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Economic Evaluations of Childhood Hearing Loss Screening Programmes: A Systematic Review and Critique

Rajan Sharma¹, Yuanyuan Gu^{1,2}, Teresa Y. C. Ching³, Vivienne Marnane³, Bonny Parkinson¹

¹Macquarie University Centre for the Health Economy, Sydney, NSW, Australia

²Department of Economics and Related Studies, University of York, York, UK

³National Acoustic Laboratories, Australian Hearing Hub, Sydney, NSW, Australia

Abstract

Background—Permanent childhood hearing loss is one of the most common birth conditions associated with speech and language delay. A hearing screening can result in early detection and intervention for hearing loss.

Objectives—To update and expand previous systematic reviews of economic evaluations of childhood hearing screening strategies, and explore the methodological differences.

Data Sources—MEDLINE, Embase, the Cochrane database, National Health Services Economic Evaluation Database (NHS EED), the Health Technology Assessment (HTA) database, and Canadian Agency for Drugs and Technologies in Health's (CADTH) *Grey matters*.

Study Eligibility Criteria, Participants and Interventions—Economic evaluations reporting costs and outcomes for both the intervention and comparator arms related to childhood hearing screening strategies.

Results—Thirty evaluations (from 29 articles) were included for review. Several methodological issues were identified, including: few evaluations reported outcomes in terms of quality-adjusted life years (QALYs); none estimated utilities directly from surveying children; none included disutilities and costs associated with adverse events; few included costs and outcomes that differed by severity; few included long-term estimates; none considered acquired hearing loss; some did not present incremental results; and few conducted comprehensive univariate or probabilistic sensitivity analysis. Evaluations published post-2011 were more likely to report QALYs and disability-adjusted life years (DALYs) as outcome measures, include long-term treatment and productivity costs, and present incremental results.

*Rajan Sharma rajan.sharma1@students.mq.edu.au.

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Conflict of interest The authors (RS, YG, TYCC, VM, and BP) declare that they have no financial or non-financial conflict of interest in the subject matter or materials discussed in this manuscript.

Limitations—We were unable to access the economic models and, although we employed an extensive search strategy, potentially not all relevant economic evaluations were identified.

Conclusions and Implications—Most economic evaluations concluded that childhood hearing screening is value for money. However, there were significant methodological limitations with the evaluations.

1 Introduction

Permanent childhood hearing loss is one of the most common birth conditions: 1–3 per 1000 newborns have clinically significant hearing loss [1–3]. Children may also acquire hearing loss after birth due to a range of factors, including but not limited to complications from illnesses such as measles and meningitis, or ototoxic medications [4]. Childhood hearing loss can result in delays in communication, cognition, language, reading, and social and emotional development [5]. These delays impact other lifetime sequelae, such as education and employment opportunities [5]. Advances in technology have made it possible to detect the presence of hearing loss reliably in children [6]. This can result in early intervention for hearing loss with the goal of improving child outcomes [7]. Early intervention leads to improved language, communication abilities and spontaneous speech [8–12].

Universal newborn hearing screening (UNHS) is now implemented in many countries around the world, including the USA, the UK and Australia [13–15]. Government decisions to fund screening programmes are generally determined by comparative assessment of safety and effectiveness, and sometimes cost effectiveness. Hearing screening at later ages may detect cases missed by UNHS or acquired hearing loss.

Two systematic reviews of this literature have been undertaken so far: Langer et al. [16] identified 21 economic evaluations published between 2000 and April 2012, and Colgan et al. [17] identified 22 evaluations published up to March 2011. The primary aim of Langer et al. was to develop broad guidelines for assessing and improving methodological quality regarding economic evaluations of any type of newborn screening programme, and consequently only provided a brief overview of past evaluations of newborn hearing screening [16]. Colgan et al. provided a more detailed review of different aspects (such as laterality, prevalence rates, type of hearing loss, diagnostic criteria, and resource use) of economic evaluations related to newborn hearing screening [17]. Colgan et al. found that the evaluations largely concluded UNHS to be cost effective. Both Colgan et al. and Langer et al. observed that few evaluations considered long-term costs and benefits. One of the reasons behind this was the unavailability of high-quality evidence regarding the long-term efficacy of UNHS [18]. Thus the value for money of UNHS remains unclear. Other than this, neither systematic review explored in detail the methodological differences among the evaluations that might have influenced the conclusions.

Anderson argued that simply reporting the results of economic evaluations is uninformative for decision makers due to high levels of variation in methods and limited applicability [19]. Methodological differences in evaluations may affect the incremental cost-effectiveness ratio (ICER), which is often used to inform decision making. There is a need to understand how the methodological differences among the evaluations might have driven or biased the

conclusions. For example, assuming that a ‘no screening strategy’ would have zero costs would underestimate the true costs as non-screened children may eventually be diagnosed and treated.

This review included evaluations of childhood screening at later ages as mild hearing loss may progress after birth and not all hearing loss is present at birth, which were excluded by the reviews by Colgan et al. and Langer et al. Furthermore, the influence of methodological differences among cost–benefit analyses (CBAs) related to childhood hearing screening has not been previously explored as Colgan et al. and Langer et al. did not identify any CBAs matching their inclusion criteria [16, 17]. CBAs form an important part of decision making in some countries—such as the USA, where cost-effectiveness analyses (CEAs) and cost-utility analyses (CUAs) are not widely used at the policy level [20].

Accordingly, the first aim of this paper was to update and expand previous systematic reviews by Colgan et al. and Langer et al. by conducting a systematic review of economic evaluations comparing screening strategies for childhood hearing loss published up to August 2017, including evaluations using CBAs, CEAs and CUAs. The second aim was to explore the way in which methodological differences among the economic evaluations might have influenced reported outcomes. The implications of methodological difference among economic evaluations will be discussed together with recommendations for future economic evaluations to enhance usability by policy-makers. This review broadens the search strategy employed by the past reviews by including hearing screening at later childhood ages.

2 Methods

2.1 Literature Search

Medline, EMBASE, the Cochrane database, National Health Services Economic Evaluation Database (NHS EED), the Health Technology Assessment (HTA) database, and Canadian Agency for Drugs and Technologies in Health’s (CADTH) *Grey matters* were searched on 29 August 2017. In addition, hand searching of references of identified economic evaluations was conducted to identify additional relevant economic evaluations on 18 October 2017. We used the following terms in title, abstracts and keywords: hearing loss; hearing impairment; deaf; child; infant; newborn; neonates; young; newborns; selective screening; risk factor screening; mass screening; universal screening; newborn’s hearing screening; economics (and related terms); costs and cost analysis (and related terms); cost minimisation; cost utility; economic evaluation; cost outcome; cost analysis; economic analysis; budget impact analysis; cost–benefit analysis; and cost-effectiveness analysis. See the Electronic Supplementary Material for more information. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of the search process is shown in Fig. 1.

2.2 Eligibility Criteria

The inclusion and exclusion criteria that were applied are summarised in the Electronic Supplementary Material. Articles were included if they were: (1) economic evaluations reporting costs and outcomes for both the intervention and comparator arms related to

childhood hearing-loss screening strategies; (2) published in English; (3) peer-reviewed or evaluations conducted by HTA agencies, such as the National Institute for Health and Care Excellence (NICE) in the UK, the German Agency of Health Technology Assessment (DAHTA) in Germany and the Medical Services Advisory Committee (MSAC) in Australia. Articles were excluded if they were editorials, correspondence, expert opinions, comments, reviews, and conference abstracts. Articles were also excluded if they only reported cost per case screened, but were included if they reported the cost per true positive case detected—considered to be an intermediate outcome. One author (RS) conducted the initial search and applied the inclusion/exclusion criteria. The inclusion of final papers was based on discussion with other authors (YG and BP).

3 Results

A total of 572 articles were retrieved, of which 29 articles were identified as appropriate for the review. These contained 30 economic evaluations [21–49] (see Fig. 1), including one by NICE [45], one by MSAC [37], one by the DAHTA [35] and one by the Institute of Health Economics. Of 30 evaluations included in this review, nine evaluations were published since the publications of Colgan et al. and Langer et al. [16, 17]. Only one evaluation considered the screening of school-aged children [45], two evaluations considered screening at 8–10 months [22, 34], with the rest all focusing on newborns. We excluded three evaluations that were included in the review by Colgan et al. as they did not meet the current inclusion criteria (one non-English, two cost analyses). Further, we excluded seven evaluations that were included in the review by Langer et al. for similar reasons (four non-English; three not reporting costs and outcomes for both intervention and comparator arms).

A summary of the economic evaluations is provided in Table 1.

