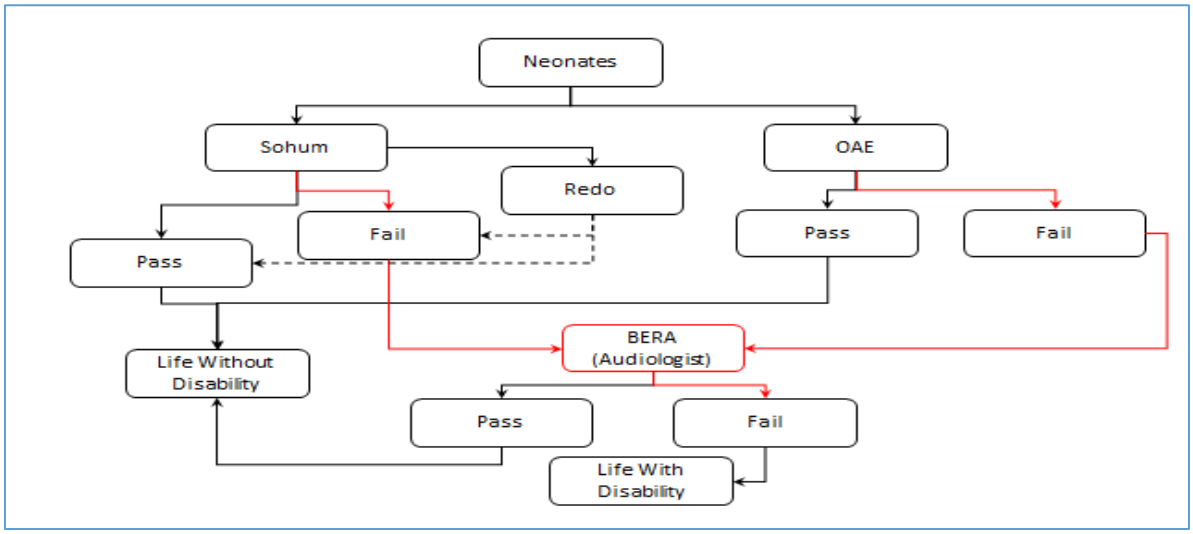
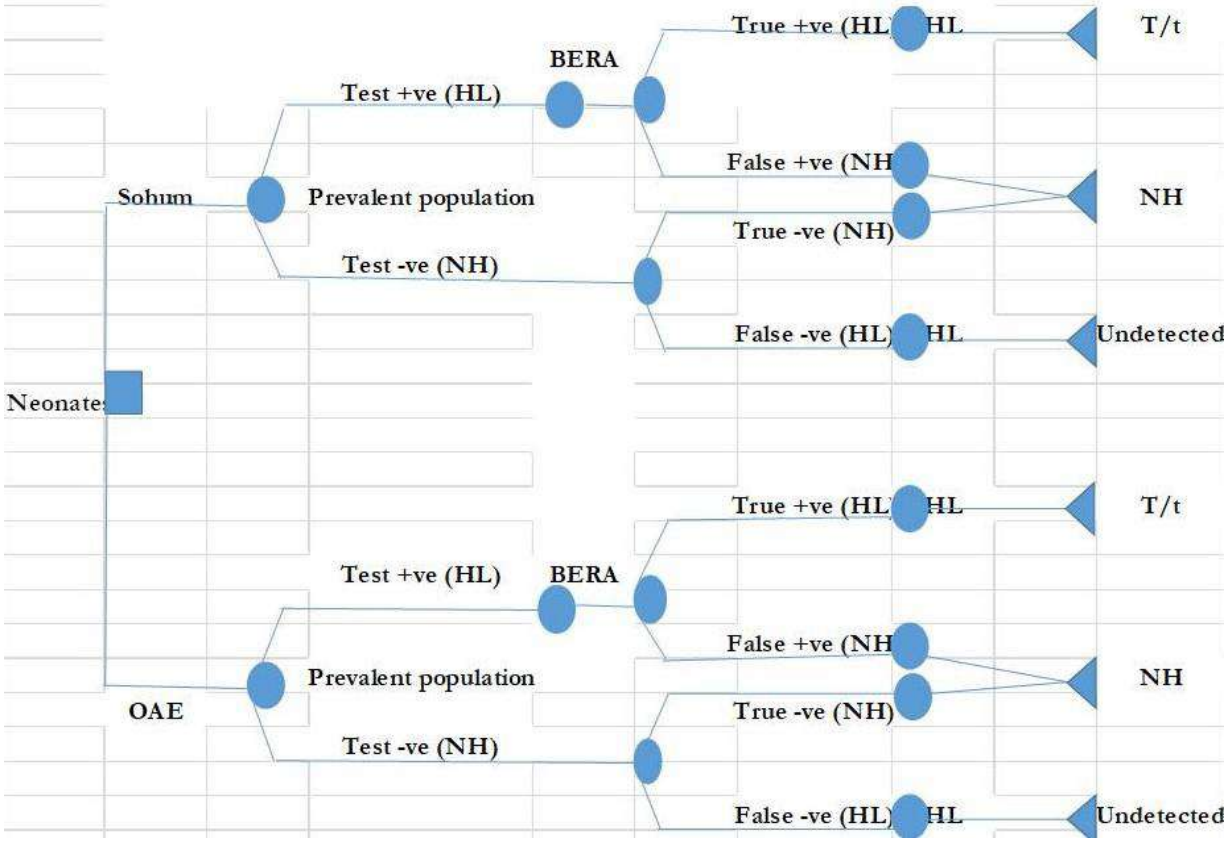


Figure 2.3.3 shows the pathways for the screening of hearing impairment which shows that how neonates has been diagnosed with the Portable Automated ABR and OAE devices, which normally gives the results in terms of pass, fail or redo. In case an infant fails the test in either device, he is considered with presence of hearing impairment and is further tested with the gold standard BERA. BERA gives the final confirmation on the presence of hearing impairment or not. However, in case the infants have been diagnosed as pass in spite of having hearing impairment, they have to live a life with disability.

