

Economic Evaluation and Research Prioritization of Adult Hearing Screening in the  
United States

by

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Dissertation submitted in partial fulfillment of  
the requirements for the degree of Doctor  
of Philosophy in the Department of  
Population Health Sciences in the Graduate School  
of Duke University

2022

ABSTRACT

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## **Abstract**

Hearing loss affects over 500 million people globally, is the fourth leading cause of years lived with disability worldwide, and carries an economic burden of over \$700 billion annually.<sup>1-3</sup> In the United States (US), one in three persons over the age of 60 have hearing loss, yet only 20% of those with hearing loss utilize a hearing aid.<sup>4,5</sup> This treatment gap leaves 80% of hearing-impaired older adults without treatment that has proven effectiveness in enhancing quality of life, reducing loneliness, and potentially improving physical and cognitive health.<sup>6,7</sup> While early hearing aid provision and use is associated with better long-term hearing outcomes, patients may wait on average 10-15 years before seeking treatment for hearing loss due to several factors including psychosocial factors, cost, and lack of awareness of their hearing loss.<sup>8,9</sup>

Adult hearing screening programs have the potential to address the failure in detection and diagnosis that contributes to the majority of patients with hearing loss not receiving effective treatment. One randomized trial of a hearing screening program in US veterans found increased uptake of hearing aids in screened patients.<sup>10</sup> However, current US clinical guidelines on adult hearing screening are conflicting, with some recommending frequent screening and others giving no guidance due to sparse data.<sup>11</sup>

While international stakeholders have increasingly called for investment to alleviate the impact of hearing loss, US policymakers do not currently have sufficient

quantitative evidence around long-term clinical and economic effects of adult hearing screening programs.<sup>12-14</sup> Further, both the NIDCD and National Academy of Medicine have called for research identifying cost-effective strategies for hearing loss diagnosis and treatment. Decision analysis is one quantitative method that can synthesize existing evidence to clarify long-term dynamics and trade-offs inherent in hearing health policy decisions. Indeed, decision models have had wide-reaching policy implications in the hearing health care space.<sup>15</sup> For example, these models have demonstrated the projected cost-effectiveness of pediatric and adult cochlear implantation and newborn hearing screening, informing coverage decisions of cochlear implants and newborn hearing screening guidelines in the US and internationally. Decision analysis can also identify optimal areas for future research investment through value of information (VOI) analysis. However, there is a dearth of evidence regarding long-term impacts of adult hearing screening policies: a recent systematic review identified no decision models that evaluate adult hearing screening programs in the US.<sup>16</sup> This dissertation addresses this evidence gap via three specific aims with the long-term goal of helping policymakers identify the most effective and cost-effective adult hearing screening strategies for their populations.

*Aim 1: To develop and validate a decision modeling framework of adult hearing screening, diagnosis, and treatment.*

We collaborated with the Lancet Commission on Hearing Loss to outline model structure, identify input data sources, and calibrate/validate DeciBHAL-US (Decision model of the Burden of Hearing loss Across the Lifespan). We populated the model with literature-based estimates and validated the conceptual model with key informants. We validated key model endpoints to the published literature, including: 1) natural history of sensorineural hearing loss (SNHL), 2) natural history of conductive hearing loss (CHL), and 3) the hearing loss cascade of care. We reported the coefficient of variance root mean square error (CV-RMSE), considering values  $\leq 15\%$  to indicate adequate fit. For SNHL prevalence, the CV-RMSE for model projected male and female age-specific prevalence compared to sex-adjusted National Health and Nutrition Examination Survey (NHANES) data was 4.9 and 5.7%, respectively. Incorporating literature-based age-related decline in SNHL, we validated mean four-frequency average hearing loss in the better ear (dB) among all persons to longitudinal data (CV-RMSE=11.3%). We validated the age-stratified prevalence of CHL to adjusted NHANES data (CV-RMSE=10.9%). We incorporated age- and severity-stratified time to first hearing aid (HA) use data and HA discontinuation data (adjusted for time-period of use) and validated to NHANES estimates on the prevalence of adult HA use (CV-RMSE=10.3%). Our results indicate adequate model fit to internal and external validation data. Future incorporation of cost and severity-stratified utility data will allow for cost-effectiveness

analysis of US hearing healthcare interventions across the lifespan. Further research might expand the modeling framework to international settings.

*Aim 2: To project clinical and economic effects of adult hearing screening programs in the US.*

We sought to estimate long-term clinical and economic effects of alternative adult hearing screening schedules in the US. Our design was a model-based cost-effectiveness analysis simulating current detection and linkage of persons with HL to hearing healthcare (Current Detection; CD) compared to alternative screening schedules varying by age at first screen (45 to 75 years) and screening frequency (every 1 or 5 years). Simulated persons experience yearly age- and sex-specific probabilities of acquiring HL, and subsequent hearing aid uptake (0.5-8%/year) and discontinuation (13-4%). Quality-adjusted life-years (QALYs) were estimated according to hearing level and treatment status. Costs include screening (\$30-120; 2020 USD), HL diagnosis (\$300), and hearing aid devices (\$3,690 year 1, \$910/subsequent year). The intervention was alternative screening schedules that increase baseline probabilities of hearing aid uptake (base-case 1.62-fold; range 1.05-2.25-fold). We found that CD resulted in 1.20 average person-years of hearing aid use compared to 1.27-1.68 with the screening schedules. Lifetime total per-person undiscounted costs were \$3,300 for CD and ranged from \$3,630 for 5-yearly screening beginning at age 75 to \$6,490 for yearly screening beginning at age

45. In cost-effectiveness analysis, yearly screening beginning at ages 75, 65, and 55 years had ICERs of \$39,100/QALY, \$48,900/QALY, and \$96,900/QALY, respectively. Results were most sensitive to variations in hearing aid utility benefit and screening effectiveness. We conclude that yearly hearing screening beginning at age 55 is cost-effective by US standards.

***Aim 3: To inform future research prioritization through value of information analysis.***

We sought to project the monetary value of future research clarifying uncertainties around the optimal adult hearing screening schedule. We used a validated decision model of hearing loss natural history, diagnosis, and treatment (DeciBHAL-US) to simulate current detection and linkage of hearing loss versus several hearing screening schedules. Key model inputs included hearing loss incidence (0.06-10.42%/year), hearing aid uptake (0.54-8.14%/year), screening effectiveness (1.62x hearing aid uptake), utility benefits of hearing aids (+0.11), and costs of hearing aid devices (\$3,690). We assigned distributions to uncertain model parameters to conduct probabilistic uncertainty analysis (PUA). We used value of information analysis to estimate the expected value of perfect information (EVPI), and expected value of partial perfect information (EVPPI), using a willingness-to-pay (WTP) of \$100,000/quality-adjusted life-year (QALY). EVPI and EVPPI estimate the upper bound of the dollar value of a future research project. The intervention was screening schedules beginning at

ages 45, 55, 65, and 75 years, and frequencies of every 1 or 5 years. The PUA demonstrated high uncertainty around the optimal screening schedule. Yearly screening beginning at age 55 was the optimal screening schedule in 38% of simulations, and other schedules in 62%. The population EVPI, or value of reducing all decision uncertainty, was \$8.2-12.6 billion varying with WTP and the EVPPI, or value of reducing all screening effectiveness uncertainty, was \$2.6 billion. We conclude that there is large uncertainty around the optimal adult hearing screening schedule and future research is likely justified.

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# 1. Introduction

Hearing loss (HL) is a pressing global health challenge. The number of people with disabling HL worldwide is expected to at least double by 2050, while rates of treatment remain low.<sup>17</sup> Prevalence of hearing loss in the US reaches 29% by age 50, and over 90% by age 80.<sup>4</sup> The continued impact of HL significantly affects patient and caregiver quality of life and can present a barrier to human communication and fulfillment. Furthermore, recent evidence points to an association between HL and cognitive impairment.<sup>18</sup> Treatment for HL exists, though the effectiveness and costs of different hearing interventions may vary. Hearing aids, especially when initiated early in the course of hearing loss, improve patient quality of life, potentially mitigate cognitive decline, and are widely accepted as a worthwhile investment.<sup>6,7,19-21</sup> Additional components of hearing health care include re/habilitation with audiology and speech pathology, as well as cochlear implantation for severe and profound hearing losses. Detecting adults with hearing loss through screening programs has the potential to increase patient awareness of hearing loss, improve uptake of effective treatment, and lead to downstream and spillover health benefits.<sup>10,19,22</sup>

Evidence from clinical trials around adult hearing screening has been limited by shorter follow-up periods and non-generalizable study populations.<sup>23</sup> Additionally, while hearing aid effectiveness on quality of life is established, the screening trials were not powered to detect changes in quality of life outcomes.<sup>7</sup> Due to sparse evidence,

conflicting guidelines exist around US hearing screening. While several Societies, including the American Geriatrics Society, advise regular hearing screening, a 2020 US Preventative Services Task Force evidence review concluded that they do not have sufficient data to make an informed recommendation.<sup>11,23</sup> As current rates of HL detection and linkage to effective treatment are woefully inadequate, with 80% of adults with HL remaining without treatment, the burden of untreated HL in the US remains unchecked.<sup>5</sup>

Policymakers and public health officials may be reticent to implement adult hearing screening in the US due to an absence of high-quality evidence around their expected long-term clinical and economic effects. A decision modeling analysis can extend current evidence reviews and address major concerns by synthesizing evidence across studies, projecting clinical outcomes over a longer time horizon, simulating a more generalizable population, and characterizing uncertainty in results. Additionally, value of information analysis can inform researchers and policymakers of the optimal areas for further patient-centered research investments.

The overall objective of this dissertation is to provide a quantitative framework and estimates to help policymakers identify effective and cost-effective adult hearing screening strategies in the United States. The dissertation is organized into six chapters. Chapter One is this introduction. Chapter Two is a systematic literature review and critical appraisal of existing decision models of hearing loss, intended to inform the

development and innovation of a novel decision model. The findings and conclusions of this systematic review indicated the need for a decision model of hearing loss across the lifespan, and in particular in low- and middle-income settings. While the subsequent Chapters of this Dissertation focus on model development, validation, and application in the United States, I am leading efforts outside of the current work are extending and validating decision modeling frameworks to low- and middle-income settings. Chapter Three reports the development and validation of the Decision model of the Burden of Hearing loss Across the Lifespan (DeciBHAL-US), a novel microsimulation model of hearing loss prevention, natural history, diagnosis, and treatment. Chapter Four is the first application of DeciBHAL-US to conduct a cost-effectiveness analysis of alternative adult hearing screening schedules in the US. Chapter Five extends these modeling efforts to conduct value of information analysis and inform future research prioritization. Lastly, Chapter Six summarizes the policy implications of the dissertation as a whole and outlines steps for future research. In sum, this body of work will promote adult hearing screening as a public health strategy and identify opportunities for decisionmakers to alleviate the immense global burden of hearing loss.

At the time of submission of this Dissertation, Chapters Two and Three were published in *eClinicalMedicine* in 2021 and 2022, and I was the first author on both publications. Chapter Four is under review, and I am the first author. Chapter Five is in preparation for submission, and I am the first author on the resulting manuscript.

Throughout each of the Chapters, I collaborated with the Lancet Commission on Hearing Loss, an international group of experts in hearing healthcare (Appendix A has a full listing of the Commissioners). The Commissioners served as clinical and policy experts reviewing my proposed decision model structure and identified published data to parameterize the decision modeling framework. They additionally helped refine the policy implications and recommendations of the resulting research. While the Commission played a critical role in the critical review and dissemination of the work in this Dissertation, I led and performed all aspects of the analysis, interpretation, and writing in the following Chapters.

## **2. Evidence Gaps in Economic Analyses of Hearing Healthcare: A Systematic Review**

### ***2.1 Introduction***

Hearing loss is the fourth leading cause of years lived with disability worldwide, affecting nearly one in five people.<sup>1,3</sup> Severity of hearing loss can range from mildly affecting communication to profoundly affecting all aspects of daily life.<sup>24,25</sup> Furthermore, the estimated global yearly economic costs of unaddressed hearing loss for the health sector alone exceed \$100 billion.<sup>26</sup> Inclusion of lost productivity increases that cost to \$750-790 billion annually.<sup>5</sup> Appropriately, policymakers are focusing attention on cost-effective interventions in hearing healthcare to reduce this burden of disease.<sup>12,13</sup>

In 2019 a Lancet Commission was convened “to examine how to reduce the global burden of hearing loss,” including investigating the economic efficiency of alternative treatment and prevention opportunities in hearing healthcare.<sup>12</sup> The Commission identified cost-effectiveness analysis as one element that could guide policymakers in the careful allocation of scarce resources to prevent and treat hearing loss. Decision models have long informed cost-effectiveness analyses and have provided significant insight in the field of hearing healthcare.<sup>27,28</sup> However, a systematic assessment of the decision modeling methodologies and qualities that inform these analyses across hearing loss interventions has yet to be performed. Understanding the

state of current evidence, as well as the limitations therein, is important for the development of decision models addressing hearing healthcare.

This systematic review seeks to: (1) investigate the methods and quality of model-based cost-effectiveness analyses addressing hearing loss; (2) identify evidence gaps; and (3) inform economic modeling for the Commission.