3.1 Variations in Interventions and Comparators Across Evaluations

The evaluations mostly compared multiple interventions and comparators and thus were counted more than once. Twelve evaluations (40%) compared UNHS to targeted or no screening, nine (30%) compared different stages of screening, 16 (53%) compared different screening technologies (such as Otoacoustic Emissions (OAEs) to Automated Auditory Brainstem Response (AABR)), five (17%) compared screening locations (such as screening in hospital vs home) and three (10%) compared different screening ages (such as at birth or at 8 months of age).

Fourteen evaluations (47%) compared other strategies to ‘no screening’. Of these, a few evaluations such as that by Tobe et al. considered the ‘no screening’ strategy as ‘doing nothing’ where costs and the improvement in health outcomes were assumed to be zero. Health-related quality of life (HRQoL) and costs would be underestimated in such evaluations as some hearing-loss cases would be later identified and treated.

3.2 Variations in Perspectives Across Evaluations

The outcomes and types of resource use depend on the perspective considered. Some evaluations reported the results from more than one perspective. Most evaluations (12, 40%) adopted a societal perspective, followed by a health system perspective (10, 33%), a hospital

perspective (five, 17%), a payer perspective (three, 10%) and a government perspective (two, 7%). Five evaluations (17%) did not explicitly report the evaluation perspective. Among evaluations that adopted a societal perspective, most, although not all, included productivity costs or education costs (i.e. special education). None explicitly included family caregiving costs. Two evaluations included education costs even though they did not adopt a societal perspective. One evaluation included productivity costs (in terms of parents' travel time) although it also did not adopt a societal perspective.

3.3 Methodological Differences: Data Synthesis

Evaluations can conduct a within-study analysis or use a model to synthesise data from different sources. Model-based evaluations are typically used when it is not possible to collect all relevant health resource use and outcomes data from a single study.

The review found that 20 employed model-based evaluations, of which 16 used a decision tree (80%), and four used a Markov model (20%). The rest used a within-study analysis. The model structure can have a substantial impact on the outcome of evaluations. While decision trees are one of the simplest decision models, Markov models are better suited to capturing events that occur over time, such as progression and remission [50].

Model structures may differ in terms of: (1) the testing pathway; (2) whether downstream impacts and long-term health outcomes were included; (3) whether costs and outcomes differed by the severity of hearing loss; and (4) whether acquired cases or remission after screening were considered.

The testing pathway differed across the economic models, especially in terms of number of hearing screening stages. Screening limited to only one stage may be associated with high false-positive rates, which increase resource use in terms of diagnostic assessments, thus increasing the ICER. For example, Burke et al. found that one-stage (compared to two-stage) screening led to the detection of over 13,000 extra false-positive cases [42]. False-positive rates also depend on the technology used for screening. Lin et al. found that using OAE alone would lead to more false-positive cases (and hence more referral rates) compared to OAE-AABR or AABR alone [38].

Decision makers are best informed if economic models incorporate the downstream impact of screening on resource use in terms of treatment of hearing loss, productivity or education, and long-term health outcomes. Seventeen (57%) evaluations estimated the impact of screening on downstream resource use. The time horizon considered in the evaluations varied from a year to a lifetime. Short time horizons may not be sufficient to capture longer-term HRQoL and costs, and so may bias the ICERs. For example, if only screening costs are included but interventions are not, then total costs would be underestimated thus underestimating the true ICER. Pre-2011, only 29% (six out of 21) evaluations considered long-term treatment (medical and rehabilitation) costs (see Table 2). However, this trend improved markedly post-2011 (eight out of nine, 89%). Similarly, pre-2011, three evaluations included long-term productivity costs (16%), while post-2011, four included long-term productivity costs (44%). This shows that overall long-term costs are still rarely

considered by evaluations. These trends are presented in the Electronic Supplementary Material.

Costs and outcomes that differ by severity were included in 53% (nine of 17) of evaluations that included downstream resource use (e.g. Chiou et al. used a Markov model that included parameters related to hearing severity, and included transitions from mild to normal (remission) [46]). The remaining evaluations assumed that treatment costs and health outcomes were the same, regardless of the severity of hearing loss (e.g. Grill et al. [37]). In contrast, a cost analysis of a matched cohort of 120 hearing-impaired and 63 controls reported an approximate twofold rise in cost with increasing severity level of hearing loss [51]. This assumption may overor underestimate treatment costs and health outcomes, depending on the severity of hearing loss targeted by the screening strategy.

Finally, none of the evaluations included acquired hearing loss cases in the economic model. Only one evaluation included remission [46]. The mild hearing loss in children not identified by UNHS may progress or hearing loss may be caused after the UNHS by injury or disease. Excluding these acquired cases may result in underestimated hearing-loss treatment costs as children would be eventually identified and treated, and thus overestimated cost savings. Excluding acquired cases may also result in overestimated health outcomes, and thus health gains, as models often assume that these children have no hearing loss and thus apply utilities associated with the general population. This would underestimate the ICER. The reverse would be true if remission was excluded from the economic model. It should be noted that hearing loss acquired in adult years is unlikely to impact the ICER in the presence of discounting.

3.4 Methodological Differences: Resource Use and Costs

All evaluations included resource use and costs associated with screening instruments (primarily, Transient-Evoked OAE (TEOAE) and AABR) and diagnostic assessment (see Table 2). However, the inclusion of other resource use and costs varied widely across the evaluations. For example, 40% (12 of 30) of evaluations included costs associated with screening and diagnostic follow-up, but did not include treatment costs [21, 23–28, 32, 38, 40, 41, 52]. The ICERs reported in these evaluations, while not factually incorrect, may not be particularly useful for policy-makers who are interested in the costs of the entire treatment pathway.

None of the models included adverse event (AE)-related costs relating to screening, false positives, false negatives or treatments. Some evaluations discussed AEs related to false-positive cases, but they did not quantify associated costs in the model [23, 30, 36, 37, 45]. However, there may be significant AE-related costs involved in treatments for hearing loss. For example, a UK study reported 37 different AEs during cochlear implantation among 9% of the participants. Treatments for AEs ranged from administering antibiotics and permanent explantation to replacing electrodes and wound revision. Exclusion of costs associated with these AEs would underestimate the ICER.

Nine evaluations (75%) that adopted a societal perspective included (longor short-term) productivity impacts and nine (75%) included educational savings (see Table 2). A further

two evaluations (11%) estimated educational costs even though they did not take a societal perspective [31, 43]. Owing to the lack of data, some evaluations assumed the productivity costs. For example, one evaluation applied societal costs based on findings by Keren et al. [29], who had relied on an expert panel to estimate productivity costs based on language quotients for high and low-risk infants [42].

3.5 Methodological Differences: Definition of Hearing Loss

Almost all evaluations pre-specified the type and extent of hearing loss being identified by the screening strategy, and these differed across the evaluations. Evaluations presenting evaluation outcomes for subgroups included: severity levels (one, 3%), type of hearing loss (none) and laterality (three, 10%).

The most common definition adopted was 40 decibels (dB) hearing level (HL) in the better ear (12, 40%). The World Health Organization has adopted a similar definition [54]. Other evaluations adopted an alternative definition (such as 30 dB HL or 35 dB HL) (nine, 30%), or did not clearly specify the definition (nine, 30%). A hearing level > 40 dB largely reflects the focus of many UNHS programs. However, if cases < 40 dB HL are excluded, then the ICER would be underestimated if children with mild hearing loss are assumed to have no treatment costs and similar health outcomes to children without hearing loss.

Additionally, not all evaluations considered screening for unilateral and bilateral hearing loss. Half of the evaluations included bilateral cases only (14, 47%), a third considered unilateral and bilateral cases (11, 37%), and the remainder did not explicitly mention the type of hearing loss (five, 17%). The inclusion of bilateral cases largely reflects the focus of many UNHS programs. However, if unilateral cases are excluded, the ICER would be underestimated if children with unilateral hearing loss are assumed to have no treatment costs and similar health outcomes to children without hearing loss.

3.6 Methodological Differences: Screening and Diagnostic Strategy

The more accurate the screening method, the better the health outcomes and the fewer the resources wasted, and thus the more likely the intervention is cost effective, all else being equal. This review observed that diagnostic accuracy of OAEs and ABRs, the most commonly used screening methods, varied widely across the evaluations. The sensitivity of OAEs ranged between 77% [48] and 100% [37] and that of ABRs ranged between 80% [37] and 98% [46] (see Table 3). The specificity values of OAEs ranged between 84% [46] and 99% [33] and that of ABRs ranged between 90% [42] and 97% [52]. Only one evaluation estimated testing accuracy from a meta-analysis [52]. The other evaluations based estimates of testing accuracy on a single study.