Rationale of the Model: In this model, initially we have diagnosed 100000 neonates with both Portable Automated ABR and OAE. These devices identify the screened neonates as pass (normal or NHL) or refer (abnormal or having HL). This detection may be true or false, and its possibility depends on the prevalence of the HL, and the sensitivity and specificity of the concerned devices (Figure 2.3.4).

Figure 2.3.4: The decision tree model for the hearing screening



Here, HL was defined as permanent congenital bilateral HL exceeding 35 dB, presuming that the screening has been performed by an audiologist. Therefore, no error occurs due to the operator's insufficient skills (chance node). The newborns detected as positive (whether true or false) by the BERA device-as the gold standard-are considered to be definitely diagnosed. An audiologist performs this test, and the model presumes that its accuracy is 100%. The remaining newborns, whose results are negative (whether true or false) are discharged and not followed up (terminal node).

Each device has two branches which refers to the BERA nodes which are divided into four end nodes from each device BERA test termed as true (+), true (-), false (+), and false (-) along with their expected cost is determined as follows:

1. True (+) Branch: The cost of screening and definite diagnosis of newborns, reflecting with true positive HL, is included under this branch.

2. False (-) Branch: The cost of screening for newborns, showing false negative HL, is included under this branch.

3. True (-) Branch: The cost of screening and definite diagnosis of newborns, showing false positive normal hearing, is included under this branch.

4. False (+) Branch: The cost of screening for newborns, showing true negative normal hearing, is included under this branch.

2.3.4. Model Parameters

The main inputs of this model include the prevalence of HL in India, device sensitivity and specificity, the cost of screening, and definite diagnosis of each newborn (Table 2.3.1 and 2.3.2).

Table 2.3.1: Clinical parameters and Quality of Life (QoL)

Clinical Parameters	**Value**	**Sources**
Prevalence of HL per 1000	5	WHO 2013
Sensitivity of Portable Automated ABR	100%	Primary data Maulana Azad Medical College, Delhi (2018 -2019)
Specificity of Portable Automated ABR	97%	
Positive Predicted Values(PPV) for Portable Automated ABR	52%	
Negative Predictive values (NPV) for Portable Automated ABR	100%	
Sensitivity of OAE	69%	Primary data Maulana Azad Medical College, Delhi (2018 -2019)
Specificity of OAE	68%	
Positive Predicted Values(PPV) for OAE	7%	
Negative Predictive values (NPV) for OAE	98%	
QoL Weights		
Normal Hearing (may have other health problems)	0.95	Primary data RMRC, Bhubaneswar using Infant health related Quality of life Instrument (IQI) by Jabrayilov et al. 2018
HL (Unilateral and Bilateral)	0.77	
Unilateral HL	0.85	
Bilateral HL	0.69	
Cohort and case detection		**Value**
Neonatal Population (Cohort)		100000
Cases detected by Portable Automated ABR		***262***
Cases detected by OAE		***38***
Life Expectancy (2012-2016)		
At Birth		69.2

Table 2.3.2: Final parameters, sensitivity, specificity values for Portable Automated ABR and OAE

Sensitivity and specificity of devices				
	BERA			
Portable Automated ABR	**+ve**	**-ve**		
+ve	11	0	1.000	***Sen***
-ve	10	346	0.972	***Spec***
	0.52381	1.000	0.000	***1 – Sen***
	PPV	***NPV***	0.028	***1 – Spec***
	0.47619	0		
	1 - PPV	***1 - NPV***		
	BERA			
OAE	**+ve**	**-ve**		
+ve	11	5	0.688	***Sen***
-ve	135	284	0.678	***Spec***
	0.075342	0.983	0.313	***1 – Sen***
	PPV	***NPV***	0.322	***1 – Spec***
	0.924658	0.017301038		
	1 - PPV	***1 - NPV***		

Table 2.3.3: Variables Required for Estimating the Costs

Variables Required for Estimating the Costs (in INR)						
Variables	**Portable Automated ABR**	**OAE**	**Gold standard (BERA)**	**Portable Automated ABR**	**OAE**	**BERA**
The device's lifespan	6 years	6 years	6 years	6	6	6
Average duration of test for one newborn (grey in hours)	15 minutes	10 minutes	90 minutes	0.25	0.17	1.5
Average duration of device function in one day	As per the number of tests performed					
Mean screening of newborn in one day	24 infants	36 infants	4 infants	24	36	4
Average number of working days in a year	260 days			260	260	260
Mean screening of newborns in one year	6240	9360	1040	***6240***	***9360***	***1040***

The life spans of the concerned devices along with the gold standard were almost 6 years. Portable Automated ABR takes almost 15 minutes to complete the test of ears in one infant, which is 10 minutes for the OAE, and 90 minutes for BERA. On the basis of average 260 working days, OAE (n=9360), Portable Automated ABR (n=6240) and BERA (n=1040) infants can be tested annually (table 2.3.3).