## ***2.2 Methods***

The methods for this systematic review followed the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines.<sup>29</sup> To define the research questions for this review, we collaborated with the Lancet Commission on Hearing Loss.<sup>12</sup> Our research questions were: 1) what are the methods and quality of published model-based cost-effectiveness analyses that address hearing loss?, and 2) what are the evidence gaps in these methods or qualities? This occurred in person in November 2019, through a multi-national, multi-stakeholder meeting and subsequently in virtual conferences for the full Commission or groups within it. After the initial creation of our research question, our research objectives and preliminary results were presented to the full Commission in July 2020 for discussion and refinement of the policy implications. The Commissioners affiliate with over 14 distinct countries and include perspectives from clinicians, health policy experts, health economists, epidemiologists, patients, and

others. Please see Appendix A for a complete listing of the Commissioners and their affiliations. This study was not registered with PROSPERO.

### **2.2.1 Data Sources and Study Selection**

We searched MEDLINE, EMBASE, Cochrane Library, and Global Index Medicus for relevant literature. Search terms were related to hearing loss and cost-effectiveness, and filtered to include full text articles (Appendix B). The searches were performed on 14 June 2020.

Prespecified inclusion criteria were 1) English-language, 2) original research cost-effectiveness analyses that consider both outcomes and costs, 3) studies that assessed hearing healthcare interventions (preventative, diagnostic, and therapeutic), and 4) studies that included a decision model. We only considered model-based cost-effectiveness analyses because a primary goal of this study is to inform future decision model frameworks of hearing healthcare interventions. However, we did include cost-effectiveness analyses based on clinical trials that utilized a decision model to project the cost-effectiveness of their intervention. We excluded conference abstracts and other types of cost analyses. Please see Appendix C for a population, intervention, comparison, outcome, time, and study design (PICOTS) table of the inclusion criteria. Before initiation of our search, we determined that we would review the bibliography of included systematic reviews and meta-analyses identified by the search strategy for

relevant articles not included in the search strategy to incorporate into our screening process.

Articles were screened independently for inclusion at the abstract and full text level by two reviewers (EDB, MMD). Exclusion criteria at the abstract level were articles unrelated to hearing loss or articles that were not cost-effectiveness analyses. Exclusion criteria at the full text level comprised of those at the abstract level as well as articles that did not use a decision model. All inclusion/exclusion conflicts were resolved by discussion between the original reviewers or by discussion with a third investigator (EDB, MMD, OO, GDS). Every effort was made to obtain full text versions of articles not available through Duke University Library. However, there was one citation for which we were unable to access a full text version and thus that article was excluded from further analyses.

### **2.2.2 Data and Extraction**

Data were abstracted from articles included at the full text level. All abstractions were vetted by a second investigator (EDB, MMD), with disagreements settled by a third investigator (EDB, MMD, OO, GDS). We used the Consolidated Health Economic Evaluation Reporting Standards (CHEERS), a checklist detailing essential components of a health economic evaluation, and simulation modeling best-practice frameworks to guide our data abstraction.<sup>30,31</sup> We abstracted data related to analysis setting and

population, interventions simulated, model type, clinical input parameters, and main cost-effectiveness findings that were included the Abstract (Appendix D). Decision model types abstracted included decision tree diagrams, Markov models (that include a time component to the analysis), and other model types (e.g., diagram, probabilistic, or net-cost). The risk of bias within the modeling studies was determined using components from the CHEERS checklist. Specific components of the checklist which corresponded to potential risk of biased included statement of perspective of analysis, model validation, methods of characterizing of uncertainty, funding source, and disclosure of potential conflicts. After the initial data abstraction, we collected additional data points for studies examining the three interventions most common across all included studies and reported each study separately. We reported acoustic (i.e., traditional) hearing aids and bone-conduction devices in the same table because of their comparison to cochlear implantation and similar data abstraction structure. Studies exploring all other interventions are reported in aggregate and without additional data collection.

### **2.2.3 Quality Assessment**

One investigator read each identified paper and abstracted quality indicators (EDB, MMD). A second investigator then independently read the included paper and noted any disagreements (EDB, MMD). Disagreements not resolved by consensus were

settled by a third investigator's review (EDB, MMD, OO, GDS). We used a previously developed quality measure that examined 16 components of the decision model and cost-effectiveness analysis and yielded a score from 0 to 100, with 100 representing a full quality score.<sup>32,33</sup> The components assessed for quality were related to transparency of modeling and data abstraction methods, clarity and appropriateness of model structure and input data, and correct comparison of assessed interventions (see Appendix E for a complete description of the quality measure). This measure was selected because it was developed specifically for quality ratings of decision models and incorporated differential weighting (one point to eight points) for each aspect of quality.<sup>30,32</sup> This measure does not assign qualitative indicators to numerical scores, so we report individual article quality scores. Major methodologic or reporting deficits were defined as those components receiving a weight of six or more points on the quality rating measure (see Appendix E).

#### **2.2.4 Presentation of Cost Parameters**

All abstracted cost parameters were converted to 2019 USD. Cost parameters were first adjusted to 2019 local currency units using local consumer price indices, then converted to USD using the World Bank currency conversion rates.<sup>34</sup> When articles did not list the currency source year (n=22), we assigned the year of publication for the adjustments.

**Table 1: Batched citations of references in the systematic review.**

<b>Batch Number</b>	<b>Citations</b>
1	28,35-150
2	28,35-129
3	66,130-150
4	28,36-39,42,46,49-51,56,58,61-67,70,71,73,74,76,77,79,81,84,85,87,88,92-96,101-103,107,110,111,114,117,118,122,124,128,132,133,136,139-142,144,146-150
5	35,45,47,55,57,59,68,75,78,82,83,89-91,98,100,104,105,108,109,112,113,115,116,119-121,123,125,126,129,130
6	40,41,43,44,48,52-54,60,69,72,80,86,97,99,106,127,131,134,135,137,138,143,145
7	37,42,49,51,56,58,63,64,66,73,74,76,79,81,83,90,91,94,101,102,107,111,113,117,118,121,122,134-138,141,148,149
8	28,36,38,41,44-46,48,52-55,57,60,77,82,93,96-100,104,105,110,112,123,127,133,139,142,144,146,150
9	35,36,38,45-47,53,54,57,59,65,69,71,75,78,80,82,87-89,96,98,100,120,129,135,137,150
10	40,43,50,61,62,67,70,85,86,92,95,108,114-116,124,131,132,140,143,145,147
11	39,42,65,68,71,72,84,87,88,102,103,106,109,110,119-122,125,126,128-130,133-135,142,144,146
12	28,40-42,44,48,49,55-58,61,63-66,68-70,72,73,77,79,81,86-89,92,94,97,99-112,114,115,117-120,122-128,131,133,136,137,139-142,144-149
13	35-39,43,45-47,50-53,59,60,62,67,69,74-76,78,80,82-85,90,91,93,95,96,100,116,120,121,130,132,138,140,143
14	36,38,39,41,44-48,50,52-55,57,60,63,67-70,80,81,85,86,89,92,93,95-101,103-105,107,109,111-115,119-123,126,128-132,137-139,143,148
15	28,35,37,40,42,43,46,49,51,52,56,58,59,61,62,64,66,70,75,77-79,84,92,94,95,106,110,114-116,127,133-138,140-142,144-147,150
16	37,42,49,56,63,64,66,74,76,79,81,94,101,102,107,111,117,118,122,136,138,141,148,149
17	51,58,64,73,134,135,137
18	83,90,91,113,121,134,135,137
19	37,49,63,66,76,79,107,118,136,138,141,148,149
20	49,66,76,79,118,136,141,149
21	58,73,134,135
22	42,49,56,63,64,66,74,76,79,81,94,102,107,111,117,118,122,148
23	49,56,58,63,64,81,102,107,111,113,117,118,137,148
24	28,36,38,41,44-46,48,52-55,57,60,77,82,93,96-100,104,105,110,112,123,127,133,139,142,144,146,150
25	57,60,77,82,93,96-100
26	28,52-55,104,105,110,112,123,127,144,146
27	36,38,41,139,142
28	44-46,48
29	28,36,41,44-46,48,52-55,57,60,77,82,93,96-100,104,105,110,112,123,127,133,139,142,144,146,150
30	45,52,55,60,82,93,98,100
31	36,38,96,100
32	110,133,142,144,146
33	38,45,46,53,54,57,82,98,139,150
34	36,45,60,93,98
35	28,38,45,46,48,52,53,55,57,60,82,93,96,98-100,104,105,110,112,133,139,142,146
36	35,36,38,45,46,54,57,59,65,71,75,78,82,87-89,96,98,100,120,129,135,137,150
37	47,53,69,80,89



## **2.3 Results**

### **2.3.1 Summary of Included Studies**

Our search yielded 1,437 unique articles, of which 117 unique studies with decision models (Table 1, Batch 1) and 17 systematic reviews<sup>152-168</sup> met the inclusion criteria (Figure 1). Model-based studies were predominately set in high-income countries (n=96, 82%; Table 1, Batch 2; Table 2), with fewer studies in low- and middle-income countries (LMIC; n=22, 19%; Table 1, Batch 3). One study was set in both a high- and low- and middle-income setting.<sup>66</sup> Sixty-one studies evaluated hearing loss strategies exclusively in pediatric populations (<18 years, 52%; Table 1 Batch 4), 32 in adults (27%; Table 1, Batch 5), and 24 in both (21%; Table 1, Batch 6). The interventions assessed included hearing screening (n=35, 30%; Table 1 Batch 7), cochlear implantation (n=34, 29%; Table 1, Batch 8), hearing aid use (n=28, 24%; Table 1, Batch 9), vaccination (n=22, 19%; Table 1, Batch 10), and other aspects of hearing healthcare (n=29, 25%; Table 1, Batch 11); some studies included more than one intervention (see Appendix F for a diagram of comparisons made among included studies). The most common decision model types were tree diagrams (n=72, 62%; Table 1, Batch 12) and Markov models (n=41, 35%; Table 1, Batch 13). In studies published since 2010, decision trees remained the most commonly used decision model (58%) and the proportion of Markov models used increased slightly to 42%. Sixty-one studies (52%; Table 1, Batch 14) were

conducted from a healthcare payer perspective and 46 (39%; Table 1, Batch 15) from a societal or modified societal perspective (inclusive of costs and benefits relevant to

**Table 2: Characteristics of included studies in the systematic review.**

<b>Characteristic</b>	<b>Number of Studies (n=117 in all)*</b>
<b>Setting</b>	
Africa	6 (5%)
Asia	18 (15%)
Australia and New Zealand	10 (9%)
Europe	47 (40%)
North America	35 (30%)
South America	2 (2%)
<b>Population</b>	
Pediatric only, <18 years	61 (52%)
Adult only, >18 years	32 (27%)
Mixed	24 (21%)
<b>Hearing loss intervention assessed</b>	
Hearing screening	35 (30%)
Cochlear implantation	34 (29%)
Hearing aid use	28 (24%)
Vaccination	22 (19%)
Other	29 (25%)
<b>Decision model type</b>	
Tree diagram	72 (62%)
Markov state transition	41 (35%)
Other	8 (7%)
<b>Perspective</b>	
Healthcare payer	61 (52%)
Societal and modified societal	46 (39%)

\*Not all categories sum to 117 (or 100%) as some studies may be represented more than once.

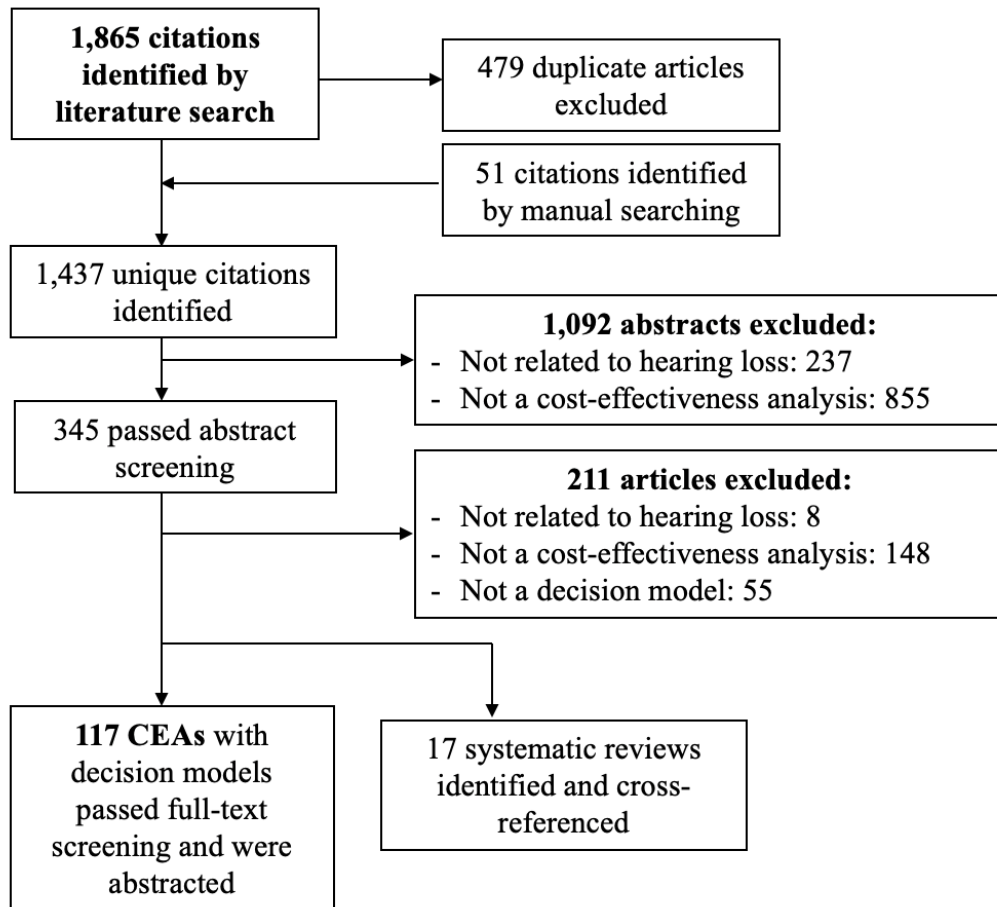


Figure 1: PRISMA literature flow diagram for the systematic review

society in general, such as productivity benefits or family and caregiver effects). Main cost-effectiveness findings from each included study are reported in Appendix G and a summary of funding sources for included studies are in Appendix H.