3.7 Methodological Differences: Health Outcome Measures and Utilities

Early identification and treatment of hearing loss may lead to gains in HRQoL due to earlier communication between infants and parents in the short term and social and psychological benefits of normal communication for children with hearing loss and adults in the long term [29]. The majority of evaluations adopted 'detected true-positive cases' as the main outcome measure (21, 70%). 'Detected true-positive cases' does not consider the impact on HRQoL,

and cannot be used to compare across other treatments or conditions, thereby making it difficult to use the information to guide decisions on funding across treatments or conditions. The remaining evaluations reported outcomes in terms of QALYs gained (three, 10%), DALYs averted (three, 10%), quality-weighted child months (QCM) in addition to 'detected true-positive cases' (one, 3%), and cost-benefit ratios (two, 7%). In addition to the two evaluations included in Colgan et al. and Langer et al. [16, 17], we found that five subsequent evaluations measured HRQoL in terms of QALYs or DALYs (see Electronic Supplementary Material). Evaluations reporting DALYs applied disability weights from Mathers et al. (three, 10%) [54]. These weights were based on expert opinion and might not provide an accurate reflection of the patients' HRQoL. Conversely, QALYs are considered to better reflect gains in HRQoL [55].

None of the evaluations conducted within-study surveys to estimate the impact of childhood hearing screening on QALYs gained. Instead, all of the evaluations used modelling approaches. Three approaches to estimating the QALY gain through modelling are possible: (1) additional children with hearing loss are identified and thus treated for hearing loss with hearing aids and cochlear implants who would not otherwise be identified and treated [56], (2) children with hearing loss are identified earlier and thus treated for hearing loss earlier, which directly results in utilities gained, and (3) children with hearing loss are identified earlier, which has a long-term impact on expressive and receptive language scores, which indirectly results in utilities gained through mapping.

None of the evaluations obtained utility values directly from children, and the utility values were also not always estimated using multi-attribute utility instruments (MAUIs) or survey methods involving trade-offs between HRQoL and overall survival, such as standard gamble (SG) and time trade-off (TTO) [57]. For example, utilities were assumed by the authors themselves in two evaluations. Furthermore, one evaluation used expressive and receptive language scores of 7-to 8-year-old Australian children [58] as utility scores [46]. These utilities may also not be an accurate reflection of the true HRQoL.

The use of different utility values may also impact the final outcomes. This is because higher utilities reduce the potential for QALYs to be gained, and thus reduce the ICER. This was shown in two evaluations that adopted significantly different utilities for moderate to very severe levels [0.827, 0.744 and 0.597 (based on language scores) vs. 0.677, 0.616 and 0.485 (based on survey instruments EQ-5D, HUI3 and SF-6D)], which resulted in very different QALY gains [45, 46]. This indicates how QALY gains may be impacted based on the measure used to estimate utilities. For example, Barton et al. found that the mean utility gain before and after hearing-aid provision differed vastly for the EQ-5D (mean change = 0.01) and HUI3 (mean change = 0.06) [59]. Finally, none of the evaluations reported disutilities surrounding the false-positive cases or AEs, such as among children receiving cochlear implants (see Table 4). Their exclusion may underestimate the ICER.

3.8 Variations in Study Conclusions

Most evaluations reported childhood hearing screening to be cost effective. While nine evaluations concluded universal childhood hearing to be cost effective compared to targeted

screening or no screening (30%), one evaluation found ‘no screening’ to be cost effective (3%). Five evaluations did not conclude which strategy was cost effective (13%).

Three evaluations reported childhood screening at different ages. While Uus et al. found screening at birth to be more cost effective than screening at 8 months of age [34], Brown et al. found screening at 10 months to be more cost effective than screening at 8–9 months of age [22]. Fortnum et al., who reported screening among school-entry children, reported that no screening dominated the other screening strategies [45].

Evaluations that compared the cost effectiveness of screening methods had conflicting results. While seven evaluations (six comparing OAEs and ABRs and one comparing ABRs with Crib-O-Gram) concluded ABRs to be cost effective (23%), two concluded two-stage or three-stage OAEs to be cost effective (7%). Screening using OAE followed by AABR was more cost effective than OAE alone in two evaluations (7%). The rest (three, 10%) concluded screening with an alternative protocol other than UNHS, a community-based screening and a home-based screening to be cost effective. The conclusions about the cost effectiveness of hearing screening may be misleading [19]. For example, those evaluations determining the cost effectiveness of hearing screening strategies without considering downstream costs may have very little policy relevance.

Most evaluations reported incremental cost per true-positive case detected (21, 70%). While six evaluations reported incremental cost per QALYs gained or DALYs averted (20%), two evaluations reported cost–benefit ratios (7%) and the remainder conducted an incremental analysis per QCM (1, 3%) (see Table 1, Table 5 and Electronic Supplementary Material). It is difficult to interpret outcome measures such as ‘per true-positive case detected’ and ‘per QCM’ due to the lack of a threshold value, and hence may not be relevant for decision makers. Incremental cost per QALYs gained or DALYs averted are more accepted at the policy level [62]. For example, Fortnum et al. based their conclusion on the threshold (ICER between £20,000 and £30,000 per QALYs gained) [45]. Chiou et al. considered the threshold of \$20,000 per QALYs gained [46]. These evaluations may have more policy relevance as they reported the cost effectiveness as well as the threshold value.

Only 15 evaluations (50%) performed incremental analyses, whereby the incremental costs and outcomes were estimated compared to the next cheaper strategy. However, a trend was observed regarding this among the evaluations published pre- or post-2011. While seven out of nine (post-2011) evaluations (78%) reported incremental results, only eight out of 21 evaluations (38%) did pre-2011. This trend is illustrated in the Electronic Supplementary Material. For evaluations not reporting incremental results, we calculated incremental results from the reported results wherever possible (see Table 5 and Electronic Supplementary Material). Comprehensive sensitivity analysis surrounding the relevant parameters increases the transparency of the results for decision makers. Probabilistic Sensitivity Analysis (PSA) is preferred over univariate analyses as it considers all parameter uncertainties at once and it can be used to estimate the probability of a strategy being cost effective at a certain threshold [63]. The majority of evaluations conducted univariate deterministic sensitivity analyses (18, 60%), and only four evaluations conducted PSA (13%). Eight evaluations did not report the results of any sensitivity analyses (27%). Trend analysis showed that two evaluations each

published pre- (14%) and post-2011 (22%) carried out PSAs. This trend is also illustrated in the Electronic Supplementary Material. Moreover, a few evaluations overlooked important variables in the sensitivity analyses, for example, ‘the proportion of children treated’ [26, 36]. Around one in five (17%) evaluations excluded ‘loss to follow-up’ (attendance at diagnostic assessment after referral from screening) in the sensitivity analysis [33, 42, 47, 48] (includes two evaluations from Burke et al. [42]).

In general, the parameters that most impacted the evaluation outcomes were: prevalence rates, the diagnostic accuracy of devices, coverage, diagnosis, follow-up, referral and intervention rates, and cost of screening (see the Electronic Supplementary Material).

4 Discussion and Implications

This paper presents an update and expansion of earlier systematic reviews of economic evaluations related to screening of childhood hearing-loss screening. Previous reviews had focused on CEAs and CUAs for newborn hearing screening programs and found that they were cost effective overall [16, 17]. The major concern for these evaluations was the lack of long-term data, which may make it difficult for decision makers to decide whether screening represents value for money over the long term. Similar findings for these types of evaluations have also been reported in this review. We also included two CBAs [39, 47] that demonstrated alternative methods to evaluate costs and outcomes of screening programmes. Both studies concluded the screening programs evaluated resulted in a net benefit. Our review found that publications post-2011 are increasingly including downstream costs in terms of treatment, productivity or education impacts. This suggests an improvement in evaluation methodologies in terms of capturing costs to individuals, the community and the government, as well as the increasing access to longer-term data.

The primary objective of this review, however, was to identify the methodological differences among the evaluations and discuss the influence of these differences on outcomes. After extensive examination of different methodological aspects of included evaluations, we identified six major areas for potential improvement. We discuss them in the following and make recommendations for future practice to help reduce methodological biases and produce outcomes that are more easily interpretable by policy-makers.