Cost parameters: The economic analysis in this study was conducted from the perspective of the healthcare system and societal perceptive on evaluating cost-effectiveness (Table 2.3.4).

Table 2.3.4: Total and per unit cost for implementation of Portable Automated ABR, OAE and BERA (In INR) along with treatment and procedural cost

Cost Head	Portable Automated ABR	OAE	BERA
Human Resource	421000	421000	1291000
Medical Consumables	104520	140400	174720
Non-Medical Consumables	0	0	4000
Medical Equipment	74736	58883	187107
Non-Medical Equipment (Including building/space)	0	0	139354
Overheads	2400	2400	30000
Total Cost	602656	622683	1826181
No. of cases per year	6240	9360	1040
Unit Cost (HS)	97	67	1756
Societal Unit	898	868	2557
Cost of T/t with Cochlear Implant (incl. hearing aid, therapy services)			**1230000**
Cost of Hearing Aid (including therapy services)			**700000**
Therapy cost			50000
Services of specialists (Counsellor, ENT, Therapist)			630000
Total(Therapy cost +services)			680000
Cochlea Implant cost			550000
Hearing aid cost			20000

2.3.5. Cost-Effectiveness Analysis

Finally, upon examining the probability of uncertainty concerning the inputs, particularly cost data and the prevalence rate of HL, sensitivity analysis was calculated in view of the maximum and minimum values of these parameters (with the assumption of keeping the other parameters constant). Final model was based on the parameters mentioned in table 2.3.1 to 2.2.3. Information is given for the prevalence of neonatal hearing impairment, its incidence, neonatal population of India, along with sensitivity and specificity of Portable Automated ABR, OAE and BERA. Based on the WHO reports on HL the prevalence of congenital HL in India varies from two to eight in 1,000 live births, which has been estimated to be five in 1,000 live births on average.

Table 2.3.5 presents the results from the decision tree model. Model shows the prevalence targeted population of the neonates screened by the Portable Automated ABR and OAE followed by the BERA. The models also included a cost for those patients who achieved a false positive screening result. This is the proportion of positive test results that are really negative events. False-positive result may cause parental anxiety and result in unnecessary follow-up tests and occasionally unnecessary interventions. In this analysis it is assumed these infants incur an additional cost of an

outpatient audiologist visit. According to the decision tree and the data presented in table 2.3.5, if hearing screening is performed in 100000 infants with the prevalent cohort population 500, using the Portable Automated ABR device, it will entail the following probable outcomes:

1. 500 newborns will be detected correctly with positive HL
2. 99738 newborns will be detected with negative HL or NH
3. Out of 500 cases which are referred to the gold standard BERA, 262 newborns will be detected true positive HL correctly, 238 will be detected negative for HL incorrectly.
4. The under detection HL is 0

Similarly using the OAE device, it will entail the following probable outcomes:

1. 344 newborns will be detected correctly with positive HL (HL)
2. 99971 newborns will be detected with negative HL (NH)
3. Out of 344 cases which are referred to the gold standard BERA, 26 newborns will be detected true positive HL correctly, 318 will be detected negative for HL incorrectly.
4. The under detection HL is 3

The under detection is more for OAE as compared to the Portable Automated ABR device if the newborns are diagnosed for the hearing impairment.

Table 2.3.5: Results from the decision tree model for prevalent population (Targeted)