### **2.3.2 Studies Evaluating Screening**

Thirty-five of the selected studies examined hearing screening strategies, with 24 studies considering neonatal screening (Table 1, Batch 16), seven studies considering child screening (Table 1, Batch 17), and eight studies considering adult hearing screening (Table 1 Batch 18). The most commonly evaluated screening strategy in newborn studies was universal newborn screening (n=13; Table 1, Batch 19), followed by targeted or risk-based newborn screening (n=8; Table 1, Batch 20). School screening was evaluated in four of the seven child screening analyses (Table 1, Batch 21). The eight studies that included adult screening analyses varied in the age at first screen, the frequency of screening, and the screening test modality. Eighteen of the 24 cost-effectiveness analyses of neonatal hearing screening (Table 1, Batch 22), one child screening analysis,<sup>64</sup> and two adult screening analyses<sup>113,121</sup> projected a main clinical outcome other than quality-adjusted life-years (QALYs) or disability-adjusted life-years (DALYs), often choosing an intermediate outcome such as number of cases identified. Forty percent of included screening studies across the lifespan evaluated across a time horizon of less than 10 years (Table 1, Batch 23).

### **2.3.3 Studies Evaluating Cochlear Implantation**

Thirty-four identified analyses considered cochlear implantation (CI) as a comparator intervention (Table 1, Batch 24). Locations of analyses included 10 in Europe (Table 1, Batch 25); thirteen in North America (Table 1, Batch 26); five in Asia (Table 1, Batch 27); four in Australia or New Zealand (Table 1, Batch 28); one in South America;<sup>150</sup> and one in Africa.<sup>133</sup> The most commonly studied interventions were unilateral and bilateral CI (33 studies, 97%; Table 1, Batch 29), with eight studies directly comparing unilateral vs. bilateral CI (Table 1, Batch 30). Other interventions included bimodal hearing technology (CI+HA; four studies; Table 1, Batch 31), deaf education (five studies; Table 1, Batch 32), and hearing aids (HA) (ten studies; Table 1, Batch 33). Simultaneous CI implantation was compared to sequential CI implantation in five studies (Table 1, Batch 34). Abstracted economic parameters included one-time CI device and procedure costs (including costs of surgery/anesthesia, and initial audiology programming of device) as well as recurring costs for CI processor updates. CI device and procedure costs ranged from \$11,560-63,970, differing by setting and analysis. Seventy-one percent of studies (n=24) included CI processor update costs, and these costs were aggregated and assessed either yearly or once per lifetime (Table 1, Batch 35).

### **2.3.4 Studies Evaluating Hearing Aids**

Twenty-eight studies conducted cost-effectiveness analyses that included hearing aids as an intervention. Acoustic (i.e., traditional) hearing aids were included in

24 studies (Table 1; Batch 36), while five studies evaluated bone conduction devices (Table 1, Batch 37). Hearing aids were most commonly evaluated in comparison to cochlear implantation (n=9; Table 1, Batch 38). Eight studies compared hearing aid provision to no intervention, assessing the cost-effectiveness of acoustic hearing aids themselves (Table 1, Batch 39). Costs for non-implantable hearing aid device and fitting ranged from \$40-7,130, again varying by setting (LMIC vs. high-income country) and analysis. Sixteen of the 28 studies (57%) included recurring costs for hearing aid batteries, device replacement, device repairs, or combinations of these costs (Table 1, Batch 40).

### **2.3.5 Health Outcome Measures**

Quality-adjusted life-years were the most commonly reported health outcome measure from included decision models, with 62% of studies reporting the main health outcome in QALYs (Table 1, Batch 41). Twelve percent of studies reported DALYs (Table 1, Batch 42), 5% reported life-years (Table 1, Batch 43), and 24% reported other outcome measures (Table 1, Batch 44). Utility values incorporated into economic analyses varied widely in terms of the impact of hearing loss on patient quality of life and the impact of hearing loss treatment on quality of life. Of the 86 studies that reported QALYs or DALYs, 24 derived their own utility values to calculate these health outcomes (Table 1, Batch 45).

### **2.3.6 Indirect Economic Costs**

Untreated hearing loss has significant effects on labor force participation and educational attainment, and economic analyses may take such costs into account.<sup>169</sup> Forty-one studies (35%) incorporated indirect economic effects into the economic analysis (Table 1, Batch 46). Effects of hearing loss on employment and productivity were considered in 21% of studies (n=24; Table 1, Batch 47), education costs in 20% (n=23; Table 1, Batch 48), caregiver or family effects in 11% (n=13; Table 1, Batch 49), and transportation costs in 9% (n=11; Table 1, Batch 50).

### **2.3.7 Quality of Included Studies**

Median quality rating of all included studies was 92, IQR [72-100], and the mean was 83, standard deviation (SD)=20. When only studies published since 2010 were included, the median quality score increased slightly to 94, IQR [79-100] and the mean increased to 87, SD=17. When only studies published since 2000 were included, the median quality score was 94, IQR [79-100], and the mean was 86, SD=18. The most frequent reasons we applied quality deductions were failure to assess interventions incrementally (i.e., failing to compare each studied intervention's costs and benefits to the next most effective intervention after eliminating dominated options. Interventions are considered dominated if they are more costly but less effective than an alternative (strong dominance), or when a combination of two interventions is better than a third

intervention (weak or extended dominance); n=29, 25%; Table 1, Batch 51), absence of statement of perspective of analysis (i.e., healthcare payer perspective, societal perspective, etc.; n=25, 21%; Table 1, Batch 52), absence of explicit consideration of biases (n=33, 28%; Table 1, Batch 53), and lack of model structure transparency and justification (n=34, 29%; Table 1 Batch 54) (Figures 2 and 3). Forty-nine studies (42%) had two or more major methodologic or reporting deficits (Table 1, Batch 55). Please see Appendix I for a breakdown of quality scores in each intervention category.

### 2.3.8 Modeling Methods

Almost all of the identified decision models used sensitivity analysis to characterize uncertainty in their model-based results (n=109, 93%; Table 1, Batch 56). The methods used included one-way deterministic (n=97, 83%; Table 1; Batch 57), multi-way deterministic (n=31, 26%; Table 1, Batch 58), and probabilistic sensitivity analysis (n=49, 42%; Table 1, Batch 59). The proportion of studies that included probabilistic sensitivity analyses increased to 58% when only studies published since 2010 were analyzed. We found that 15% of analyses (n=17) explicitly reported validation exercises in their methods or results sections (Table 1; Batch 60).<sup>36,38,39,41,47,50,51,58,64,71,73,74,79,84,108,117,134</sup>

<sup>36,38,39,41,47,50,51,58,64,71,73,74,79,84,108,117,134</sup> Seven studies reported face validity (Table 1, Batch 61), seven reported external (or “predictive”) validation exercises (Table 1, Batch 62), and three reported internal validation exercises (Table 1, Batch 63).

The proportion of studies that reported any validation efforts did not change when only studies published since 2010 were evaluated.



Reference	Study objectives (7 pts.)	Perspective (4 pts.)	Source of variable estimates (8 pts.)	Subgroup (1 pt.)	Uncertainty analysis (8 pts.)	Incremental analysis (9 pts.)	Data abstraction methodology (5 pts.)	Time horizon (7 pts.)	Cost measurement (8 pts.)	Primary outcomes measures (6 pts.)	Health outcomes measures (7 pts.)	Display of economic model (8 pts.)	Statement and justification of choices (7 pts.)	Direction and magnitude of potential biases (6 pts.)	Conclusions (8 pts.)	Disclosure of funding (2 pts.)	Total quality score (100 pts.)
Kitano, 2017																	77
Kosaner 2017																	100
Kruvt, 2020																	100
Kuznik, 2017																	86
Langer, 2012																	93
Laske, 2019																	81
Le, 2015																	100
Lea, 1995																	28
Leeds, 2019																	100
Lieu, 2000																	100
Linszen, 2015																	94
Liu, 2011																	52
Lundqvist, 2005																	97
McIntosh, 2003																	97
Melegaro, 2004																	100
Merlin, 2007																	100
Mohiuddin, 2014																	100
Mohiuddin, 2015																	100
Monksfield, 2011																	82
Montes, 2017																	68
Moradi-Lakeh, 2012																	80
Morris, 2013																	100
Morris, 2011																	55
Navas, 2005																	100
Newall, 2016																	100
Nguyen, 2015																	94
Ning, 2018																	91
Ontario HTA, 2018																	100
Ontario HTA, 2020																	100
Perez-Martin, 2017																	86
Prager, 1987																	68
Prusa, 2017																	100
Pugh, 2019																	79
Qiu, 2017																	100
Rivera, 2017																	72
Rob, 2009																	86
Salo, 2005																	94
Saunders, 2015																	80
Schopflicher, 2007																	100
Schnippel, 2018																	100
Semenov, 2013																	94
Sharma, 2014																	67
Simon, 2016																	100
Summerfield, 1995																	74
Summerfield, 1997																	51
Summerfield, 2002																	69
Summerfield, 2010																	100
Theriou, 2019																	100
Tobe, 2013																	72
Turner, 1992																	30
UK CI Group, 2004																	87
Vallejo-Torres, 2015																	100
Veenstra, 2007																	77
Williams, 2015																	93
Williamson, 2009																	99
Wong, 2000																	32
Wong, 2017																	49
Wyatt, 1995 (1)																	91
Wyatt, 1995 (2)																	75
Wyatt, 1996																	76

Figure 3: Quality of included studies in the systematic review, authors Kr-W.

## ***2.4 Discussion***

This systematic review identified a large body of literature that explores the economic efficiency of interventions in hearing healthcare. The most frequently examined interventions were related to prevention of hearing loss from infectious causes, i.e., vaccination studies; detection of hearing loss through screening strategies; and treatment of hearing loss, including cochlear implantation and hearing aid provision. These interventions were most frequently examined in high-income settings.<sup>1</sup>

The median quality score of included studies was high and we found that more recent studies had slightly higher quality than earlier studies. However, almost half of all included studies had two or more major methodologic or reporting deficits. Some studies did not compare alternative interventions incrementally, rather compared multiple interventions to a set best practice or current standard of care. While this approach might be helpful for policymakers in some circumstances, a formal cost-effectiveness analysis should compare all studied intervention alternatives incrementally to identify the intervention that maximizes expected benefit for its cost. Incremental comparison is recommended by cost-effectiveness guidelines and failing to compare incrementally can affect the validity of cost-effectiveness conclusions and subsequent policy recommendations.<sup>151</sup> Sensitivity analysis is a crucial component of decision analysis and almost all included studies incorporated sensitivity analysis of some form, with a higher proportion of studies published after 2010 including probabilistic

sensitivity analysis. That said, model validation exercises were not reported in over 80% of studies, and this proportion did differ between more recently published studies and earlier studies. Including validation exercises in model-based analyses follows modeling best-practice guidelines and can increase the transparency and applicability of the results.<sup>31,151</sup>

The data synthesis and analysis in the systematic review reveal several evidence gaps. First, despite over 80% of the global burden of hearing loss lying in LMIC, the vast majority of the included studies (82%) were conducted in a high-income setting. This is of particular importance as health policy decisions in LMIC are increasingly made based on prioritization approaches such as health technology assessments that include cost-effectiveness analyses. Additionally, the lack of studies in LMIC reveals that disproportionately lower efforts and resources are being invested to identify solutions to the hearing healthcare problems in regions of the world where the burden of hearing loss is highest. The reason for this dearth of evidence in LMIC may be due to relatively sparse setting-specific clinical or economic data or to workforce shortages of hearing health professionals.<sup>1</sup> Future decision analyses that seek to alleviate the global burden of hearing loss should evaluate hearing interventions in LMIC. Decision scientists may partner with local hearing health researchers and clinicians to collect data to inform model developments and the parameters selected for the models. Indeed, decision models are particularly useful in settings where data are sparse or highly variable.

Nearly all decision models included in this review evaluated a single intervention or a set of interventions aimed at a single etiology of hearing loss. Out of all included studies, we identified two studies performed by the same lead author that directly compared the cost-effectiveness of interventions targeting hearing loss prevention and treatment from multiple etiologies and across the lifespan.<sup>134,135</sup> These studies considered child and adult screening strategies, antibiotic administration for meningitis-associated hearing loss, and antibiotics or aural toilet for chronic otitis media. When considering optimal resource allocation in conditions of scarcity, policymakers and finance ministers will benefit from analyses and models that compare interventions targeting hearing loss across etiologies and the lifespan. Future research should explore how a decision model that considers numerous etiologies of hearing loss from beginning to end of life might provide such information.