First, only six (20%) evaluations measured benefit or gain using QALYs or DALYs [64], which are often recommended by reimbursement agencies to assess value for money decisions [65]. Among these evaluations, however, the approaches used to estimate the utilities or disability weights for constructing QALYs and DALYs were not based on well-established methods (MAUIs, SG or TTO) [66]. Moreover, none of the evaluations measured utilities directly from children. Utilities obtained by surveying adults may not be a good proxy of the children’s true utilities as children understand health quite differently from adults—they imply a greater emphasis on well-being and psychological health in contrast to adults whose focus is on the absence or presence of a chronic illness or disability [67]. Therefore, the utility measures developed for adult populations may not be representative of children’s utility measures as they may not include dimensions that children consider an important aspect of HRQoL [68]. Examples of utility instruments measuring HRQoL from

children include Child Health Utility-9D (CHU9D) [69–71] and EQ-5D-Y [72, 73]. We recommend that future works adopt QALYs or DALYs as the measure of benefit instead of those intermediate outcomes such as ‘detected true positive cases’ and consider utilities measured by instruments designed for children.

Second, costs and disutilities surrounding the AEs, such as those related to cochlear implantation, were not included in the evaluations, probably because only a small proportion of children experienced AEs that need re-admission and/or revision surgery post-cochlear implant. However, evidence suggests that there are sizeable costs associated with the AEs, especially in the year following implantation [74, 75]. Therefore, we recommend that future work include costs and disutilities associated with AEs whenever possible.

Third, none of the models included costs and outcomes related to acquired cases that occur post-screening. Since the hearing loss among these children would eventually be identified and treated, it could lead to underestimated hearing-loss treatment costs. Thus, we recommend that future evaluations explore the significance of excluding these cases on the ICER using scenario analysis.

Fourth, evaluations included in the review appeared to present results only at aggregated levels instead of subgroup levels. We recommend that subgroup analyses be conducted to inform decision makers about different potential screening strategies (such as in terms of unilateral vs. bilateral, type of hearing loss or different definitions of hearing loss according to dB HL). For example, it is known that greater severity of hearing loss is associated with more resource use and poorer health outcomes [38], so we recommend future evaluations to estimate differential costs and outcomes according to the severity of hearing loss.

Fifth, evaluations included in the review also tended to consider a single age group to be screened (e.g. newborn or school age). Only three evaluations compared different screening ages, but the range of age was somewhat limited (before 12 months). We therefore recommend that future evaluations also use scenario analysis to compare a broader range of ages, such as screening at birth compared to screening at later stages.

Last but not least, only four evaluations carried out PSA or included important variables such as ‘loss to follow-up’ and ‘proportion of children treated’ in sensitivity analyses. PSA can help estimate the probability of a strategy being cost effective at a given threshold value [63]. Moreover, when important variables are not included in the sensitivity analysis, it may add further uncertainty to the economic evaluation outcome. To alleviate uncertainty and better inform policy decisions, conducting PSA using all relevant parameters is warranted.

There are some limitations to our review. First, we were unable to access the economic models and original calculations that would otherwise help us to clarify the modelling issues raised in this review. Second, even though we employed an extensive search strategy covering all potentially useful information sources, it remains possible that not all relevant economic evaluations were identified. Third, we were unable to make a clear recommendation regarding the optimal screening strategy due to methodological limitations, although this was not the aim of our review. Finally, there were very few evaluations carried

out in low- and middle-income countries and the recommendations made in this review may not address all methodological differences and requirements of such evaluations.

5 Conclusion

Most economic evaluations concluded that childhood hearing screening is value for money; however, this review identified several methodological issues with the evaluations, which were illustrated with examples. Future evaluations should focus on improving methodological approaches regarding utility estimates, the inclusion of acquired hearing loss and remission, resource use and costs related to AEs and treatment, the use of subgroup analysis, and conducting comprehensive sensitivity analyses.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

RS, YG, and BP designed the systematic review. RS and BP applied the selection criteria to the identified studies. RS extracted and synthesised the data with input from BP. RS drafted the manuscript, with input from YG, TYCC, VM and BP. RS acts as guarantor for the paper and accepts full responsibility for the conduct of the review and decision to publish.

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Key Points for Decision Makers

This review updated and expanded the past reviews by including cost-benefit analyses and including hearing screening at later childhood ages, with particular focus on explaining how different aspects of the methodology on the economic outcomes.

This review provides recommendations for future economic evaluations of childhood hearing-loss screening. This should facilitate decision-makers to understand about possible uncertainties surrounding the results of related economic evaluations before making decisions. Additionally, it should result in economic evaluations that have less methodological issues and produce outcomes that are more easily interpretable by policy-makers.

Fig. 1.
Overall process of literature search

Table 1

Study design and synthesis method

Economic evaluation	Country	Population	Testing strategies	Synthesis methods	Time horizon	Discount rate	Perspective	Reported outcomes
Prager et al. (1987) [21]	USA	Infants	Targeted screening using: 1. ABR 2. Crib-O-Gram	Decision tree	NR	NR	NR	Incremental cost per detected true positive cases
Brown (1992) [22]	UK	Infants	1. Conventional screening policy (screen at 8–9 months, diagnostic assessment at 10 months) 2. Alternative policy (screen at 10 months when required/concerned) 3. No screening	Decision tree	NR	NR	Third payer	Incremental cost per detected true positive cases
White et al. (1995) [23]	USA	Infants	UNHS using: 1. TEOAE (1-stage)	Within study	NR	NR	NR	Incremental cost per detected true positive cases
Friedland et al. (1996) [24]	USA	Infants	Screening at 1. Mount Sinai Hospital 2. Other hospitals	Decision tree	NR	0%	Hospital and governmental	Incremental cost per detected true positive cases
Kemper et al. (2000) [25]	USA	Infants	UNHS using: 1. TEOAE (1-stage)	Decision tree	< 1 year	NA	health system	Incremental cost per detected true positive cases
Kezirian et al. (2001) [26]	USA (32 states)	Infants	1. 1-stage: S-ABR, 2-stage: S-ABR 2. 1-stage: S-ABR, 2-stage: None 3. 1-stage: OAE, 2-stage: OAE 4. OAE then S-ABR (those failing OAE), 2-stage: None	Decision tree	< 2 year	NR	Hospital	Incremental cost per detected true positive cases
Boshuizen et al. (2001) [27]	Netherlands	Infants	1. 2- or 3-stage AABR 2. 2- or 3-stage OAE (at home, clinic or home + clinic; and for unilateral and bilateral or bilateral only cases)	Decision tree	NR	NR	Payer and societal (partly)	Incremental cost per detected true positive cases
Vohr et al. (2001) [28]	USA	Infants	UNHS using: 1. TEOAE (1-stage) 2. AABR (1-stage) 3. TEOAE + AABR (2-stage)	Within study	1 year	NA	Hospital	Incremental cost per detected true positive cases
Keren et al. (2002) [29]	USA	Infants	1. UNHS 2. Targeted screening 3. No screening	Decision tree	Lifetime	3%	Societal	Incremental cost per detected true positive cases 6 months
Herrero and Monero-Terrero (2002) [30]	Spain	Infants	UNHS, targeted and no screening: 1. 2-stage: UNHS1 (TEOAE then AABR) UNHS2 (OAE then S-ABR) Targeted screening1 (TEOAE then AABR) Targeted screening2 (OAE then S-ABR)	Decision tree	Lifetime (74 years)	5%	Hospital, health system and societal	Incremental cost per QALY gained

Economic evaluation	Country	Population	Testing strategies	Synthesis methods	Time horizon	Discount rate	Perspective	Reported outcomes
			2. 3-stage: UNHS3 (OAE + OAE + OAE) Targeted screening 3 (OAE + OAE + OAE) 3. No screening					
Hessel et al. (2003) [31]	Germany	Infants	1. Targeted screening 2. Universal screening 3. No screening	Markov model	10 years	3%	Health system	Incremental cost per detected true positive cases
Lin et al. (2005) [32]	Taiwan	Infants	1. 1-stage TEOAE 2. 2-stage (TEOAE and AABR)	Within study	NR	NA	NR	Incremental cost per detected true positive cases
Grill et al. (2006) [33]	UK	Infants	1. Hospital-based screening 2. Community-based screening 3. No screening	Markov model	10 years	Costs: 6%, Outcomes: 1.5%	Health system	Incremental cost per QCM gained Incremental cost per detected true positive cases
Uus et al. (2006) [34]	UK	Infants	1. Screening at birth (OAE and AABR) 2. Screening at 8 months of age	Within study	10 year	NR	Societal	Incremental cost per detected true positive cases
Schnell-Inderst et al. (2006) [35]	Germany	Infants	1. UNHS 2. Targeted screening 3. No screening	Decision tree	10 years	3%	Health system	Incremental cost per detected true positive cases
Schoepflocher et al. (2007) [36]	Canada	Infants	1. 1-stage (AOAE/AABR) 2. 2-stage (AOAE + AABR)	Decision tree	Lifetime	NR	Societal	Incremental cost per detected true positive cases
Merlin et al. (2007) [37]	Australia	Infants	1. UNHS 2. Targeted screening 3. No screening If UNHS was adopted: 1. AABR-AABR 2. OAE-AABR	Decision tree	18 years	5%	Societal	Incremental cost per detected true positive cases
Lin et al. (2007) [38]	Taiwan	Infants	1. 1-stage AABR 2. 1-stage TEOAE 3. 2-stage (TEOAE and AABR)	Within study	1 year	NA	Hospital	Incremental cost per detected true positive cases
Porter et al. ³ (2009) [39]	USA	Infants	1. UNHS involving 1-stage (DPOAE alone) 2. UNHS involving 2-stage (DPOAE followed by AABR) 3. No screening	Within study	Lifetime	NR	Societal	Benefit–cost ratio
Olusanya et al. (2009) [40]	Nigeria	Infants	UNHS and Targeted screening: 1. Community-based 2. Hospital-based	Within study	NR	NR	NR	Incremental cost per detected true positive cases
Uilenburg et al. (2009) [41]	Netherlands	Infants	3 stage UNHS at: 1. At home plus screening for metabolic diseases (4–7 days of birth) 2. At home (plus home visit) (< 3 weeks)	Within study	NR	NR	Health system	Incremental cost per detected true positive cases