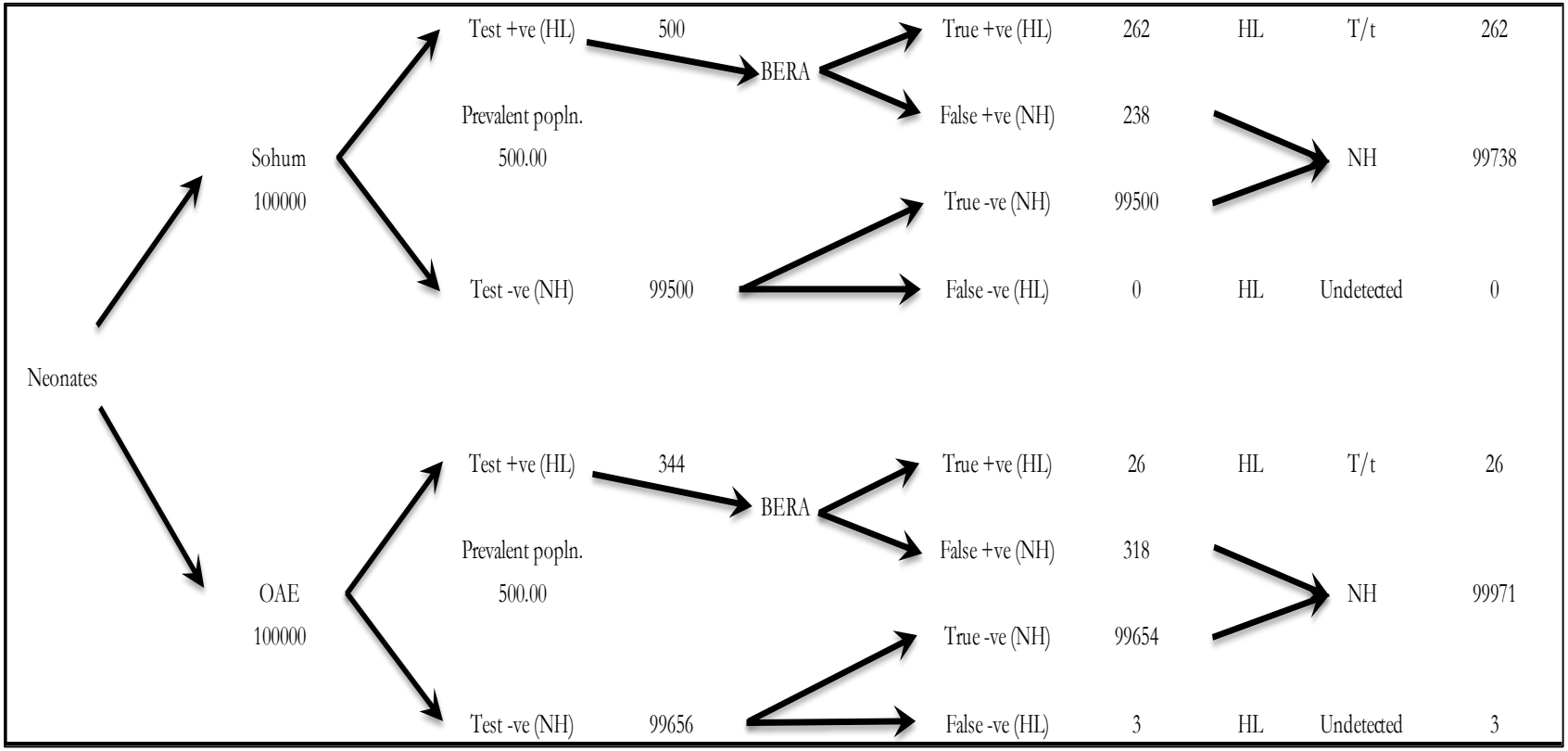


Table 2.3.6: Estimation of health system cost for human resources and consumables for implementation of OAE, Portable Automated ABR and BERA (annual)

Human resources	Monthly Salary	Time spend exclusively for screening(in hour per day)	overall working hours (Monthly)	overall working hours (yearly)	Monthly time on screening (in hours)	Apportioning statistic	Monthly cost to system	Annual cost (In INR) OAE	Portable Automated ABR	BERA
Audiologist	50000	8	176	2080	176	1	50000	**0**	**0**	**600000**
Staff nurse	15000	8	176	2080	176	1	15000	**180000**	**180000**	**180000**
Data Entry Operator/technician	18000	8	176	2080	176	1	18000	**216000**	**216000**	**216000**
Paediatrician or Anaesthesiologist	90000	2	176	2080	44	0.25	22500	**0**	**0**	**270000**
Post service training per person (lump sum) annually								**25000**	**25000**	**25000**
Consumables										
Medical										
Disposable electrodes, lead, ear trips and other (single use per baby)								**140400**	**104520**	**18720**
Sedatives(Triclofos)								**0**	**0**	**156000**
Non-medical										
Stationary, cartridge and other items								**0**	**0**	**4000**
Building and space										
Soundproof room								**0**	**0**	**408000**
Building rent(including patient waiting area and others)								**0**	**0**	**48000**
Overhead										
Electricity and water per annum								**2400**	**2400**	**30000**
Direct cost total (health system)								**563800**	**527920**	**1955720**
Cross-tally								***563800***	***527920***	***1955720***

Table: 2.3.7: Estimation of health system cost for annual non-consumables for implementation of OAE, Portable Automated ABR and BERA

Non-consumables	OAE	Portable Automated ABR	BERA	Expected Life	Units	Unit Price	Total cost	Discount factor (DF)	Annual maintenance rate (AMR)	Annualization Factor (F)	EUAC Capital	Annual Maintenance cost (AMC)	Present worth maintenance	Total annual cost
Medical								0.03	0.05	0.1846	60917.18	16500	13818.49	***74735.67***
	Portable Automated ABR													
								0.03	0.05	0.1846	47995.35	13000	10887.30	***58882.65***
	OAE													
Device cost	**260000**	**330000**	**826184**	**6**	**1**	As mentioned		0.03	0.05	0.1846	152511.50	41309.2	34595.80	***187107.31***
Non-medical														***BERA***
Other Infrastructure(computer, printer, Table, chair, Air conditioner, light arrangements)	0	0	**152000**	**Expected Life**	**Units**	**Unit Price**		**Discount factor(DF)**	**Annual maintenance rate (AMR)**	**Annualization Factor (F)**	**EUAC Capital**	**Annual Maintenance cost(AMC)**	**Present worth maintenance**	**Total annual cost**
Computer	0	0		5	1	20000	20000	0.03	0.05	0.2184	4367.09	1000	862.61	5229.70
Air conditioner	0	0		10	2	36000	72000	0.03	0.05	0.1172	8440.60	3600	2678.74	11119.33
Printer	0	0		5	3	3000	9000	0.03	0.05	0.2184	1965.19	450	388.17	2353.37
Table	0	0		5	2	9000	18000	0.03	0.05	0.2184	3930.38	900	776.35	4706.73
chair	0	0		5	3	3000	9000	0.03	0.05	0.2184	1965.19	450	388.17	2353.37
stool	0	0		5	2	1000	2000	0.03	0.05	0.2184	436.71	100	86.26	522.97
Bed	0	0		5	1	8000	8000	0.03	0.05	0.2184	1746.84	400	345.04	2091.88
Almirah	0	0		7	1	10000	10000	0.03	0.05	0.1605	1605.06	500	406.55	2011.61
Tube lights and others	0	0		2	2	2000	4000	0.03	0.05	0.5226	2090.44	200	188.52	2278.96
	0	0											***Total***	***32667.92***
Soundproof room	0	0	**408000**	5	**1**	**408000**	408000	0.03	0.05	0.2184	89088.67	20400	17597.22	106685.88
	0	**0**											***BERA***	***139353.80***
	OAE	***Portable Automa***												

		ted ABR												

Table 2.3.8: Final outcomes for CEA with OAE and Portable Automated ABR devices for number of cases detected, per case detection and total cost