Health economic analyses traditionally report clinical outcomes in terms of QALYs or DALYs to allow for comparison of value across multiple conditions. The majority of decision models we identified did report health outcomes in QALYs or DALYs; however, there was no uniform source for utility values used to calculate QALYs and DALYs. Over one quarter of studies reporting QALYs or DALYs used their own methods to determine utility values of decision model health states. This variability highlights the high degree of uncertainty around this model input, and the lack of a definitive source for parameterizing model-based utility values. While utility values

should be specific to the population under study, common approaches to incorporating utility values of hearing health states in decision models may provide consistency and comparability between studies. Future research might explore the creation of appropriate and well-developed utility values of hearing loss – that also bear the appropriate study populations in mind – to inform decision models and reduce this model input uncertainty.

We also identified an evidence gap in inclusion of the indirect economic effects of hearing loss. Around one third of included studies incorporated indirect economic effects into their cost-effectiveness analysis as recommended by the Second Panel on Cost-Effectiveness in Health and Medicine.<sup>151</sup> Exclusion of the effects of hearing loss on economic productivity, education, and social support may underestimate the true economic burden of hearing loss and the potential for amelioration of the burden. Emerging evidence that associates hearing loss with cognitive decline and other medical comorbidities may further increase the indirect economic effects associated with hearing loss, such as caregiver and family burden.<sup>170</sup> There is a need for high-quality estimates of the impact of hearing loss on indirect economic outcomes that can be incorporated into decision modeling analyses.

Lastly, we found that many economic analyses of newborn hearing screening forecast clinical and economic outcomes over an abbreviated time horizon and included intermediate clinical outcomes such as hearing loss cases identified. While we did not

deduct quality scores for shorter time horizons in screening analyses, we recognize that time horizons less than ten years may not fully incorporate important downstream clinical or economic outcomes that affect the cost-effectiveness of the intervention.

The evidence gaps uncovered by this review suggest several specific recommendations for future decision model development and cost-effectiveness analysis in hearing healthcare. Future decision models should assess hearing healthcare interventions across the lifespan and might synthesize high-quality model structures identified by this review. Analysts should also ensure that models are able to assess hearing healthcare interventions that are relevant for LMIC to address the large burden of unaddressed hearing loss in those settings. Finally, model-based analyses should follow modeling best practice guidelines, incorporating validation exercises and comparing interventions incrementally, and predict comparable clinical and economic outcomes (i.e., currency/QALY) over a time horizon that can capture important downstream effects.

Our results may have clinical and policy implications that are of immediate importance to international stakeholders in hearing healthcare. To our knowledge, this is the first systematic review that includes model-based cost-effectiveness analyses across all interventions in hearing healthcare. The comprehensive compilation and quality evaluation of cost-effectiveness analyses presented herein can help decision makers identify the most relevant and highest-quality analyses to guide their decision

making on hearing healthcare provision. With the current evidence, decision makers might compare the published cost-effectiveness ratios from high quality studies with thresholds to identify setting-specific hearing healthcare interventions that are a worthwhile investment. Additionally, the identified evidence gaps can inform data collection and research priorities in hearing health.

This systematic review has several limitations. First, we did not extract cost-effectiveness results from identified studies, as the goals of this review were to examine the methods used and the implications for future modeling efforts in hearing healthcare. Future studies might consider reviewing and synthesizing the cost-effectiveness of specific interventions in hearing healthcare. Second, we only included model-based cost-effectiveness analyses to inform future decision model framework development. Cost-effectiveness analyses based on randomized controlled trials that did not use a decision modeling framework, for example, may be synthesized in future research. Third, the quality measure we used depended on author reporting of specific study characteristics and, as such, our measures of quality should be interpreted as both methodologic and author reporting quality. Fourth, we required publications to be in English, which might have reduced the number of studies from non-English speaking countries. Lastly, we did not perform a detailed analysis of all included studies (for example, vaccination studies), but rather on the three most commonly assessed interventions. All references

were included in reported summary measures, however, and the identified evidence gaps based on aggregate measures can be considered for all studies.

In conclusion, model-based cost-effectiveness analyses have been performed widely in hearing healthcare, and many are of high quality. By addressing the evidence gaps uncovered by this review, such as including LMIC study settings, future decision models will better guide clinicians, advocacy groups, and policymakers toward optimal interventions to alleviate the large global burden of hearing loss.

### **3. Development and Validation of DeciBHAL-US: A Novel Microsimulation Model of Hearing Loss Across the Lifespan in the United States**

#### ***3.1 Introduction***

One in three US adults over the age of 60 have hearing loss, and the prevalence of hearing loss climbs to over 90% by age 80.<sup>4</sup> Hearing loss has a significant impact on quality of life, learning and early development, and emerging evidence suggests hearing loss may negatively impact general and cognitive health.<sup>24,25,171,172</sup> Furthermore, persons with hearing loss have higher medical costs compared to those without hearing loss and the annual direct medical costs of hearing loss in the US range from \$3.3-12.8B, varying with age and method of estimation.<sup>169,173,174</sup> Lost economic productivity due to hearing loss may cost up to \$194B per annum.<sup>169</sup> Effective treatments for hearing loss exist, yet recent estimates suggest many are severely underutilized.<sup>175</sup> As innovations in hearing healthcare service delivery and technology are developed, frameworks to understand their potential clinical and economic impacts are increasingly important.

Cost-effectiveness analysis in hearing healthcare can guide policymakers towards optimal resource allocation and diverse stakeholders have called for research into the cost-effective provision of hearing healthcare in the US and abroad.<sup>1,176,177</sup>

Decision modeling is a quantitative method that underlies many cost-effectiveness analyses and allows for evidence synthesis to simulate alternative policy or treatment

interventions over a long time horizon.<sup>178</sup> However, almost all currently available decision models do not consider prevention, diagnosis, and treatment of hearing loss across the lifespan, which limits the generalizability and applicability of their results to policymakers and hearing healthcare providers.<sup>179</sup> A decision model that allows for consideration of numerous different interventions across ages and etiologies of hearing loss would provide better information on optimal implementation of hearing healthcare interventions.

Our objective was to develop and validate a decision analytic model of hearing loss natural history, prevention, diagnosis, and treatment in the US across the lifespan to inform policymakers and providers on the expected clinical and economic outcomes of alternative hearing healthcare strategies. This work was conducted as a part of an ongoing Lancet Commission on Hearing Loss, and contributes a US-specific component to the broader Commission goal of generating a decision model of hearing loss across the lifespan that can be populated with setting-specific data and applied in various international settings.<sup>12</sup>

## ***3.2 Methods***

### **3.2.1 Analytic Overview**

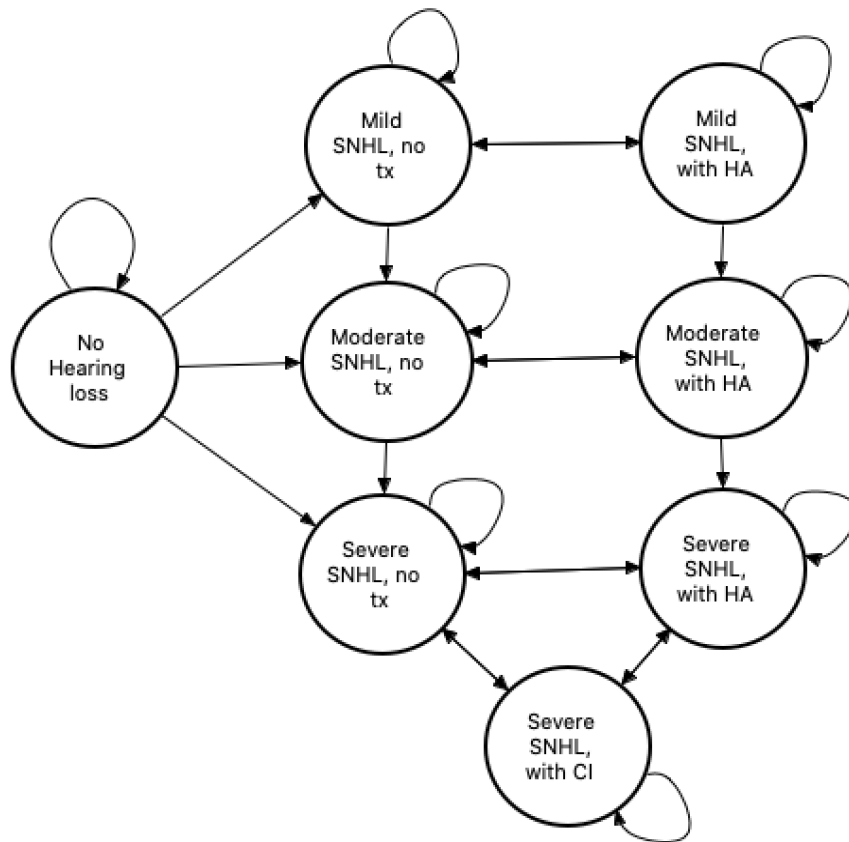
This study was motivated by stakeholder engagement through the Lancet Commission on Hearing Loss and a recent systematic review, both revealing a gap in the

current hearing healthcare decision modeling literature.<sup>179</sup> To address this gap, we set out to develop and validate DeciBHAL-US (Decision model of the Burden of Hearing loss Across the Lifespan) as a policy simulation model. We first consulted with hearing loss clinicians, public health, and policy experts to define the health states of the model. We then populated the model with literature-based estimates of the incidence and prevalence of sensorineural hearing loss (SNHL) and conductive hearing loss (CHL), natural histories of SNHL and CHL, and treatment probabilities. We then performed validation exercises, specifically in three key areas: 1) natural history of SNHL, 2) natural history of CHL, and 3) the hearing loss cascade of care. Wherever possible, we followed the Assessment of the Validation Status of Health-Economic decision models (AdViSHE) framework to guide our validation efforts (Appendix J).<sup>180</sup>

### **3.2.2 Model Overview and Hearing Loss Health States**

DeciBHAL-US is an individual-level microsimulation model implemented in TreeAge software (Williamstown, MA). Model health states are based on: 1) presence of hearing loss, 2) hearing loss type (SNHL, CHL, chronic suppurative otitis media (CSOM)-associated CHL), and 3) treatment modality if applicable. Figure 4 shows a schematic for the SNHL health states for post-lingual hearing loss (e.g., hearing loss after the time of language acquisition). Hearing loss severity is categorized based on better

ear pure tone average (PTA) thresholds at 500, 1,000, 2,000, and 4,000 hertz: 26-40 decibel (dB) is mild, 41-60 dB is moderate, 61-80 dB is severe, and 81+ dB is profound hearing



**Figure 4: Sensorineural hearing loss health state diagram.**

loss.<sup>4</sup> Simulated persons are assigned set characteristics and experience yearly probabilities of acquiring hearing loss, progression or cure of their hearing loss, and receiving or leaving treatment. Traditionally, hearing loss is classified as 1) SNHL, due to damage or degeneration of the inner ear or neural structures proximal to the inner ear, 2) conductive hearing loss (CHL), due to pathology involving the outer or middle ear, and 3) mixed SNHL and CHL. DeciBHAL assumes independence between SNHL and CHL and simulated persons may acquire SNHL, CHL, or both at each yearly time step. To clearly delineate the etiologies that contribute to SNHL and CHL across the lifespan, we collaborated with hearing health experts to create an etiology framework of hearing loss (Appendix K). Age- and sex-specific mortality rates from 2017 US lifetables were incorporated into the model.<sup>181</sup> SNHL and CHL are tracked for each simulated person in PTA thresholds and utility is dependent on the more severe of the two. Each year of the model, a cohort of newly born persons can enter the simulation. The model runs for 100 cycles (years) or until all simulated persons are in the death state.