Economic evaluation	Country	Population	Testing strategies	Synthesis methods	Time horizon	Discount rate	Perspective	Reported outcomes
Burke et al. (2012) ¹ [42]	UK and India	Infants	3. Screening at clinic (<4 weeks of birth) 1. UNHS 2. Targeted screening	Decision tree	Unclear-seems a year cost from health system perspective as well as lifetime from societal	NR	Health system and societal	Incremental cost per detected true positive cases
Burke et al. (2012) ² [42]	UK and India	Infants	1. 1-stage universal screening (TEOAE only) 2. 2-stage universal screening process (TEOAE and AABR)	Decision tree	Unclear-seems a year cost from health system perspective as well as lifetime from societal	NR	Health system and societal	Incremental cost per detected true positive cases
Huang et al. (2012) [43]	China (8 provinces)	Infants	1. UNHS 2. Targeted screening (OAE + AABR) 3. No screening	Decision tree	15 years	NR	NR	Incremental cost per DALY averted
Tobe et al. (2013)[44]	China	Infants	1. UNHS (OAE + AABR) 2. UNHS (OAE) 3. Targeted (OAE + AABR) 4. Targeted (OAE) 5. No screening	Decision tree	NR	3%	Government	Incremental cost per DALY averted
Fortnum et al. (2016) [45]	UK	School-age children	School entry screening using 1. Hearcheck (HC) 2. Pure tone screening (PTS) 3. No screening	Decision tree	4 years	3.50%	Health system	Incremental cost per QALY gained
Chiou et al. (2017) [46]	Taiwan	Infants	1. UNHS with TEOAE 2. UNHS with AABR 3. No screening	Markov model	Lifetime	3%	Societal	1. Incremental cost per QALY gained 2. Monetary net benefit (MNB)
Chen et al. ³ (2017) [47]	China	Infants	Short-term and long-term costs and benefits of UNHS (and intervention) compared to no screening (at initial stage)	Within study	Two different time periods mentioned: 1. Birth-15 years 2. Lifetime	3%	Societal	Benefit-cost ratio
Heidari et al. (2017) [48]	Iran	Infants	1. UNHS (AABR) 2. UNHS (TEOAE)	Decision tree	1 year	NA	Health system	Incremental cost per detected true positive cases
Rivera et al. (2017) [49]	Philippines	Infants	1. UNHS 2. No screening	Decision tree	Lifetime	3%	Public payer and societal	Incremental cost per DALY averted

AABR Automated Auditory Brainstem Response, AAOE Automated Otoacoustic Emissions, DALY disability-adjusted life year, DPOAE Distortion Product Otoacoustic Emissions, HC HearCheck, NA not applicable, NR not reported, PTS pure tone screening, QALY quality-adjusted life year, QCM quality-weighted child months, S-AABR Stacked Auditory Brainstem Response, TEOAE Transient Evoked Otoacoustic Emissions, UNHS Universal Hearing Screening

Cost-benefit analyses

ξ

2-stage vs. 2-stage model

I_2

Universal vs. Targeted

I_1

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Table 2

Resource use and costs

Economic evaluation	Screening	Diagnostic assessment	Treatment of hearing loss ^b	AEs	Productivity impacts ^b	Education impacts ^b	Other costs
Prager et al. (1987) [21]	Not explicitly reported	ABR and COG Diagnostic assessment (included testing for perinatal infections, behavioural testing, impedance tympanometry and physicians fees)	None	None	None	None	None
Brown (1992) [22]	Time: For screening	Screening costs (instrument unspecified) Diagnostic assessment Referral costs Overheads	Not clearly specified	None	Productivity short-term: parents	None	None
White et al. (1995) [23]	Not explicitly reported	OAE and ABR Diagnostic assessment Staff training Overheads	None	None	None	None	Administrative costs
Friedland et al. (1996) [24]	Time: Audiologist	ABR Diagnostic assessment Salary (audiologist) and benefits	None	None	None	None	Maintenance of ABR
Kemper et al. (2000) [25]	Not explicitly reported	ABR and TEOAE Diagnostic assessment Cost of maintaining HR registry	None	None	None	None	None
Kezirian et al. (2001) [26]	Clerical work (including tracking and scheduling follow-up testing)	S-ABR and OAE Diagnostic assessment of 3 stages Tracking Overheads	None	None	None	None	None
Boshuizen et al. (2001) [27]	Not explicitly reported	OAE and AABR Diagnostic assessment Staff salary (for personnel) Transport costs of personnel Staff training	None	None	Productivity short-term: parents	None	depreciation of equipment Consumables/repairs of AAE and AABR Costs of invitations Helpdesk/monitoring
Vohr et al. (2001) [28]	Time: Audiologist	TEOAE and AABR Diagnostic assessment Staff training Salary	None	None	None	None	Administrative costs/ clerical Consumables Hours in the hospital
Keren et al. (2002) [29]	Time for nurse to question parents (to identify risk factors)	AABR and TEOAE Diagnostic assessment Tracking Machines, supplies, tracking software Salary	Medical long term (treatment: NR) Rehabilitation	None	Productivity long term: children	Special education	Assistive devices
Herrero and Monero-Ternero (2002) [30]	Not explicitly reported	TEOAE, AABR, S-ABR, targeted screening Diagnostic assessment	Medical long term (treatment: Hearing aid Cochlear implants) Rehabilitation	None	None	Special education	Disability allowance for children

Economic evaluation	Screening	Diagnostic assessment	Treatment of hearing loss ^b	AEs	Productivity impacts ^b	Education impacts ^b	Other costs
Hessel et al. (2003) [31]	Not explicitly reported	S-TEOAE/S-S-ABR Diagnostic assessment Consumables (probe tips, couplers, electrode) Tracking	Medical (but not clear about long term) (treatment: Cochlear implants Hearing aid) Rehabilitation	None	None	Special education	None
Lin et al. (2005) [32]	Time: for screening the lifespan of machine equipment	TEOAE and AABR Diagnostic assessment (ABR) Salary: initial screener	None	None	None	None	Consumables Administrative costs
Grill et al. (2006) [33]	Time Visit frequency Quantity, make and model of computers and printers Quantity and make of consumables	Screening cost σ (device: NR) Diagnostic assessment (ABR) Salary Staff training (initial and refresher) Recruitment	None	None	None	None	IT costs, capital costs such as building, direct over-heads (lighting, heating, cleaning)
Uus et al. (2006) [34]	Number and duration of Staff training sessions	TEOAE and AABR Diagnostic assessment False positive audiological costs Salary (rural technician) Staff training Staff travel costs Consultation fees for hearing specialist	Not clearly specified	None	Productivity short-term: parents and children	None	IT costs, overheads, building capital and equipment costs, lighting, heating and cleaning
Schneil-Inderst et al. (2006) ** [35]	Not explicitly reported	TEOAE and AABR Diagnostic assessment	None	None	None	None	None
Schofflocher et al. (2007) [36]	Time taken to screen/baby by an audiologist	AABR and AOAE Diagnostic assessment Specialist visit (audiologist)	Medical long term (treatment: Hearing aids Cochlear implants) Rehabilitation [Source: Keren et al.]	None	None	None	Costs associated to delayed language skills
Merlin et al. (2007) [37]	Time: coordinator, clerk, screener and audiologist Screening time	AABR and OAE Diagnostic assessment Tracking Salary (per hour) for programme coordinator	Medical long term (treatment: Cochlear implants Hearing aids) Rehabilitation	None	Productivity long term: children (but lack of data cited)	Special education	None
Lin et al. (2007) [38]	Lifespan of machine equipment	TEOAE and AABR Diagnostic assessment Salary: initial screener	None	None	None	None	Consumables Administrative costs
Porter et al. (2009) [39]	Employee time to screen babies/hour	DPOAE and AABR (both stages) Diagnostic assessment (ABR) Disposable tips Salary/hour	Medical long term (treatment: NR)	None	Productivity long term: children	Special education	None
Olusanya et al. (2009) [40]	Not explicitly reported	TEOAE and AABR Diagnostic assessment (ABR, tympanometry and visual reinforcement audiometry)	None	None	None	None	Consumables (electrodes, earphones, shipping and duty charges, printer, computer, accessories and software)