Health Systems				
Portable Automated ABR/OAE + BERA				
Device	Costs (with cochlear implant)	QALYs (with cochlear implant)	Costs (with hearing aid)	QALYs (with hearing aid)
Portable Automated ABR	332678772.18	6574000.00	193869248.38	6574000.00
OAE	39111934.20	6573966.33	25385478.72	6573966.33
Difference	293566837.98	33.67	168483769.65	33.67
ICER		8718388.30		5003654.15
Societal				
Portable Automated ABR/OAE + BERA				
Device	Costs (with cochlear implant)	QALYs (with cochlear implant)	Costs (with hearing aid)	QALYs (with hearing aid)
Portable Automated ABR	413235150.18	6574000.00	274425626.38	6574000.00
OAE	119543069.08	6573966.33	105816613.60	6573966.33
Difference	293692081.11	33.67	168609012.78	33.67
ICER		8722107.79		5007373.64
	Cost of detecting 1 case	Total Cost (HS) w/o T/t	Cases Detected	Cost Per Case Detection
	With Portable Automated ABR	10535915	262	40228
	With OAE	7256198	26	280173
Final ICER	97407.69			

Diagnosis and management of hearing impairment has a positive impact on children's quality of life (QoL) as measured using the QALY. The QALYs accruing to children with no hearing impairment is 0.95 and HL is 0.77. The results show that not having a screening program results in lower QALYs than having early detection of hearing impairment associated with the highest QALY gains. In order to determine the cost-effectiveness of each method of screening, the ICER needs to be calculated. The ICER presents the ratio of the marginal gain of the intervention over the counterfactual in terms of both costs and benefits (2.3.6 to 2.3.8). Table 2.3.8 indicates the incremental health system cost and societal cost, and QALYs for the two screening approaches for health system and societal values and resultant ICERs for health system and Society for the hearing screening with Portable Automated ABR and OAE devices respectively. For the clear understanding the results has been divided into four scenarios:

1. Based on the perspective: Health system and Societal.
2. Based on the treatment scenarios: on treatment with either cochlear implants (CI) or with just hearing aids (HA)

The health system and societal cost for treatment with Portable Automated ABR and OAE will be as follows:

1. The CI cost for health system will be INR 332678772 and with HA it will be INR 193869248 if the child is screened by Portable Automated ABR.
2. The CI cost for health system will be INR 39111934 and with HA it will be INR 25385478 if the child is screened by OAE.
3. The resultant QALYs for health system will be 6574000 for CI and 6574000 for HA for Portable Automated ABR and 6573966 and 6573966 for OAE respectively. The resultant ICERs from QALYs from CI will be 8718388, and for HA it will be 5003654.
4. ICERs with cost without true positive cases (Including primary QoL scores) will be 739000 for Portable Automated ABR and 739004 for OAE, resulting into ICER value of 97407.69.

Final outcomes for CEA with OAE and Portable Automated ABR devices for number of cases detected, per case detection cost and total cost for treatment with Portable Automated ABR and OAE will be as follows:

1. The total cost to the health system irrespective of true positive cases with Portable Automated ABR will be INR 10535915and for OAE it will be INR 7256198.

2. The total number of cases detected with Portable Automated ABR will be 262, while it will be 26 by OAE.
3. The cost for per case detection from Portable Automated ABR will be INR 40228 and by OAE it will be INR 280173.

In the base case, it is appropriate to report an ICER, as Portable Automated ABR dominates (is more effective and less costly than) OAE screening approach for UNHS. In the context of our research question, the results indicate that Portable Automated ABR is more cost-effective compared with OAE. It indicates that it will cost less to the system if they implement Portable Automated ABR along with BERA. Similarly, from the societal perspective it will cost less to the system if they implement Portable Automated ABR along with BERA. The number of cases detected would be also more for Portable Automated ABR which will help in UNHS along with significantly lower cost for per case detection and overall lower cost for both health system and from societal perspective.

Based on the findings, the unit cost of screening per newborn of the Portable Automated ABR was higher compared to the OAE device. The high diagnostic accuracy of Portable Automated ABR compared to OAE, and the fact that it entails less costs, the Portable Automated ABR device may prevent delayed interventions in newborns and the subsequent complications that may ensue. The number of false positive results (i.e., the newborns who were healthy but falsely detected as cases) was far less in the Portable Automated ABR method than in the OAE method, imposing less costs (direct, indirect and intangible), stress and anxiety on the newborns' families. In this study, effectiveness was defined as the percentage of newborns, whose hearing status was correctly detected by each of the two devices. In addition to the lower direct medical and intangible costs of the Portable Automated ABR compared to the OAE device, the number of referred false positives was also significantly smaller. Though the unit cost of newborn screening is slightly higher in the Portable Automated ABR technique than in the OAE technique, its referred cases are fewer. The Portable Automated ABR is a good substitute for the OAE, as it entails fewer referred cases and lower total costs per screened newborn. The minimum and maximum costs of the gold standard also indicated that the Portable Automated ABR costs less and has greater effectiveness. Upon considering the minimum costs of the OAE or the maximum costs of the Portable Automated ABR, the screening procedure employing the Portable Automated ABR is associated with higher costs and effectiveness.