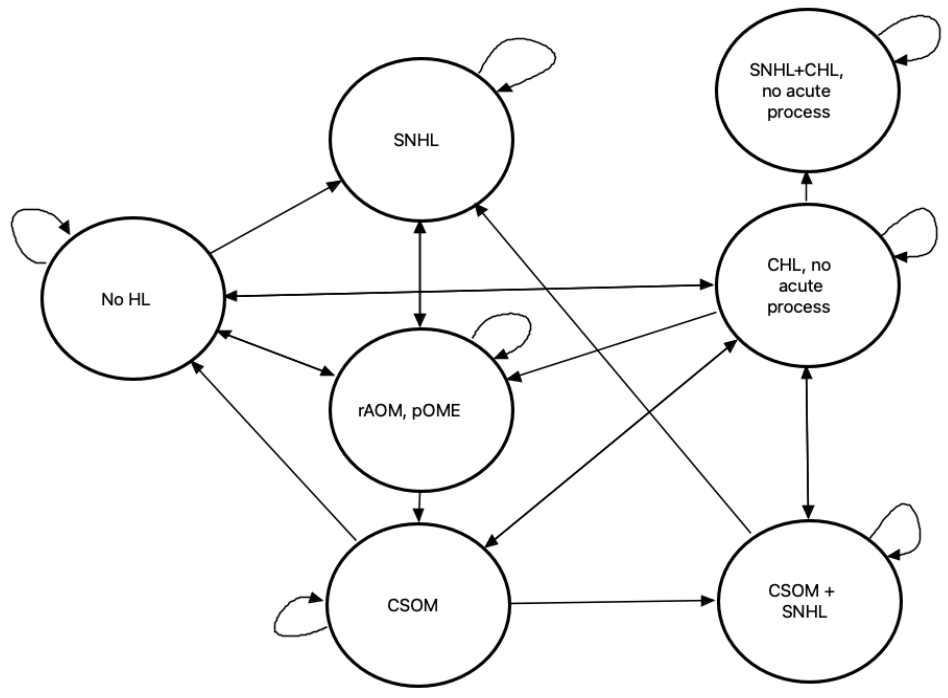
### **3.2.3 Natural History of SNHL**

We derived age- and sex-specific incidences of bilateral SNHL from recent prevalence estimates from the National Health and Nutrition Examination Survey (NHANES) and US lifetables, assuming a lifetime duration after acquisition of SNHL (Appendix L).<sup>4,181-184</sup> We only simulate bilateral SNHL to remain consistent with input

data definitions of hearing loss based on better-ear PTA and other economic analyses of hearing healthcare. Upon acquiring SNHL, the age-specific etiology is divided proportionally between ototoxic (e.g., after cisplatin or aminoglycoside use), meningitis, and age-related and other causes. We assumed simulated persons can only experience one cause of SNHL in their lifetime. After acquiring SNHL of any cause, simulated persons receive a SNHL PTA severity in dB; assumed to be  $\geq 25$  dB hearing loss (HL) for age-related hearing loss and, for the other etiologies, based on the average hearing loss PTA for each etiology (Table 3).<sup>185,186</sup> Age-specific decline in hearing loss is incorporated as a yearly PTA increase in dB (mean=1.05dB/year; SD=0.4) for persons ages 35+ years and is based on longitudinal studies.<sup>187</sup> This PTA determines hearing loss severity, which subsequently affects other model parameters as described, such as hearing aid (HA) uptake and health state utilities.

### **3.2.4 Natural History of Otitis Media-Related and Other CHL**

DeciBHAL incorporates acute otitis media (AOM), persistent otitis media with effusion (OME), and chronic suppurative otitis media (CSOM) as explicit etiologic contributors to CHL, and simulates all other causes of CHL in aggregate (Figure 5). All persons in the model, except those with active CSOM, experience age- and region-specific yearly probabilities of at least 1 episode of AOM.<sup>188</sup> We assumed simulated persons that have at least 1 episode of AOM during ages 0-12 years experience an



**Figure 5: Conductive hearing loss health state diagram.**







hearing aid; HL: hearing loss; OME: otitis media with effusion; PTA: pure tone average;

SD: standard deviation; SNHL: sensorineural hearing loss; y: year.

average of 2.8 episodes per year, and those older than age 12 experience 1 episode per year.<sup>189</sup> The model stratifies two risk groups of persons based on AOM history during the first 2 years of life: persons experiencing 2 or more episodes of AOM receive double the risk of subsequent AOM and OME throughout their lifetime.<sup>200,201</sup> In the absence of adult-specific data, we assume that 17% of all simulated patients who have at least 1 episode of AOM in a year develop recurrent AOM (defined as  $\geq 3$  episodes in 1 year) and transition to the recurrent AOM/persistent OME health state the subsequent year (described below).<sup>189</sup>

In the model, persistent OME may occur after an episode of AOM or spontaneously. Based on a meta-analysis of placebo controlled AOM trials, 26% of simulated patients experience OME of  $\geq 3$  months after an episode of AOM.<sup>189</sup> Of OME episodes that persist for  $\geq 3$  months, 71% of episodes resolve before 1 year.<sup>190</sup> OME episodes that persist for at least one year are assumed to have a mean duration of 21 months, with 75% of patients experiencing spontaneous resolution after 2 years, and 25% after 3 years.<sup>202</sup> Spontaneous rates of OME were calibrated to attain estimates of persistent OME prevalence. In the absence of US-specific data on OME prevalence lasting  $\geq 3$  months, by age group, we calibrated to Dutch data and assumed similar demographic characteristics to the US.<sup>191,203</sup> As outlined by US treatment guidelines, OME persisting for  $\geq 3$  months of known duration is considered for surgical management.<sup>190</sup> We assumed 26% of patients with OME  $\geq 3$  months receive treatment

with tympanostomy tubes within 1 year, and treatment reduces the proportion with effusion at 1 year by 53%.<sup>204,205</sup> The remainder have persistence of their OME for  $\geq 1$  year despite treatment, or spontaneous resolution or persistence without treatment (See Appendix M for the decision nodes of OME, including surgical treatment).<sup>202</sup>

Simulated patients with recurrent AOM (defined as  $\geq 3$  episodes in the previous 12 months) or OME that persists  $\geq 1$  year enter a distinct health state (*recurrent AOM and persistent OME*). We simulated these conditions as a single health state due to clinical expert opinion positing the state as a continuum rather than two distinct entities.

Patients in this state experience yearly probabilities of acquiring CSOM, based on CSOM incidence data from the US and Canada.<sup>188</sup> The average duration of CSOM (including the US mix of treated and untreated CSOM), 3 years, was calibrated to attain estimates of the US CSOM prevalence ( $< 1\%$ ).<sup>206</sup> Probabilities for surgical intervention (including tympanoplasty and mastoidectomy) for CSOM are not explicitly incorporated, rather are included in the average duration of CSOM, and costs for baseline rates of surgical intervention will be estimated as the average yearly costs of patients with CSOM. CSOM results in a PTA of 34 dB hearing level CHL during active disease, and after resolution a proportion has a residual CHL (Mean=17 dB air conduction threshold, SD=18.6 dB).<sup>192,193</sup> The probability of residual CHL after CSOM was calibrated to attain literature-based estimates.<sup>188</sup> Permanent CHL not due to CSOM is simulated in aggregate and incidences

are derived to attain adjusted NHANES estimates of US CHL-prevalence, with average PTA assumed to be 40 dB hearing level (Table 3).<sup>207</sup>

### **3.2.5 Mixed Hearing Loss**

We recognize that some etiologies that cause CHL can also subsequently cause SNHL, however due to an absence of data on the temporal relationship and quantified audiometric effects of this relationship, we assumed independence between etiologic contributors to SNHL and CHL. As such, all patients in the model may acquire both SNHL and CHL through similar age- and sex-specific incidences. DeciBHAL tracks SNHL in dB hearing level and CHL in dB hearing level independently, and severity-dependent parameters are based off the more severe PTA.

### **3.2.6 Pre-lingual Hearing Loss**

For persons with pre-lingual hearing loss, intervention before the time of language acquisition has different downstream outcomes than interventions for persons losing their hearing after language acquisition. In the model, simulated children with bilateral, profound hearing loss with an onset before age 2 years who do not receive a cochlear implant, enter a separate health state with a pathway of sign language education, and remain for their lifetime (not shown). In the context of pre-lingual severe and profound hearing loss, DeciBHAL primarily addresses the impact of early diagnosis

and intervention on efforts to improve access to spoken language and the acquisition of verbal communication. The costs and utilities in these health states will be informed by the published literature detailing the benefit of early intervention for severe and profound hearing loss.<sup>172,208</sup>

### **3.2.7 Hearing Loss Cascade of Care**

In conjunction with expert stakeholders on the Lancet Commission on Hearing Loss, we mapped a conceptual framework for the hearing loss cascade of care (Appendix N). Simulated persons with hearing loss experience yearly probabilities of going on or off treatment derived from the literature. While there are multiple complex factors influencing treatment access and uptake, transition probabilities in DeciBHAL are based on the final step – treatment uptake or not. Specific intermediary points in the treatment uptake cascade might be incorporated within the treatment uptake probability as needed in future analyses. We considered hearing aids, and re/habilitation (for example, including early speech and language development for children, aural rehabilitation), as treatment for all causes of hearing loss. We included cochlear implantation (i.e., the device and the surgery) for patients with severe and profound SNHL. For patients with CHL, we included non-implantable and implantable bone conduction devices as a proportion of the amplification therapy. The age- and hearing loss severity-specific yearly probabilities of all adult hearing aid acquisition were based

on estimates of the average time to uptake of hearing aids after hearing loss onset (mean=8.9 years).<sup>5,9</sup> Hearing aid discontinuation rates were derived from an National Institute on Deafness and Other Communication Disorders/Veteran's Affairs longitudinal study and adjusted to account for a high rate of hearing aid discontinuation in the first year after acquisition, and declining rates thereafter (13-4%/year).<sup>197,198</sup> We incorporated a delay to diagnosis factor, calibrated to achieve NHANES prevalence estimates of adult hearing aid use. We calibrated the yearly probability of cochlear implantation for persons with severe to profound hearing loss to achieve yearly estimates of cochlear implantation in US children and adults (n=18,000).<sup>199</sup> We incorporated a 1% annual probability of cochlear implant discontinuation in adults, and 0.2-1.8% per year in children depending on age at implantation.<sup>209,210</sup>

For pediatric hearing aid use, we incorporated time to uptake data to inform yearly probabilities of acquiring hearing aids (age 1 year: mean=15.8 months, SD=16.8 months; ages 2-5 years: 31.68 months, SD=18.32 months).<sup>194,195</sup> We assumed a linear decline in hearing aid acquisition from age 5 years to adulthood. Combined with a discontinuation rate of 3%/year, we projected the yearly proportion of children with aidable hearing loss (defined as PTA $\geq$ 25 dB in the better ear) using hearing aids.<sup>196,211,212</sup> The yearly probability of pediatric cochlear implantation was calibrated to achieve 50% of eligible patients provided with a cochlear implant by age 18 years.<sup>199,213</sup>

### **3.2.8 Internal Validation**

We performed internal validation exercises as recommended by AdViSHE. Co-authors who are experts in decision modeling independently reviewed the model code and programming for accuracy. We undertook extreme value testing and report our results in Appendix O. We examined over 20 patient trace files to ensure the logic of the model and present two annotated patient trace files in Appendix P.

### **3.2.9 External Validation**

All model outcomes were reviewed by hearing health expert co-authors and collaborators on the Lancet Commission on Hearing Loss for face validity. Expert reviewers analyzed DeciBHAL output data in virtual meetings and the model logic and input data were refined based on their feedback. We then focused our external validation efforts on validation to published data as described above. Cohort characteristics for external validation simulations were adjusted for each validation scenario and are described in the Results. We used coefficient of variance root mean square error (CV-RMSE) to compare model projected outcomes with the published literature, and considered  $CV-RMSE \leq 15\%$  to indicate adequate model fit.<sup>214,215</sup> We also compared model-projected results with published 95% confidence intervals whenever possible. For select model outcomes, we present low and high ranges based on input value computed 95% confidence intervals in Appendix Q.

### ***3.3 Results***

#### **3.3.1 Prevalence of Sensorineural Hearing Loss by Age and Sex**

We validated our age- and sex-stratified incidences of bilateral SNHL at each decile to published NHANES estimates adjusted to remove CHL stratified by sex as an internal validation exercise (Table 4). We simulated males and females separately from birth to death and collected the prevalence of bilateral SNHL at each decile. The CV-RMSE for model-projected male and female age-specific prevalence compared to adjusted NHANES data was 4.9% and 5.7%. No estimates were outside of the adjusted NHANES 95% confidence intervals.

#### **3.3.2 Progression of Sensorineural Hearing Loss**

DeciBHAL incorporates age-related decline in SNHL from published longitudinal data. We simulated 35-year-old males and females without any hearing loss throughout their lifetime, applying SNHL incidences and age-specific progression of SNHL to the PTA in dB hearing level. We assumed that persons without hearing loss had a linear decline in their dB hearing level from 0-20 dB hearing level between ages 35-85 years. The model projected population average hearing loss, measured as the PTA in dB hearing level, at each decile was compared to published data from the Baltimore Longitudinal Study on Aging (Figure 6).<sup>216</sup> The CV-RMSE of model data compared to published data was 11.3%.

**Table 4: Model validation results.**

Age	Bilateral SNHL Prevalence, Males		Bilateral SNHL Prevalence, Females		CHL Prevalence, Males and Females		Hearing Aid Use Prevalence, % of persons with hearing loss	
	Model Outcome, %	NHANES, % (95% CI*)	Model Outcome, %	NHANES, % (95% CI*)	Model Outcome, %	NHANES, %	Model Outcome, %	NHANES, % (95% CI)
15	0.13	0.16 (0.07-0.28)	0.08	0.16 (0.07-0.28)	0.46	0.37	-	-
25	0.38	0.39 (0.0-0.97)	0.31	0.39 (0.0-0.97)	0.59	0.59	-	-
35	2.4	2.5 (0.2-3.1)	2.4	2.5 (0.2-3.1)	0.41	0.41	-	-
45	9.9	9.7 (6.4-13.6)	3.0	3.0 (2.0-4.2)	0.56	0.62	-	-
55	20.0	20.3 (15.1-25.9)	6.6	6.3 (4.7-8.1)	1.03	1.14	3.8	4.3 (0-8.8)
65	36.7	37.2 (31.2-43.9)	17.5	16.9 (14.2-20.0)	1.31	1.45	7.8	7.3 (3.6-10.9)
75	64.4	66.5 (60.5-73.7)	45.6	43.7 (39.8-48.5)	1.26	1.43	14.7	17.0 (12.4-21.6)
85	89.7	86.4 (83.7-90.9)	79.4	77.0 (74.6-81.0)	1.30	1.39	21.0	22.1 (18.5-25.8)

Abbreviations: B/l: bilateral, CHL: conductive hearing loss, CI: confidence interval, NHANES: National Health and Nutrition Examination Survey, SNHL: sensorineural hearing loss.