Economic evaluation	Screening	Diagnostic assessment	Treatment of hearing loss ^b	AEs	Productivity impacts ^b	Education impacts ^b	Other costs
Uilenburg et al. (2009) [41]	Time: Staff	Salary (project coordinator, screeners, support staff, back-up staff member, data entry clerk) TEOAE and AABR Diagnostic assessment Salary Staff training	None	None	None	None	Transport (parents) Administrative costs
Burke et al. (2012) ¹ [42]	Time for coordinator, screener, clerk, audiologist	TEOAE and AABR Diagnostic assessment Components of TEOAE per infant (probe tips, probes, supply costs) Components of AABR per infant (electrodes, machine calibration, supply costs, false positive)	Medical long term (treatment: NR) Rehabilitation	None	Productivity long term: children	Special education	Assistive devices
Burke et al. (2012) ² [42]	Time for coordinator, screener, clerk, audiologist	TEOAE and AABR Diagnostic assessment Components of TEOAE per infant (probe tips, probes, supply costs) Components of AABR per infant (electrodes, machine calibration, supply costs, false positive)	Medical long term (treatment: NR) Rehabilitation	None	Productivity long term: children	Special education	Assistive devices
Huang et al. (2012) [43]	Not explicitly reported	AABR and OAE Diagnostic assessment (ABR device) Staff training Salary	Medical long term (treatment: Hearing aids Cochlear implants Drugs) Rehabilitation	None	None	Special education	Transportation charges for diagnosis and treatments Capital costs [#] Recurrent costs [*] Capital investments ^δ
Tobe et al. (2011) [44]	Not explicitly reported	OAE and AABR Diagnostic assessment Database management Salary Staff training	Medical long term (treatment: Cochlear implants Hearing aids) Rehabilitation	None	None	None	Transportation charges for diagnostic procedures and treatments Capital investments in buildings, furniture, and equipment Staff transport
Fortnum et al. (2016) [45]	Average duration of screening test	PTS and HC screener Diagnostic assessment Salary	Medical long term (treatment: Hearing aids Digital and bone anchored Cochlear implants (unilateral and bilateral) Others: Grommet surgery (middle ear)	None	None	None	Travel cost for parents and children
Chiou et al. (2017) [46]	Compliance rate	TEOAE and AABR Diagnostic assessment	Medical long term (treatment: Hearing aids) Rehabilitation	None	Productivity long term: children	Special education	None

Economic evaluation	Screening	Diagnostic assessment	Treatment of hearing loss ^b	AEs	Productivity impacts ^b	Education impacts ^b	Other costs
Chen et al. (2017) [47]	Not explicitly reported	TEOAE and AABR Diagnostic assessment Components of hearing aids and cochlear implants (per year) Initial screening/infant Re-screening/infant	Medical long term (treatment; Hearing aids Cochlear implants Hospitalisation) Rehabilitation	None	Not explicitly reported	Special education	Disability allowance for children
Heidari et al. (2017) [48]	Average number of working days in a year for the employees Devices lifespan Average duration of screening device in a day Mean number of screening/year	AABR and OAE Diagnostic assessment (ABR device) Location (rent) Monthly overhead costs Salary	None	None	None	None	OAE and AABR related Maintenance-AABR and OAE
Rivera et al. (2017) [49]	Lifetime of hearing aid Number of hearing aids needed in lifetime Number of rehabilitative sessions needed per early age and late age Years of education (early and late)	OAE and AABR Diagnostic assessment (ABR) Consultation fees for hearing specialist	Medical long term (treatment; Hearing aids) Rehabilitation	None	Productivity long term: children	Elementary and high school education Special education	None

AABR Automated Auditory Brainstem Response, AEs adverse events, AOAE Automated Otoacoustic Emissions, COG Crib-O-Gram, DALY disability-adjusted life year, DPOAE Distortion Product Otoacoustic Emissions, HC HearCheck, IT information technology, NHS National Health Service, PTS pure tone screening, QALY quality-adjusted life year, QCM quality-weighted detected child months, S-ABR Stacked Auditory Brainstem Response, TEOAE Transient Evoked Otoacoustic Emissions, UNHS Universal Hearing Screening

Costs related to office buildings, furniture and equipment

* Costs related to materials and supplies, utilities, equipment maintenance, database management

δ Capital investments of office buildings, furniture and equipment were annualized by depreciation

σ Home and hospital-based screening compared

** The full report is in German, so it was not possible to be specific about the cost types included in the evaluation

^a Long-term cost saving based on observational data and expert opinion

^b Considered to have included downstream resource use: (i) treatment of hearing loss; (ii) long-term productivity; and (iii) education impacts

¹ Universal vs. Targeted

² 1-stage vs. 2-stage

Table 3

Diagnostic accuracy and prevalence rates

Economic evaluation	Sensitivity			Specificity			Source	Hearing loss prevalence
	OAEs	ABRs	Others	OAEs	ABRs	Others		
Prager et al. (1987) [21]	–	100%	COG: 75%	–	86%	COG: 71%	Single study	0.2%
Brown (1992) [22]	–	–	8–9 months: Conventional/alternative: 60% 10 months: Conventional/alternative: 60%	–	–	8–9 months: Conventional/alternative: 97% 10 months: Conventional/alternative: 95%	Single study	NR
White et al. (1995) [23]	NR	NR	NR	NR	NR	NR	NR	0.595%
Friedland et al. (1996) [24]	NR	NR	NR	NR	NR	NR	NR	0.15–0.6%
Kemper et al. (2000) [25]	80%	98%	Targeted screening: 59%	92	96%	Targeted screening: 95%	Single study	0.11%
Kezirian et al. (2001) [26]	95%	95%	OAE then S-ABR: 90.25% **	90%	95%	OAE then S-ABR: 95%	Single study	0.35%
Boshuizen et al. (2001) [27]	NR	NR	NR	NR	NR	NR	NR	NR
Vohr et al. (2001) [28]	NR	NR	NR	NR	NR	NR	NR	0.2%
Keren et al. (2002) [29]	95%	95%	–	85%	90%	–	Single study	HR: 0.83% LR: 0.6%
Herrero and Monero-Ternero (2002) [30]	NR	NR	UNHS: 78.4–90.25% TNHS: 46.3–53.2%	NR	NR	UNHS: 95–99.6% TNHS: 99.8–99.9%	Single study	Two rates considered for analysis: 0.11% and 0.35%
Hessel et al. (2003) [31]	–	–	S-TEOAE/S-ABR: 96%	–	–	S-TEOAE/S-ABR: 89%	Single study	0.15%
Lin et al. (2005) [32]	NR	NR	Diagnostic ABR:	NR	NR	NR	NR	Bilateral (TEOAE): 0.22%; Unilateral (TEOAE): 0.23% Bilateral (TEOAE + AABR): 0.1% Unilateral (TEOAE + AABR): 0.2%
Grill et al. (2006) [33]	96%	–	–	99%	–	–	Single study	0.15%
Uus et al. (2006) [34]	–	–	Screening at birth > 90%	–	–	Screening at 8 months of age 95%	Single study	NR
Schnell-Inderst et al. (2006) [35]	NR	NR	Range reported for: Echoscreeen/S-TOAE, GSI60/D-DPOAE, Blitzbera/AABR, Erosca/S-DPOAE modus, S-TOAE modus: 99.4–100%	NR	NR	Range reported for: Echoscreeen/S-TOAE, GSI60/D-DPOAE, Blitzbera/AABR: 82.4–92.3%	Multiple studies	0.15%
Schopfloch et al. (2007) [36]	80%	98%	Targeted screening: 59%	92	96%	Targeted screening: 95%	Single study	0.11%