2.3.6. Budgetary Implications

The number of healthcare facilities in India (as on 2017) is given in figure 2.3.5. There are 476 medical college hospitals, 779 district hospitals, 1108 sub-divisional hospitals, 5624 community health centres and 25650 primary health centres in India. Expected budget implication for implementation of 'potable Automated ABR' and OAE at a primary health centre is provided in In Table 2.3.9, and expected budget implication for implementation of Potable Automated ABR at a Community Health Centre/Sub-Divisional Hospital for hearing screening is given in Table 2.3.10.

Figure 2.3.5: Number of Health Facilities in India (as on 2017)

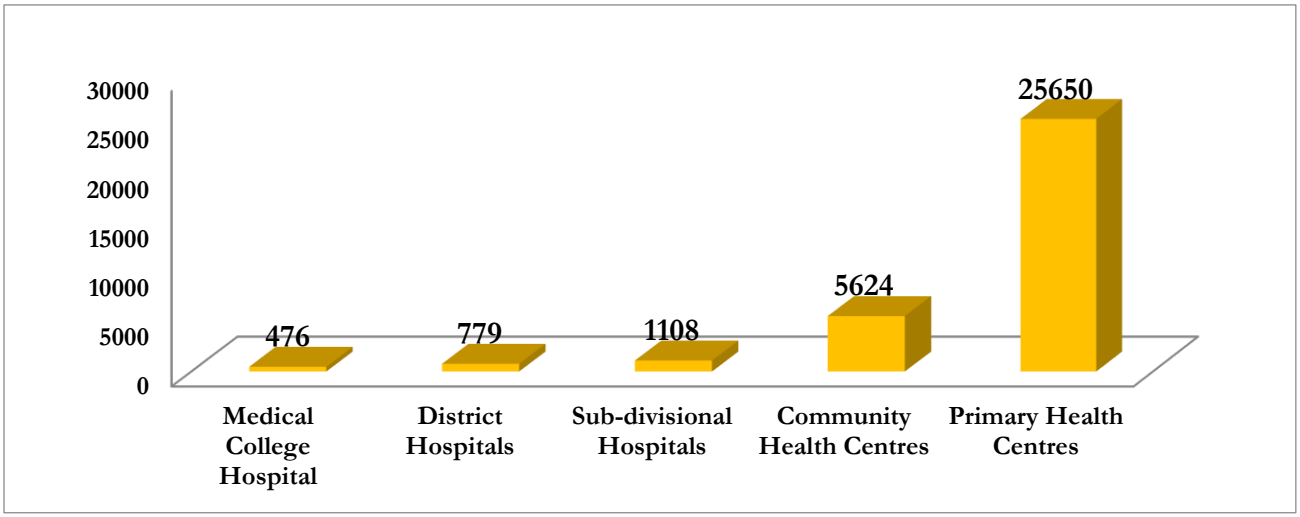


Table 2.3.9: Expected budget implication for implementation of 'Potable Automated ABR' and OAE at a Primary Health Centre

Requirements	Potable Automated ABR			OAE		
	Unit Cost (per month/per baby/per unit) in INR	Unit (HR/ device/per baby)	Annual Cost in INR per facility	Unit Cost (per month/per baby/per unit) in INR	Unit (HR/device/per baby)	Annual Cost in INR per facility
Human Resources						
Staff Nurse	15000	1	180000	15000	1	180000
Technician	18000	1	216000	18000	1	216000
Non consumables						
Medical	330000	1	330000	260000	1	260000
Nonmedical	0	0	0	0	0	0
Consumables						
Medical	16.75	300	5025	15	300	4500
Nonmedical	0	0		0	0	0
Total Cost			**731025**			**660500**
*Average number of delivery per annum is 300 (100 to 500)						

Table 2.3.10: Expected budget implication for implementation of Potable Automated ABR at a Community Health Centre/Sub-Divisional Hospital for hearing screening

Potable Automated ABR				OAE		
Requirements	**Unit Cost (per month/per baby/per unit) in INR**	**Unit (HR/device/per baby)**	**Annual Cost in INR per facility**	**Unit Cost (per month/per baby/per unit) in INR**	**Unit (HR/device/per baby)**	**Annual Cost in INR per facility**
Human Resources						
Staff Nurse	15000	1	180000	15000	1	180000
Technician	18000	1	216000	18000	1	216000
Non consumables						
Medical	330000	1	330000	260000	1	260000
Nonmedical	0	0	0	0	0	0
Consumables						
Medical	16.75	1000	16750	15	1000	15000
Nonmedical	0	0	0	0	0	0
Total Cost			**742750**			**671000**
***Average number of delivery per annum is 1000 (700 to 1200)**						

Table 2.3.11: Expected overall budget implication for implementation of Potable Automated ABR at Primary Health Centres/ Community Health Centres (CHCs)/Sub-Divisional Hospitals for hearing screening in India

	PHCs		**CHCs**		**SDHs**	
	Potable Automated ABR	OAE	Potable Automated ABR	OAE	Potable Automated ABR	OAE
Cost per facility	731025	660500	742750	671000	742750	671000
Total facilities in India	25650	25650	5624	5624	1108	1108
Total Cost (In INR)	18750791250	16941825000	4177226000	3773704000	822967000	743468000
Amount in Crore (INR)	1876	1695	418	377	82	74

In Table 2.3.11 expected overall budget implication for implementation of Potable Automated ABR at Primary Health Centres/ Community Health Centres (CHCs)/Sub-Divisional Hospitals for hearing screening in India is provided. The annual implementation cost of 'Potable Automated ABR' at a SDH/CHC will be 742750 INR and OAE will be 671000.