\*95% confidence intervals from published NHANES estimates are adjusted to derive male- and female-specific values, and to remove conductive hearing loss (see Methods). Therefore, the confidence intervals presented in this table are likely too narrow to reflect the underlying uncertainty. We presented the narrower confidence intervals here to remain conservative in assessing model fit, however any future analyses using DeciBHAL-US should use wider confidence intervals in sensitivity analysis to better reflect this uncertainty.

### **3.3.3 Acute Otitis Media, Persistent Otitis Media with Effusion, and Chronic Suppurative Otitis Media**

The model-projected incidence of at least 1 episode of AOM at each decile was consistent with the input data (CV-RMSE=6.5%).<sup>188</sup> We validated model-projected yearly prevalence of OME $\geq$ 3months during ages 0-9 years to adjusted estimates from the Netherlands (CV-RMSE=12.2%; Appendix R). The derived CSOM incidence rates produced an average yearly CSOM prevalence between ages 2-80 years of 0.4%, consistent with US estimates of CSOM prevalence.<sup>206</sup>

### **3.3.4 Prevalence of Conductive Hearing Loss by Age**

As described above, simulated persons can acquire CHL during and after CSOM, or from other etiologies modeled in aggregate. Simulating persons from birth to death, we validated model-projected age-stratified prevalence of CHL to adjusted NHANES data (CV-RMSE=10.9%).

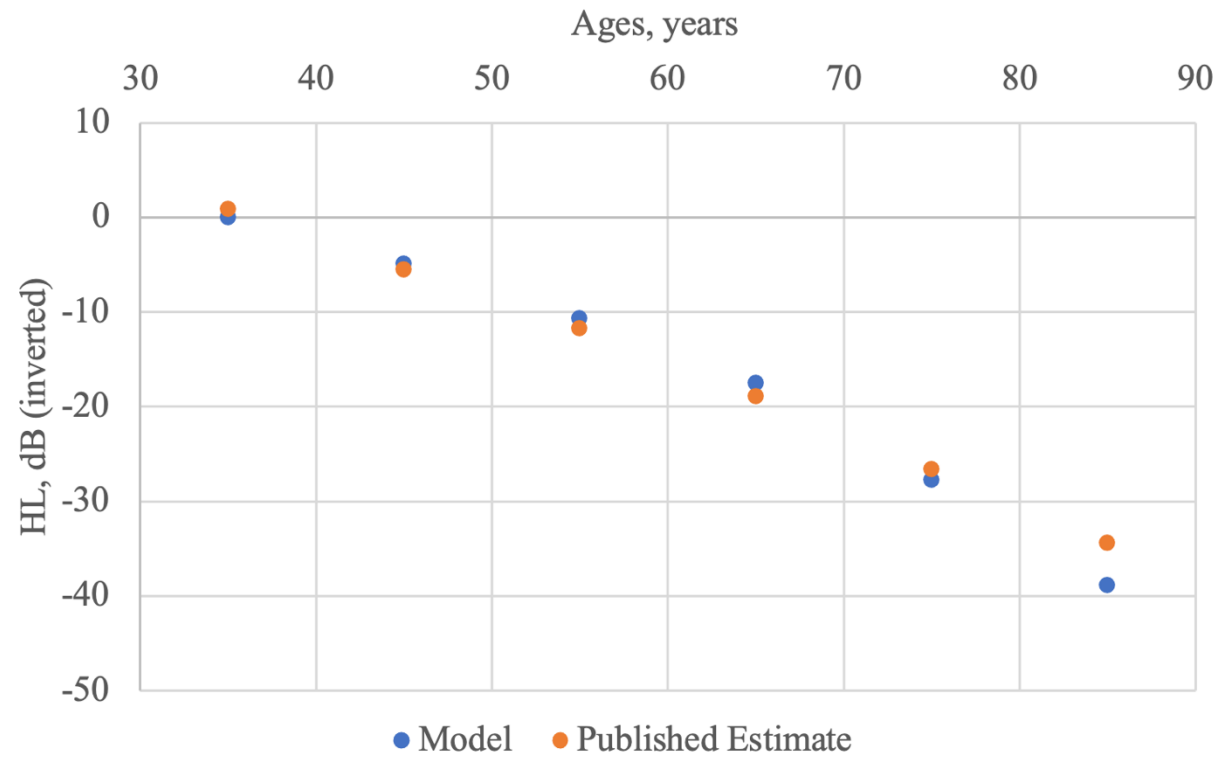
### **3.3.5 Age-Specific Hearing Aid Use**

For children, we simulated persons without hearing loss from time of birth to age 18, collecting the proportion of patients with bilateral, permanent hearing loss using a hearing aid yearly (see Appendix S). Identified estimates ranged between 54-79% in this age group, which is consistent with identified estimates from the US and other high-

income settings.<sup>196,211,212</sup> For adults, we simulated persons aged 35 years without hearing loss throughout the rest of their lifetime, collecting the proportion of people with acquired hearing loss using hearing aids at ages 55, 65, 75, and 85 (Table 4). We achieved adequate model fit compared to published NHANES data (CV-RMSE=10.3%).

### **3.3.6 Cochlear Implantation**

We adjusted the yearly probability of adults with severe-profound hearing loss receiving a cochlear implant to match yearly implantation estimates from 2019 (model=13,000, estimate=13,000).



**Figure 6: Model projected bilateral sensorineural hearing loss severity compared to the Baltimore Longitudinal Study on Aging.**

### ***3.4 Discussion***

We developed and validated DeciBHAL-US, among the first microsimulation models of hearing loss prevention, natural history, diagnosis, and treatment across the lifespan in the US. Our decision modeling framework was validated by hearing healthcare clinical and public health experts. We populated the framework with published estimates of hearing loss epidemiology and current US-based estimates on treatment uptake and discontinuation, and validated model-projected outcomes to published estimates. We demonstrated adequate fit of DeciBHAL-US projections to literature-based estimates across several validation targets, including NHANES epidemiologic estimates of the natural history of SNHL and CHL, and the hearing healthcare cascade of care.

DeciBHAL-US has several novel contributions to the hearing loss decision modeling literature. First, it simulates males and females without and with hearing loss, incorporating published NHANES epidemiologic data, across the lifespan. Most existing decision models evaluating hearing healthcare interventions begin with a cohort of persons with hearing loss and do not incorporate age-related incident hearing loss.<sup>179</sup> The use of robust epidemiologic data on incident hearing loss across the entire lifespan gives DeciBHAL-US the potential to identify optimal points of intervention for hearing healthcare, and potential effects of hearing loss prevention interventions. The population of DeciBHAL-US with US-specific health state utility values and costs will enable

projection of long-term clinical and economic effects of alternative hearing healthcare interventions and treatment scale-up. Comparing multiple hearing healthcare interventions in the same modeling structure will produce directly comparable cost-effectiveness estimates to inform policy and decision makers. DeciBHAL-US further includes both SNHL and CHL, which provides a framework to better simulate interventions targeting hearing loss prevention interventions, as well as more accurate costing analysis.

DeciBHAL-US additionally simulates the current cascade of hearing healthcare in the US, incorporating current rates of screening, diagnosis, linkage, and severity-dependent treatment uptake/discontinuation to project the number of people diagnosed and in care throughout the life course. This allows for simulation of scale-up interventions (hearing aid, CI, and other) at any point in the hearing healthcare cascade. The novel inclusion of treatment uptake and discontinuation rates allows DeciBHAL-US to simulate treatment and screening interventions over a long time-horizon, a key limitation in the current hearing loss decision modeling literature. Given the uncertainty in several important parameters informing the hearing healthcare cascade of care, for example the introduction of over-the-counter hearing aids in the US, future analyses might assign appropriate distributions to uncertain parameters to allow for value of information analysis. Value of information analysis is a quantitative methodology that estimates the monetary value of reducing decision uncertainties, and may provide

research funders an estimate of the maximum return on investment expected for their research dollars.<sup>217</sup>

DeciBHAL-US currently does not include health state utility values and medical and societal costs of hearing loss. There is large variability and uncertainty in the economic modeling literature around health state utility values and indirect economic costs for hearing loss, with many modeling analyses assigning Global Burden of Disease calculated disability-adjusted life-years (DALYs) for severity-specific hearing loss health states and assuming a 1-severity lower DALY for treated hearing loss.<sup>175</sup> While robustly measured, these DALY values might not be appropriate in all settings and treatment states. Indeed, two ongoing systematic reviews as part of the Lancet Commission on Hearing Loss are currently underway to inform untreated and treated DeciBHAL-US health state utility values, as well as the costs of lost productivity attributed to hearing loss.<sup>218,219</sup>

The natural history framework in DeciBHAL-US necessarily simplified across important hearing loss etiologies. We worked with key stakeholders to create a framework of etiologic contributors to hearing loss across the lifespan. We then built off this framework to identify published estimates and simulate hearing loss natural history in DeciBHAL. We used NHANES data as the most representative estimates of hearing loss stratified across age and severity. We made simplifying assumptions to divide the NHANES data into SNHL and CHL, given the different natural histories and treatment,

and costs of these conditions. While policymakers will not likely target treatment of persons with SNHL or CHL, rather persons with hearing loss of any etiology, the model necessarily simulates hearing loss natural history and progression. Additionally, separating by etiology provides a framework for simulating alternative hearing loss prevention interventions in future analyses. However, dividing NHANES projections into SNHL and CHL does not account for the relationship between SNHL and CHL, with some data showing that CHL predisposes persons to have SNHL earlier and at higher severities.<sup>220</sup> Additionally, we did not incorporate surgical interventions for CHL, such as stapedectomy for otosclerosis, and future model versions evaluating these interventions might incorporate a sub-module to account for hearing and cost outcomes related to otosclerosis and its treatment.

As currently structured, DeciBHAL does not explicitly consider the contributions of hearing loss to the increased risk of other physical health outcomes and dementia. Hearing loss is a modifiable risk factor with potential to affect dementia risk reduction worldwide and, therefore, prevention or treatment of hearing loss, and the associated sensory deprivation and social isolation, may reduce the incidence of dementia.<sup>171,221,222</sup> Future versions of DeciBHAL might project the potential clinical and economic benefits of those possibly averted cases of dementia and other health conditions, without necessarily simulating the natural history of these disorders.

DeciBHAL incorporates current published estimates on the prevalence of hearing aid and cochlear implant use to simulate the cascade of hearing health care. The rates of hearing aid uptake were based on estimates of time to first hearing aid after hearing loss onset in an older population, and included a calibration factor to better match NHANES estimates.<sup>5</sup> We acknowledge that hearing aid discontinuation rates could also be adjusted (increased) instead of uptake to better match NHANES estimates, and the different clinical and economic outcomes from these alternative calibration factors should be explored in any future DeciBHAL analyses. Data informing the pediatric hearing aid use prevalence were sparse, and our estimates may overestimate the true number of children with an aidable hearing loss using a hearing aid. Equally important to simulating the hearing healthcare cascade, the role of stigma in adult patient decisions to acknowledge their hearing loss and seek help for their hearing difficulties might be incorporated indirectly in DeciBHAL as an effect on age-specific hearing aid uptake rates.<sup>223</sup>

Additionally, while we based model transition probabilities on acquisition of a hearing aid or cochlear implant, hearing healthcare often involves a multidisciplinary healthcare team and longitudinal approach to achieve optimal treatment outcomes, most evident in the care pathway for children with congenital hearing loss. DeciBHAL does not explicitly simulate re/habilitation that should be provided to hearing aid and cochlear implant users, but rather models all persons with either treatment in

aggregate.<sup>224</sup> DeciBHAL's health states are inherently based on health outcomes and do not represent educational and cultural outcomes. Future model input values, such as health state utility values and costs, might incorporate the proportion of treated patients receiving appropriate re/habilitative care, and the effects of appropriate care on patient outcomes, including improved communication and quality of life, and healthcare costs. There is also the future potential to use DeciBHAL to examine the benefits of early intervention for non-auditory interventions, which may be more feasible in some contexts.

Our analysis and DeciBHAL-US have several limiting assumptions. First, as with all modeling studies we made simplifying assumptions in both the model structure and input data. We were transparent about these assumptions in this validation analysis, and any future studies using DeciBHAL-US should robustly test the effect of these assumptions on projected outcomes. One such assumption is excluding age-period-cohort effects, using cross-sectional data to project future outcomes, despite the presence of cohort effects in exposures that DeciBHAL-US does not capture. Data on cohort effects in hearing loss and methods for their application in long-term simulation modeling might be incorporated in future analyses using DeciBHAL-US. Another simplification was the exclusion of an explicit health state for impacted cerumen, a common and costly condition in the US that is associated with mild levels of hearing loss.<sup>225</sup> We chose to focus the model structure on permanent hearing loss given the

yearly time step, however future analyses might include impacted cerumen across all health states – carrying associated quality of life effects and costs – to better represent the costs of hearing care in the US. Second, we chose what we believed to be the highest-quality and most generalizable estimates to validate model-projected outcomes. These estimates were selected among other possibilities through discussions with clinical and policy experts in the Lancet Commission on Hearing Loss. Third, some model inputs did not have US-specific data and required either derivation from other known inputs, or imputation from population-based estimates from other high-income settings. In particular, US-specific estimates for pediatric hearing loss natural history and treatment were sparse and we incorporated estimates from other high-income settings (predominately Europe and Australia) to inform our model inputs.<sup>226</sup> All uncertain inputs, and especially those adjusted from a non-US setting, should be robustly tested in sensitivity analysis in future model applications.