Economic evaluation	Sensitivity			Specificity			Source	Hearing loss prevalence
	OAEs	ABRs	Others	OAEs	ABRs	Others		
Merlin et al. (2007) [37]	100%	80%	—	92%	96%	—	Single study	Bilateral: 0.13% ^{ϕ} Unilateral: 0.06% ^{ϕ}
Lin et al. (2007) [38]	NR	NR	NR	NR	NR	NR	NR	0.51%
Porter et al. (2009) [39]	NR	NR	NR	NR	NR	NR	NR	0.2%
Olusanya et al. (2009) [40]	NR	NR	NR	NR	NR	NR	NR	0.6%
Uilenburg et al. (2009) [41]	NR	NR	NR	NR	NR	NR	NR	NR
Burke et al. (2012) ¹ [42]	95%	95%	—	85%	90%	—	Single study	Overall ^{ψ} : UK: 0.15%, India: 0.496
Burke et al. (2012) ² [42]	95%	95%	—	85%	90%	—	Single study	Overall ^{ψ} : UK: 0.15%, India: 0.496
Huang et al. (2012) [43]	95%	—	—	95%	—	—	Single study	Overall: 0.30% HR: 3%
Tobe et al. (2013) [44]	90%	—	OAE + AABR: 95%	85%	—	OAE + AABR: 95%	Single study	0.2%
Fortnum et al. (2016) [45]	—	—	PTS: 95.9% HC: 88.7%	—	—	PTS: 79.8% HC: 83.8%	Single study	0.46%
Chiou et al. (2017) [46]	80%	98%	—	84%	96%	—	Single study	0.13%
Chen et al. (2017) [47]	NR	NR	NR	NR	NR	NR	NR	1.66%
Heidari et al. (2017) [48]	77%	93%	—	93%	97%	—	Meta-analysis	0.5%
Rivera et al. (2017) [49]	86%	—	—	97.3%	—	—	Single study	0.138%

AABR Automated Auditory Brainstem Response, *COG* Crib-O-Gram, *DPOAE* Distortion Product Otoacoustic Emissions testing, *GSIG* Grason-Stadler Incorporated, *HC* HearCheck, *HR* high risk, *LR* low risk, *NR* not reported, *OAE* Automated Otoacoustic Emissions, *PTS* pure tone screening, *QCM* quality-weighted detected child months, *S-AABR* Stacked Auditory Brainstem Response, *TEOAE* Transient Evoked Otoacoustic Emissions, *TOAE* Transient Otoacoustic Emissions, *TNHS* Targeted Newborn Hearing Screening, *UNHS* Universal Newborn Screening

^{ψ} HR: UK—0.800%, India—0.796%; LR: UK—0.08%, India—0.463%

* Exact source not found. The citation that closely resembles the value is the study by Mason et al., who reported the sensitivity of 90% (95% CI: 78–96)

** Calculated by multiplying the specificities for OAE and S-ABR (95% × 95% = 90.25%)

^{ϕ} Median

¹Universal vs. Targeted

²1-stage vs. 2-stages

Table 4

Utilities and disability weights

Economic evaluation	Source	Population surveyed	Country	Methods	Sample size	Results
Brown (1992) [22]	Assumed	None	NR	Assumed	NA	Hearing problems * TP: 0.6 TP10: 0.5 HL: 0.3 HL10: 0.2 FN8: 0.1 FN10: 0.0 No hearing problems ** TN8: 1.0 TN10: 0.95 NSW10: 0.925 NSW: 0.9 SW10: 0.875 SW: 0.85 FP8: 0.8
Herrero & Monero-Ternero (2002) ^a [30]	Assumed	None	Spanish tariffs used	Assumed	NA	EQ-5D *** [for 0.11% prevalence] TNHS1: 0.0019 TNHS2: 0.0022 TNHS3: 0.0021 UNHS1: 0.0033 UNHS2: 0.0038 UNHS3: 0.0035 HUI3 *** [for 0.11% prevalence] TNHS1: 0.0032 TNHS2: 0.0037 TNHS3: 0.0034 UNHS1: 0.0054 UNHS2: 0.0062 UNHS3: 0.0058
Grill et al. (2006) [33]	Expert opinion	None	UK	Expert opinion	NR	Detected < 6 months: 1.0 Not detected in one year: Moderate: 0.90, Moderate/month: 0.875 (50% of hearing disorder considered moderately impaired) Severe/profound: 0.85
Huang et al. (2012) [43]	Mathers et al. [54]	None	NR	Expert opinion	NR	Treated: 0.216 Untreated: 0.168
Tobe et al. (2013) [44]	Mathers et al. [54]	None	NR	Expert opinion	NR	NR
Fortnum et al. (2016) [45]	Barton et al. [59] (for severity)	Hearing impaired adults (before and after hearing-aid provision)	UK	EQ-5D Health Utilities Index Mark III SF-6D	609 patients	Moderate 0.677 Severe: 0.616 Profound: 0.485
Fortnum et al. (2016) [45]	Bissonni et al. [60] (for grommet surgery)	None	None	None	None	Grommet surgery 0.995
Fortnum et al. (2016) [45]	Assumed (for mild, minimal, conductive hearing loss and hearing aid)	Assumed	UK	Assumed	NA	Minimal: 1.0 Mild: 1.0 Conductive (unilateral/bilateral): 0.677 Hearing aid: 1.0
Fortnum et al. (2016) [45]	Summerfield et al. [61] for unilateral and bilateral	Adult patients undergoing unilateral implantation and	UK	Patients: Mark III (HUI3)	Patients: 202 General population: 70	Cochlear implant: Bilateral: 0.965 Unilateral: 0.934

Economic evaluation	Source	Population surveyed	Country	Methods	Sample size	Results
		general population		General population: TTO		
Chiou et al. (2017) [46]	Wake et al. [58]	Children with fitted hearing aid for congenital HL, 7–8 years ($n = 89$)	Australia	CELF language scores	89	Mild: 0.888 Moderate: 0.827 Severe: 0.744 Very severe: 0.597
Rivera et al. (2017) [49]	Mathers et al. [54]	None	NR	Expert opinion	NR	Treated: 0.12 Untreated: 0.333

CELF Clinical Evaluation of Language Fundamentals, *DALY* disability-adjusted life year, *HL* hearing loss, *HUI3* Health Utilities Index Mark 3, *NA* not applicable, *NR* not reported, *NSW* well but no symptoms, *QALY* quality-adjusted life year, *QCM* quality-adjusted child months, *SF-6D* Short-Form Six-Dimension, *SW* well but having symptoms, *TNHS* Targeted Newborn Hearing Screening, *UK* United Kingdom, *UNHS* Universal Newborn Hearing Screening

* TP: True positive; FN: False negative; HL: children with hearing loss; 8 and 10 represent screening at 8–9 months and at 10 months, respectively

** TN: True negative; FP: False positive; 8 and 10 represent screening at 8–9 months and at 10 months, respectively

*** Utilities for 0.35% not presented here

^a TNHS1 and UNHS1 protocol involved screening by TEOAE followed by AABR; UNHS2 and TNHS2 involved screening by OAE followed by S-ABR; TNHS3 and UNHS3 involved screening by 3-stage OAE

Table 5

Incremental costs and outcomes

Economic evaluation	Country, currency, price year	ICER Intervention arm	Authors' conclusions
Prager et al. (1987) [21]	USA, USD, price year not reported	Incremental cost per true positive case detected—compared to ABR: COG: \$22,591	ABR more cost effective
Brown (1992) ^b [22]	UK, GBP, 1986	Alternative policy (in terms of unit output)—Incremental cost per unit output per screened child a. Reference b. £12.47 c. £10.22 Conventional: dominated No screening not considered due to lack of information	Screening for clinical indication at 10 months cost effective
White et al. (1995) [23]	USA, USD, 1993	Incremental cost per true positive case detected: UNHS: \$979 Targeted screening: Dominated	UNHS more cost effective
Friedland et al. (1996) [24]	USA, USD 1995	Incremental cost per true positive case detected: Base case model: \$7936.83 Government: Dominated	Screening at other hospitals than at Mount Sinai Hospital cost effective
Kemper et al. (2000) [25]	USA, USD, NR	Incremental cost per true positive case detected: \$23,930	UNHS more cost effective
Kezirian et al. (2001) [26]	USA, USD, 1999	Incremental cost per true positive case detected: S-ABR/S-ABR: \$8112 S-ABR/None: \$9470 OAE/OAE: \$5113 OAE + S-ABR/None: \$7996	2- stage OAE/OAE most cost effective strategy
Boshuizen et al. (2001) ^b [27] ^{pp}	Netherlands, USD, Price year not clear	Incremental cost per true positive case detected—compared to OAE-2C(B): OAE-3C(B + U): \$1846,429 OAE-2C + H(B + U): \$208,841 OAE-2C(B + U): dominated OAE-2H(B + U): \$759,315 AABR-2C(B + U): dominated On considering only bilateral and unilateral cases (i.e. after excluding the bilateral only cases) Compared to OAE-3C(B + U): OAE-2C + H(B + U): \$208,841 OAE-2C(B + U): dominated OAE-2H(B + U): \$759,315 OAE-3C(B + U): dominated	3- stage OAEs cost effective [Inconclusive about home vs. child health clinic screening]
Vohr et al. (2001) [28]	USA, USD, 1998	Incremental cost per true positive case detected: AABR: \$1749 AABR + TEOAE: \$754	AABR more cost effective
Keren et al. (2002) ^b [29]	USA, USD, 2001	Incremental cost per true positive case detected by 6 months: \$16,000	UNHS more cost effective
Herrero & Monero-Temero (2002) ^b [30]	Spain, USD, Price year not reported	Incremental cost utility ratio: TNHS1: \$177 TNHS2: \$165 TNHS3: \$174 UNHS1: \$670	TNHS more cost effective: If direct costs only considered UNHS more cost effective: if indirect costs also considered