Chapter 3

3. Conclusions and Policy Implications

Hearing impairment is one of the leading contributors to years lived with a disability, with over 5 per cent of the world's population (360 million people) currently living with a disabling HL. Hearing impairment among infants and children across the world constitutes a particularly serious obstacle to their optimal development and education, including language acquisition. Around 5-6 in every 1000 neonates and infants have early childhood onset of sensorineural deafness or severe to profound hearing impairment with significant consequences. Deaf and hearing impaired children often experiences delayed development of speech, language and cognitive skills, which may result in slow learning and difficulty in progressing in schools and society. Congenital and early childhood onset deafness or severe to profound hearing impairment may also affect the auditory neuropath way of children at later development stage, if appropriate and optimal interventions are not provided within the critical period of central auditory pathway development. Therefore, early detection is an important element in providing appropriate support to deaf and hearing impaired babies that will help them to enjoy equal opportunities in society alongside all other children.

Ministry of Health & Family Welfare (MoHFW), Government of India, under the National Health Mission (NHM) has initiated an innovative and ambitious initiative i.e. Rashtriya Bal Swasthya Karyakram (RBSK) which aims at early identification and early intervention for children from birth to 18 years to cover 4 'D's viz. Defects at birth, Deficiencies, Diseases, Development delays including disability.

Major concern associated with the present hearing screening program under RBSK was that it is provided through the DIECs which are available at the DHH level or higher level of medical care. In India, where non-institutional deliveries are still among the prevalent practices, the vast majority of the infants are left out from the early detection and intervention for the hearing impairment. Deliveries at CHC, PHCs and community level are also among the few missed cases of hearing screening and goes without any intervention or treatment.

There were notable concerns, demand and supply side barriers in the existing hearing screening technologies in India. These points have indicated the need for a portable technology which can detect

the hearing impairment through first level of screening with better or similar diagnostic accuracy at various levels of care and at the same time it should be user-friendly also. In this context, a portable hearing screening device, "PORTABLE AUTOMATED ABR" has been developed by School of International Biodesign (SIB) start-up Portable Automated ABR Innovation Labs India Pvt Ltd under Department of Biotechnology (DBT). The device is portable in nature like OAE, and can perform the hearing test for the babies between 0-3 days with better accuracy. Also, it does not require considerable reliance on high manpower such as audiologist, junior staff nurse, and data entry operator and is user-friendly in the nature. It is perceived that 'Portable Automated ABR' is clinically efficient and cost-effective, which has been assessed in the present report.

The present study was undertaken for Health Technology Assessment (HTA) of the device and its diagnostic accuracy. We have compared the OAE hearing screening test which is commonly used under RBSK program with 'Portable Automated ABR'.

It was observed from the perspective of parents and caregivers that there is lack of awareness regarding the probable consequences of hearing impairment in India. Majority of the parents especially mothers were unaware of the long term consequences of hearing impairment and the existing government programmes on screening and treatment. It was recorded that majority of the parents are either not able to understand that hearing difficulties may be a reason for the development delay of their children, or bring them very late for the treatment. It is suggested that during the antenatal examinations, mothers and caregivers should be provided with adequate information on hearing screening in order to reduce the burden of HL and judicious demand for the hearing screening services.

The sensitivity results revealed that the 'Portable Automated ABR' device had higher sensitivity in comparison to OAE. The outcomes indicated that the sensitivity of 'Portable Automated ABR' device was 100% and specificity was 97%. The sensitivity and specificity of OAE as 69% and 68% respectively. The number of false positive cases (i.e., the newborns who were healthy but falsely detected as cases) were far less in 'Portable Automated ABR' as compared to the OAE method, resulting into lower costs (direct, indirect and intangible), and less stress and anxiety on the families new-born's. The importance of reducing the number of false negatives through screening of HL has significant impact not only on the health system but also on the society. This includes cost attributable to lost productivity, special education, vocational rehabilitation, assistive devices, and medical cost especially for cochlear implants. The societal costs are significantly higher for untreated deaf infants

so the most sustainable long terms strategy may be one which identifies the total number of cases missed i.e. the untreated.

Majority of tertiary care facilities and DHH where the hearing screening facilities are available under RBSK were located quiet far, which has significantly attributed to the increased cost on traveling for the parents of the infants who bring them for screening. Along with the travel cost it also leads to wage loss further making the situation more catastrophic. It was found that the average wage loss was highest for Medical College hospital (600 INR) or district hospital (300 INR) along with the transportation cost (441 INR). For universalizing the hearing screening services, we suggest provisioning of hearing screening services at nearest facilities such as sub-divisional hospital, CHCs, and if possible at PHCs to reduce both indirect as well as intangible cost.

The cost-effectiveness of a screening intervention is largely dependent upon two crucial factors i.e. the cost (per patient) of the intervention and the baseline prevalence (risk) of hearing impairment. In scenarios where the baseline risk is low, the intervention is less likely to be cost-effective compared to when the baseline risk is high. Further the number of false negative cases also impacts the overall cost-effectiveness of any device.