Fourth, we defined hearing loss as bilateral, based on PTA, and did not include unilateral hearing loss, which can also have significant effects on quality of life and healthcare costs. We made this assumption to remain consistent with input data sources and other economic analyses of hearing loss, and to remain conservative in our calculation of the burden of hearing loss. PTA is a commonly accepted metric for defining hearing loss, and most often found in our input data sources, however it does not directly assess functional hearing abilities and may under- or overestimate actual

hearing loss burden. Additionally, for validation purposes, we defined severities in line with NHANES, which is different than updated severity definitions from the Global Burden of Disease and the 2021 WHO World Report on Hearing.<sup>4,175</sup> Sensitivity analysis loosening these assumptions will be important in analyses utilizing DeciBHAL-US. Fifth, given the complexity of the model we were unable to assign distributions to every parameter and compute uncertainty intervals. Instead, we present several deterministic sensitivity analyses in the Appendix. Lastly, there are large, documented disparities in the provision of and access to hearing healthcare within the US, and DeciBHAL currently does not account for differential outcomes based on patient race, ethnicity, or socioeconomic status.<sup>194,227,228</sup> Future model versions should incorporate the impacts of racism, classism, and other structural inequities on hearing health outcomes.<sup>229</sup>

The vast majority of hearing loss burden lies in low- and middle-income countries, and the opportunities for hearing healthcare scale-up are equally large in these settings.<sup>1</sup> Future collaboration with clinicians and researchers from low- and middle-income countries, and select populations in high-income settings like the rural US, might allow for population of DeciBHAL with setting-specific epidemiologic and treatment parameters and expansion to other settings.<sup>230</sup> Ongoing efforts are identifying the other data inputs necessary to build a hearing loss modeling framework in international settings, and similar validation efforts will be required for those frameworks.

In conclusion, DeciBHAL-US provides a reasonable simulation of hearing loss natural history, diagnosis, and treatment when validated to published estimates. Use of DeciBHAL-US for economic analysis might provide a major advance in hearing healthcare decision modeling literature by projecting comparable cost-effectiveness ratios for multiple interventions for men and women across the lifespan. The availability of comparable and transparent cost-effectiveness estimates from DeciBHAL could help guide decision makers in the optimal allocation of resources to alleviate the substantial burden of hearing loss and limited treatment uptake in the US and ultimately in other countries and world regions.

## 4. Model-Projected Cost-Effectiveness of Adult Hearing Screening in the United States

### 4.1 Introduction

Most US adults will experience hearing loss (HL) at some point in their lifetime, with prevalence reaching 50% at age 70 years and 80% by 80.<sup>4,231,232</sup> Despite this high prevalence, hearing screening is not commonly performed in adults, leaving most affected Americans without a diagnosis. As a result, 80% of persons with HL in the US do not receive treatment.<sup>4,5</sup> Further, untreated HL has significant impacts on quality of life, cognitive impairment and other morbidity, fall risk, and patient-provider communication.<sup>233-238</sup> HL incurs yearly societal costs of upwards of \$194B due to associated and independent risk of poor general health and dementia.<sup>169,235,237</sup> Stakeholders are increasingly calling for identification of cost-effective interventions to diagnose, link, and treat persons with HL.<sup>1,13,175,176</sup>

Screening for HL in primary care settings increases diagnosis of HL and downstream treatment uptake.<sup>223,239,240</sup> However, current US screening practices are varied and include single questions, surveys, and sound tests, with some professional societies recommending regular hearing screening of older adults.<sup>241,242</sup> A recent United States Preventative Services Taskforce (USPSTF) update found that while several screening modalities successfully identify persons with HL, and that HL treatment is beneficial, there was insufficient evidence to make a recommendation on screening

asymptomatic adults over age 50 years.<sup>23,243,244</sup> A key limitation of the evidence cited by the USPSTF was the absence of a randomized trial that linked hearing screening to quality-of-life outcomes in the general population. In this study, we used a model to estimate the long-term clinical and economic effects of different adult hearing screening paradigms in the US and identify key sources of uncertainty to guide future research and policy.

## **4.2. Methods**

### **4.2.1 Analytic Overview**

We used the previously validated Decision model of the Burden of Hearing Loss Across the Lifespan (DeciBHAL-US) to simulate Current Detection (CD), e.g., current rates of symptomatic presentation and uptake of hearing healthcare, compared to different hearing screening schedules that varied by age at first screen and screening frequency.<sup>245</sup> We simulated a cohort of 40-year-old persons without HL throughout their remaining lifetime, with yearly probabilities of acquiring HL and subsequent hearing aid (HA) uptake and discontinuation. Screening effectiveness was simulated as an increase in baseline HA uptake probability during the year of screening. We measured effectiveness using quality-adjusted life-years (QALYs) and estimated health system costs in 2020 USD. In cost-effectiveness calculations, we discounted costs and effectiveness by 3%/year. We considered incremental cost-effectiveness ratios (ICERs) of

<\$100,000/QALY to be cost-effective.<sup>246,247</sup> This study followed the Second Panel on Cost-Effectiveness in Health and Medicine and Consolidated Health Economic Reporting Standards.<sup>151,248</sup>

#### **4.2.2 Model Overview**

DeciBHAL-US is a microsimulation model of HL natural history, detection, diagnosis, and treatment. Simulated persons experience yearly age- and sex-specific probabilities of acquiring bilateral sensorineural HL, conductive HL, or both, based on published National Health and Nutrition Examination Survey (NHANES) estimates.<sup>4</sup> Persons with sensorineural HL experience age-related decline in pure tone average (PTA) hearing level, and HL severity was categorized according to World Health Organization definitions (WHO; Table 5).<sup>175</sup> After acquiring HL, patients experience age- and severity-specific yearly probabilities of acquiring HAs and, once using HAs, rates of discontinuation. Adults with severe-to-profound HL may receive cochlear implantation after use of HAs for at least one year.<sup>249</sup>

#### **4.2.3 Simulated Screening Schedules**

We simulated screening schedules starting at ages 45, 55, 65, and 75 years and lasting throughout the lifetime with frequencies of screening every one and five years.

We did not simulate individual screening modalities as current, and likely future, hearing screening practices are varied across use of a single-question, survey-based, or

**Table 5: Selected model inputs for the cost-effectiveness analysis.**

<b>Clinical input parameters</b>	<b>Value</b>		<b>Reference</b>
<b>Bilateral SNHL probability, yearly, %</b>	Males	Females	4,182-184
Ages 40-45 years	0.76	0.06	
Ages 46-55 years	1.22	0.36	
Ages 56-65 years	2.33	1.25	
Ages 66-75 years	5.39	3.83	
Ages 76+ years	10.42	9.17	
<b>SNHL Progression, PTA decline in dB, mean (SD)</b>			187
Ages 35-65 years	1.05 (0.4)		
Ages 65+ years, PTA <40 dB HL	1.37 (0.4)		
<b>Yearly probability of HA uptake, %*</b>	PTA < 40dB	PTA ≥ 40 dB	5,9
Ages 40-55 years	0.54	2.35	
Age 65 years	0.51	4.60	
Age 75 years	0.60	8.14	
Age 85 years	0.71	7.20	
<b>Yearly probability of HA d/c, ages 18+, %*</b>			197,198
1 year after use	12.9		
10+ years after use	3.50		
<b>Yearly probability of CI implantation, %</b>			
Adults with severe+ HL with HAs, %	1.3		199
<b>Health state utility values</b>			4,182-184
No hearing loss	0.84		
Mild hearing loss (PTA 25-34 dB HL)	0.71		
Mild-moderate hearing loss	0.68		
Moderate hearing loss	0.65		
Moderate-severe hearing loss	0.58		
Severe hearing loss	0.54		
Profound hearing loss	0.53		
Utility benefit of hearing aids	+0.11		8,250-252
Utility benefit of cochlear implants	+0.16		250



sound test screening modality.<sup>23</sup> Instead, we incorporated test performance and cost characteristics from several modalities to create conservative cost-effectiveness estimates, as described later.

## **4.2.4 Model Input Data**

### **4.2.4.1 Natural History of Hearing Loss**

Yearly probabilities of bilateral sensorineural HL ranged from 0.8-10.4% for males and 0.1-9.2% for females.<sup>4,181-184</sup> Age-specific decline in HL is modeled as a yearly decibel (dB) increase in PTA (mean=1.05dB/year; SD=0.4).<sup>187</sup> Simulated persons may also acquire conductive HL.<sup>188-190,192,193,202,206</sup> DeciBHAL tracks sensorineural HL in dB and conductive HL in dB independently, and severity-dependent parameters are based off the more-severe PTA.

### **4.2.4.2 Hearing Aid Uptake**

Simulated persons with HL experience yearly probabilities of acquiring or discontinuing use of HAs. HA acquisition probabilities vary with age and severity (Table 5).<sup>5,9</sup> After acquiring HAs, simulated persons have yearly probabilities of discontinuation that range from 13% in year 1 after acquisition and decline to 4% in year 10.<sup>197,198</sup> These combined inputs were previously calibrated to NHANES estimates of HA use prevalence, and represent rates of symptomatic and asymptomatic detection and

linkage to care under current mixed hearing screening policies.<sup>5</sup> DeciBHAL-US projects average person-time of HA use by aggregating each year a simulated person uses a HA and dividing by the total population size.

#### **4.2.4.3 Cochlear Implant Uptake**

Patients with severe or profound HL experienced a 1.3% annual probability of cochlear implantation after at least 1 year of HA use, and a 1% probability of CI discontinuation thereafter.<sup>199,210</sup>

#### **4.2.4.4 Screening Effectiveness**

We simulated the effectiveness of HL screening schedules as a multiplier on calibrated baseline rates of HA uptake among simulated persons with HL. We based this multiplier on two randomized control trials that demonstrated increased rates of hearing healthcare uptake after screening implementation that ranged from 1.50-2.0 (using a tone-emitting otoscope or four-frequency screening device).<sup>10,240</sup> For our basecase screening effectiveness parameter (1.62), we combined the risk ratios of hearing healthcare uptake after screening versus no screening using inverse variance weighting. We assumed that among persons who failed screening, there would be a similar risk ratio for HA uptake in veterans and non-veterans (though the absolute rate is different). We varied screening effectiveness in sensitivity analysis from 1.05-2.25.

#### **4.2.4.5 Screening Test Characteristics**

We incorporated test characteristics for multiple screening test modalities, reflecting the diversity of screening methods used in practice. To estimate the number of persons without HL who might be referred for a hearing diagnostic test based on results of hearing screening, we used a false positive rate of 24%, based on pooled estimates of the Hearing Handicap Inventory for the Elderly.<sup>23</sup> We incorporated a sensitivity of 80%. These screening test characteristics affected model-projected costs, but not screening effectiveness because test characteristics were already incorporated in downstream HA uptake estimates.

#### **4.2.4.6 Health State Utilities**

We assumed a population average utility of 0.84 for persons without HL, and mild and moderate HL utility values derived from the published literature of 0.71 and 0.65.<sup>8,252,259</sup> We incorporated data from a recent systematic review on the utility benefits of HAs (+0.11) and cochlear implants (+0.17) and vary these in sensitivity analysis.<sup>8,250-252</sup>

#### **4.2.4.7 Screening Costs**

Screening test costs were applied to persons without and with HL (schedule-dependent, either yearly or every 5 years). For persons without HL, we included the cost of a screening test (\$2; device cost and personnel time amortized across all persons

screened) and the proportion of persons receiving a false positive test (24%) who would seek an audiology diagnostic test (43%; \$295), coming for a net cost of \$33.<sup>23,240,253,254</sup> For persons with HL but without hearing treatment, we included the proportion of persons that receive a true positive screen (80%) and seek an audiology diagnostic test but do not acquire HAs (51%). Along with the screening test cost (\$2) the total was \$120.<sup>240,253,254</sup>

#### **4.2.4.8 Hearing Healthcare Costs**

We included costs of an audiology diagnostic test (\$295), HA one-time purchase (\$3,690 for the device) and recurring operational and replacement costs (\$910), and costs of cochlear implantation (\$54,380 one-time, \$1,260-1,400 yearly recurring).<sup>13,208,254-256,258</sup> For HAs, we assumed 84% of fittings were binaural and accounted for the proportion of reduced cost HA fittings done through the US Department of Veteran's Affairs.<sup>13</sup> Recurring HA costs included batteries and replacement of the HA device every five years.<sup>256,257</sup>

#### **4.2.5 Sensitivity Analysis**

We performed one-way sensitivity analysis, varying model parameters across their plausible ranges, to determine their effects on the ICER of the most effective strategy with a basecase ICER < \$100,000/QALY. We then performed several multi-way sensitivity analyses, varying multiple parameters across their plausible ranges. We

included a sensitivity analysis incorporating WHO assumptions (HL treatment improves utility by 1 severity stratum) for the benefits of HA utility benefit.