Economic evaluation	Country, currency, price year	ICER Intervention arm	Authors' conclusions
Hessel et al. (2003) ^b [31]	Germany, Euro, 1999	UNHS2: \$818 UNHS3: \$730 (Strategy with the lowest ICER recommended) Incremental cost per true positive case detected UNHS: €13,395 TS: €6715	UNHS more cost effective
Lin et al. (2005) [32]	Taiwan, USD, 2004	Incremental cost per true positive case detected: AABR + TEOAE: \$917	AABR + TEOAE ³
Grill et al. (2006) [33]	UK, GBP, 2002	Incremental costs per true positive case detected: £2423 Incremental cost per QCM: £25	Hospital and community-based strategies equally cost effective
Uus et al. (2006) ^b [34]	UK, GBP, 2003	Incremental cost per true positive case detected: £12,526	UNHS more cost effective
Schnell-Inderst et al. (2006) [35]	Germany, Euro, 2004	Incremental cost per true positive case detected (compared to no screening): Targeted: €5201.05 UNHS: €4,463.42	Targeted screening more cost effective
Schopflocher et al. (2007) ^b [36]	Canada, CAD, NR	Incremental cost per true positive case detected Compared to 1-stage AABR 1-stage AOAIE: dominated 1-stage vs. 2-stage***: \$7575	AABR more cost effective
Merlin et al. (2007) ^b [37]	Australia, AUD, 2003	For birth cohort of 4000 infants/year: ICER per true positive case detected Compared to no screening: UNHS (OAE-AABR) ^f : \$9300 UNHS (OAE-AABR) ^c : \$10,100 UNHS (AABR) ^f : \$12,500 UNHS (AABR) ^c : (\$17,600) Compared to TS UNHS 2-stage (OAE-AABR) ^f : \$8800 UNHS 2-stage (OAE-AABR) ^c : \$9500 UNHS (AABR) ^f : \$14,600 UNHS (AABR) ^c : \$23,800	Short-term cost effectiveness of UNHS may be misleading. May be cost effective in the long-term
Lin et al. (2007) ^b [38]	Taiwan, USD, 2005	Incremental cost per true positive case detected: TEOAE: \$61,525 AABR + TEOAE: \$531	AABR more cost effective
Porter et al. ³ (2009) ^b [39]	USA, USD, 2004	No definite results given. Suggests that benefits outweigh costs by the ratio of 25:1 when high benefit and low costs are considered	UNHS more cost effective
Olusanya et al. (2009) [40]	Nigeria, USD, price year not reported	Incremental cost per true positive case detected—compared to community-UNHS: Community-TNHS: \$1221 Other strategies dominated If no screening strategy with \$0 cost and 0 effect was considered (as reference), the Community-UNHS would have ICER: \$26,809	Community-based screening more cost effective

Economic evaluation	Country, currency, price year	ICER Intervention arm	Authors' conclusions
Uilenburg et al. (2009) [41]	Netherlands, USD, price year not reported	Incremental cost per true positive case detected—compared to A: B: \$79,688 C: Dominated	Home screening including metabolic diseases (B) more cost effective
Burke et al. (2012) ^{1b} [42]	UK, GBP, 2010	Incremental cost per true positive case detected: £36,181 (Health system) £296,857 (societal) (cost-saving)	UNHS more cost effective
Burke et al. (2012) ^{1b} [42]	India, INR, 2010	INR-157,084 per true positive case detected Societal –INR 8418,834 (cost saving)	
Burke et al. (2012) ^{2b} [42]	UK, GBP, 2010	Incremental cost per true positive case detected: £120,972	Not explicitly reported
Burke et al. (2012) ^{2b} [42]	India, INR, 2010	INR 926,675 per true positive case detected	
Huang et al. ^a (2012) ^b [43]	China, RMB, USD, 2009	ICER per DALYs averted for UNHS: Ranged from \$18,000 for Guangdong to \$500,000 for Guangxi TS: Ranged from \$4000 for Guangdong to \$83,000 for Guangxi	UNHS and TS both demonstrated cost effectiveness in rich provinces; TS in poor provinces
Tobe et al. (2012) ^b [44]	China, USD, 2009	Compared to TS (OAE): UNHS OAE: \$55,000 OAE + AABR: \$43,000 TS OAE + AABR: \$127,000	OAE + AABR more cost effective
Fortnum et al. (2016) ^b [45]	UK, GBP, 2012–2013	PTS vs. no screening: PTS less effective and more costly HC vs. no screening: HC less effective and more costly HC vs. PTS: PTS more effective and less costly	No screening more cost effective
Chiou et al. (2017) ^b [46]	Taiwan, USD, NR	TEOAE vs. no screening: TEOAE less costly more effective AABR vs. no screening: AABR less costly more effective AABR vs. TEOAE: \$6723 per QALY gained	AABR more cost effective
Chen et al. ^a (2017) ^b [47]	China, RMB and USD, 2012	Short-term cost–benefit ratio: 1:2.01 Long-term cost–benefit ratio: 1:7.52	UNHS more cost effective
Heidari et al. (2017) [48]	Iran, USD, NR	AABR vs. OAE: AABR less costly more effective	AABR more cost effective
Rivera et al. ^a (2017) ^b [49]	Philippines, Pesos, 2015	Incremental cost per DALY gained: PhP 105,376 ^e	UNHS more cost effective

Calculation of incremental cost per true positive case detected involved the following steps: First, detected cases/screened (Yield) was obtained by dividing cost per screening by cost per cases detected. Then, the incremental cost per screening (incremental cost) was divided by incremental yield (incremental outcome) to obtain the incremental cost per true positive case detected

AABR Automated Auditory Brainstem Response, AAOAE Automated Otoacoustic Emissions, AUD Australian dollars, CAD Canadian Dollars, COG Crib-O-Gram, DALY disability-adjusted life year, DPOAE Distortion Product Otoacoustic Emissions, GBP Pound Sterling, HC HearCheck, ICER incremental cost-effectiveness ratio, INR Indian Rupees, NA not applicable, NHS National Health Service, NR not reported, PhP Philippine Pesos, PTS pure tone screening, QALY quality-adjusted life year, QCM quality-weighted detected child months, RMB Renminbi, S-ABR Stacked Auditory Brainstem Response, TEOAE Transient Evoked Otoacoustic Emissions, TNHS Targeted Newborn Hearing Screening, TOAE Transient Otoacoustic Emissions, UNHS Universal Hearing Screening, USD United States Dollars

^a Combined societal costs for Burke et al.¹ and Burke et al.²

$$\phi = \frac{(\text{cost of UNHS} - \text{Cost of NS})}{(\text{DALY loss of UNHS} - \text{DALY loss of NS})}$$
 Authors preferred to carry out sensitivity analysis surrounding the ICER instead of calculating the ICER itself. NS = no screening

Sensitivity of protocol given instead of the number of infants

^a Total instead of mean costs and outcomes reported

^b Considered to have included downstream resource use: (i) treatment of hearing loss; (ii) long-term productivity; and (iii) education impacts

^c Using couplers

^d Using probe tips

^{pp} Acronyms used include: OAE-2C for 2-stage OAE at Clinic, OAE-2C + H: 2-stage OAE at home and clinic; B + U = Bilateral and unilateral; B: Bilateral only

¹ Universal vs. Targeted

² 1-stage vs. 2-stage

³ Cost-effective alternative was decided based on the fact that TEOAE + AABR leads to reduced additional diagnostic testing. Total cases considered in the model was 100,000. □ See Table 2 for cost types included