Utilising a universal strategy, although incurring additional costs in short term through screening low risk infants for hearing impairment can have major cost saving implications in the long run. This will also significantly increase the QoL of more new-borns through less reliance on special education and vocational rehabilitation programmes. When taking a societal perspective, it should be noted that the lifetime cost of treated and untreated HL will vary substantially. In particular, the developing countries such as India are associated with relatively low level of healthcare facilities, for both the treated and untreated cases. The untreated infants tend to have higher lifetime costs due to costs incurred later in life. It was also observed that undetected cases remain untreated for the remainder of the person's life, and as such will incur relatively few healthcare costs. The economic and potential health related QoL burden from missing a case is extremely high which makes early intervention fundamental. Therefore, the choice of strategy should also depend upon the importance of minimising the number of missing cases.

Our study revealed that per unit cost for screening a newborn using 'Portable Automated ABR' was lower than that of OAE device. The Portable Automated ABR device can be considered to dominate the OAE screening strategy when considering costs that falls on health system and also on society i.e.

less costly and more effective. In this model, it is assumed that cohort size is 100000 newborns and if the universal newborn hearing screening program is conducted with the 'Portable Automated ABR' at Sub-divisional, CHCs and PHCs and Mobile Health Team, the annual health system cost irrespective of true positive cases would be approximately INR 739000 for 'Portable Automated ABR' and INR 739004 for OAE for reference newborns. It was also observed that the total detected cases would be 262 by Portable Automated ABR, and OAE can detect 26 which are almost half. Per case detection cost would be 40228 with Portable Automated ABR, and 280173 by OAE. Resultant ICERs would be 97407.69. However, initially the health system may have to experience higher cost to promote allocative and technical efficiency along with equity considerations. Findings from the cost effective analyses (CEA) indicates that implementing Portable Automated ABR in the UNHS program will help in reducing the cost for the health system in long run but also to significantly reduce the societal cost.

Identifying and managing HL in infants at initial stage is likely to result into improved health outcomes in infants along with improvements in health related QoL. The device can be used as a part of UNHS in out-reach areas due to its' minimal infrastructural and manpower requirements. The screening services could be explored in out-reach areas by replacing the BOA approach of RBSK program. The device may be implemented at all delivery point such as the PHCs, CHCs, including private hospitals to increase the coverage of hearing screening among new-born's.

We have also observed from our study that the Portable Automated ABR device has an added advantage of better sensitivity and specificity and it can also test the babies' between 0-3 days more accurately as compared to OAE. Further, the test duration of per baby was recorded between 15-20 minutes (preparation of electrode sites, impediments set-up, placement of ear phones and swipe-counts), if the baby was calm and sleeping. However, we have also noticed certain key challenges and limitations associated with the current device which is mentioned as follows:

- It requires a silent environment, as crowd or noisy environment may disrupt baby's sleep and ultimately affect the testing process.
- During the test, presence of any electronic devices such as mobile charger, computer or other electric appliances etc. interfere with the test results.
- It was difficult to screen children above six months' as they were super active and wake up with a simple touch and try to remove the electrode.

It was also observed that the hearing screening can be performed by any healthcare staffs with basic skill based training (3–5 days) with basic skill of handling a baby, about infection control practice and expertise in handling smartphone. However, the interpretation of the graphical waves and test readings were not possible without intensive training or assistance from trained audiologist. We suggest that for appropriate hearing screening, each service provider should be trained properly with hands-on practices. It is also suggested that each team should have at least two members; one of them should be preferably a staff nurse. For quality assurance of the screening program, initially a supportive supervisor should monitor the service providers for at least 1-2 months.

The 'Portable Automated ABR' device is a non-invasive, safe and simple technology which can be engaged in UNHS programs. As we have experienced from our field study that there were difficulties in engaging audiologists especially in hard to reach areas, this device can be used to meet the challenges of shortage of skilled manpower as other staffs can be easily trained to handle the device with a basic training and supervision. Further, the high sensitivity and specificity of the device, as compared to OAE, not only results into lowering the number of false referred cases for HL but also to provide a better coverage for detection of hearing impairment among children. This method will undoubtedly influence the performance of any ad-hoc referral system prompted by suspicion of HL. Meanwhile, in the stipulated time period, it is assumed that the device may achieve better clinical effectiveness.

We have highlighted the continuing evolution of evidence on the accuracy of tests for hearing impairment among newborns. We think that it would be useful to do the hearing screening with better technologies in an on-going manner, particularly for the general value of the information to health-care workers who are performing hearing screening in childhood. We thus suggest that even though it might not directly impinge on a decision about early diagnostics of hearing impairment, systematic reviews of diagnostic accuracy of devices and cost effective analysis of implementing Portable Automated ABR might be used to measure hearing deficiencies at birth and should be pursued as an opportunity for better UNHS.

The 'Portable Automated ABR' device is a non-invasive, safe and simple technology that can be employed in existing UNHS programs under RBSK. In case of shortage of skilled and expert work force, it can be easily taught to other staffs. The high sensitivity and specificity of this device, compared to that of the OAE device, not only reduces the number of falsely referred cases, but also detects a greater number of newborns with hearing loss. Eventually, better clinical effectiveness may be achieved. Furthermore, considering the annual birth rate, the prevalence rate of HL, and the high

diagnostic accuracy of this device in the long run, it can be stated that this device imposes lower costs than the OAE device. Hence, this study recommends to include the above device at SDHs, CHCs and PHCs for greater coverage of UNHS. However, there is need for small scale implementation using existing infrastructure; which will help to identify the operational feasibility of the implementation as well as prevalence of cochlear implant for furthermore budgetary implication of the treatment, and large scale implementation.

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