#### **4.2.6 Budget Impact Analysis**

We projected 5-year undiscounted incremental costs of a screening schedule for the current US adult population compared to CD. We used DeciBHAL to determine the number of people with HL, the HL severity, and the number of people in treatment at each age. We then simulated 59 cohorts of persons (ages 40-99), scaled to the US population, over 5 years to estimate 5-year costs for each schedule (Appendix T).

### **4.3 Results**

#### **4.3.1 Clinical Results**

HA use increased with earlier age of onset of screening and increased frequency of screening, ranging from 1.27 person-years under CD to 1.68 for yearly screening starting at age 45 years. Mean age at first HA with CD was 79.2 years, whereas yearly screening schedules that initiated before age 75 reduced this age by 0.2 to 0.8 years depending on the age at first screen. Per-person lifetime undiscounted QALYs for CD were 32.107 (Table 6). Compared to CD, 5-yearly schedules increased undiscounted lifetime QALYs by 0.01-0.02, and yearly screening schedules imparted increases of 0.04-0.07 QALYs.

### **4.3.2 Costs and Cost-Effectiveness**

CD had lifetime undiscounted per-person hearing healthcare costs of \$3,300, 5-yearly screening schedules had per-person costs of \$3,630-3,960 (varying with age at first screen, 45-75 years), and yearly schedules \$4,780-6,490. Using discounted costs and QALYs, annual screening beginning at ages 75, 65, and 55 years were all considered cost-effective, with ICERs of \$39,100/QALY, \$48,900/QALY, and \$96,900/QALY, respectively. Annual screening beginning at age 45 years had an ICER of \$234,600/QALY. Compared to annual screening strategies, most 5-year screening strategies had lower benefits at increased incremental costs (Appendix U).

### **4.3.3 One-way Sensitivity Analysis**

The ICER for yearly screening beginning at age 55 years was most sensitive to single parameter variations in audiology diagnostic test cost, screening effectiveness, HA device cost, screening test false positive rate, and HA utility benefit (Figure 7). Varying these parameters across their plausible ranges, the yearly screening schedule beginning at age 55 exceeded the \$100,000/QALY threshold (Figure 7, dashed line).

**Table 6: Cost-effectiveness results of alternative US hearing screening schedules.**

<b>Schedule</b> (Initial Age) q(Interval in years)	<b>Per-person undiscounted lifetime effectiveness (QALYs)</b>	<b>Per-person undiscounted lifetime costs (2020 USD)</b>	<b>ICER (\$/QALY)<sup>a</sup></b>
Current Detection	32.107	3,300	-
75 q5	32.117	3,630	37,500
65 q5	32.120	3,780	Weakly dominated <sup>b</sup>
55 q5	32.122	3,880	Weakly dominated <sup>b</sup>
45 q5	32.122	3,960	Weakly dominated <sup>b</sup>
75 q1	32.149	4,780	39,100
65 q1	32.168	5,570	48,900
55 q1	32.175	6,100	96,900
45 q1	32.177	6,490	234,600

Abbreviations: ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life-year.

<sup>a</sup>Discounted lifetime costs and QALYs at 3%/year were used calculate incremental cost-effectiveness ratios.

<sup>b</sup>Weakly dominated: Indicates an alternative combination of strategies has greater incremental effectiveness at lower incremental cost.

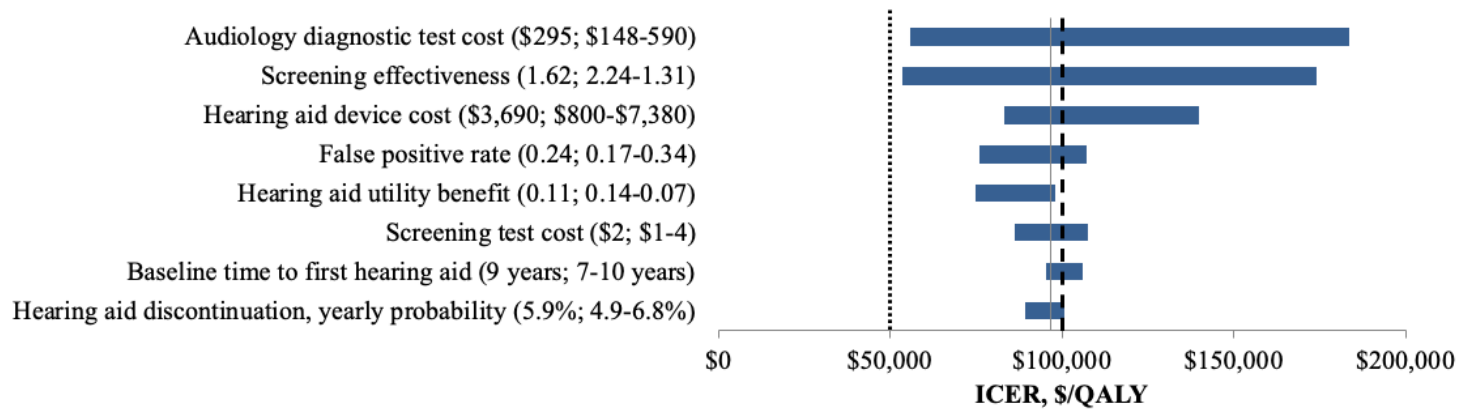


Figure 7: One-way sensitivity analysis on the cost-effectiveness of yearly screening beginning at age 55 years.

#### **4.3.4 Multi-way Sensitivity Analysis**

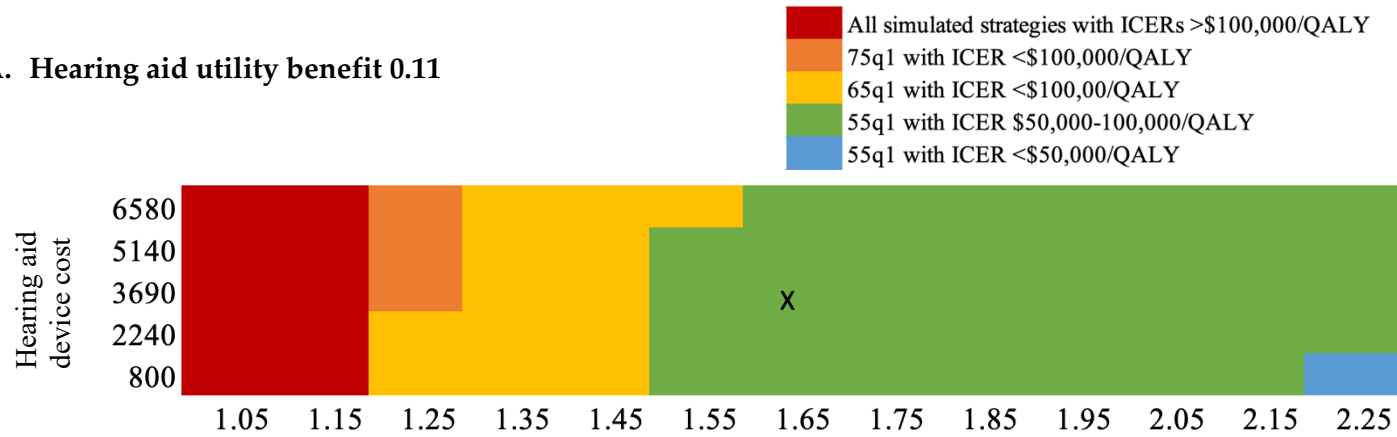
With base-case HA utility benefit inputs, yearly screening beginning at age 55 years remained under \$100,000/QALY as long as effectiveness was >1.55 and device cost was <\$6580 (Figure 8A). With screening effectiveness ranging between 1.25-1.45, yearly screening beginning at age 65 years was <\$100,000/QALY. When screening effectiveness was lowered to 1.05-1.15, none of the simulated screening schedules was cost-effective.

Lowering the HA utility benefit to match assumptions used by the WHO,<sup>175</sup> Global Burden of Disease,<sup>230</sup> and other hearing healthcare investment cases increased the base-case ICER of yearly screening at age 55 to \$169,700/QALY (Figure 8B). With these utility benefit assumptions, yearly screening at age 75 years was cost-effective (ICER=\$93,500/QALY).

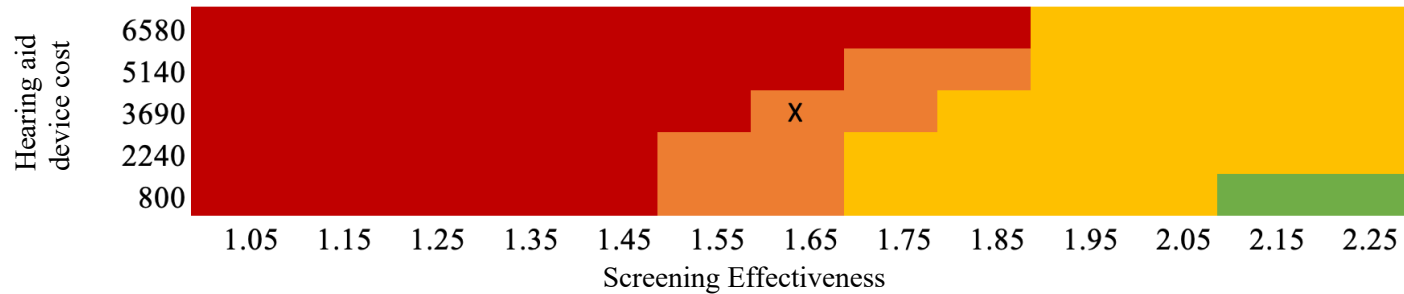
#### **4.3.5 Budget Impact Analysis**

The average annual undiscounted cost of CD over five years and for the US population over age 40 years was \$12.8B, and for yearly screening beginning at age 55 it was \$21.8B (Figure 9; Appendix V). Most differences in costs between the CD and the screening schedule were due to screening and subsequent diagnostic test costs, estimated at \$4.9B.

**A. Hearing aid utility benefit 0.11**



**B. Hearing aid utility benefit 0.01-0.07**



**Figure 8: Three-way sensitivity analysis on the cost-effectiveness of adult hearing screening schedules in the United States.**

Total Annual Cost (2020 USD)

**Figure 9: Budget Impact Analysis**

#### ***4.4 Discussion***

Our model, based on the best available evidence, predicts that hearing screening schedules for US adults would increase uptake of hearing healthcare and improve quality of life. Yearly screening at ages 55+years increased per-person undiscounted lifetime QALYs by 0.07, equivalent to extending full-health survival by 26 days (averaged across all persons without and with HL). This QALY benefit is in line with other cost-effective interventions in older adults: a recent cost-effectiveness analysis of biennial screening mammography in women over age 75 years estimated per-person QALY benefits of 3-7 days.<sup>260</sup> Compared to CD, per-person lifetime undiscounted costs increased by ~\$2,900, and the ICER was \$96,900/QALY for yearly screening beginning at age 55. Simulated screening schedules beginning later in life, such as 65 and 75 years when HL is more prevalent were even more cost-effective (ICERs<\$50,000/QALY).

In sensitivity analysis, applying less optimistic parameter values resulted in the ICER of yearly screening beginning at 55 years to exceed \$100,000/QALY. To improve the cost-effectiveness of screening, policymakers could focus on improving referral processes to hearing healthcare after screening (effectiveness) and lowering patient's costs for audiology diagnosis or purchase of HA devices. Even with lower screening effectiveness and higher HA costs, screening schedules starting later in life remained cost-effective. The cost-effectiveness of hearing screening was also sensitive to HA utility benefit assumptions. Future efforts should focus on quantifying the value of reduction in

parameter uncertainty ascertained by potential research projects through value of information analysis.<sup>217</sup>

Previous model-based cost-effectiveness analyses of adult hearing screening schedules in high-income settings have supported the economic efficiency of screening beginning at ages 55-65 years.<sup>179,253,261,262</sup> One study set in the US, based on a randomized controlled trial of  $\geq 50$ -year-old, primarily male veterans, projected a \$1,400 cost per additional HA user at one year.<sup>253</sup> Our results are not directly comparable to this study because we projected costs/QALY and over a lifetime. Two European studies projected ICERs of €3,700/QALY (\$4,700 in 2020 USD) for internet-based screening every 5-years beginning at age 50 in the Netherlands and £1,800/QALY (\$2,800 in 2020 USD) for 5-yearly primary care screening in the United Kingdom.<sup>261,262</sup> These ICERs are considerably lower than our yearly and 5-year estimates, likely due to our incorporation of audiometric evaluation costs for false positives, consideration of HA discontinuation, lower screening effectiveness assumptions, and the higher costs of HAs and healthcare in the US.

A major consideration around adult hearing screening is successful implementation in real-world settings.<sup>263,264</sup> Challenges throughout the implementation process include appropriate distribution of the hearing screening test, referral to a hearing professional, and linkage to hearing healthcare. While our base-case screening effectiveness estimates were based on comparisons to symptomatic uptake alone, they

may overestimate the effectiveness of screening in different settings and without a research infrastructure. Our sensitivity analyses varying screening effectiveness might approximate reductions in effect due to imperfect implementation. Innovative hearing screening strategies, such as availability in community settings like pharmacies and senior centers, could expand access and help to alleviate the burden on primary care settings.<sup>265,266</sup>

We simulated a combination of screening test modalities as opposed to a single modality to better represent varied practice patterns. While objective assessment measures, using tone-emitting otoscopes or four frequency screening devices, have shown better results in trials of adult hearing screening, single-question or other clinical hearing screening tests may be more feasible in a clinic setting.<sup>240,253</sup> To be conservative, we incorporated higher per person screening test costs (those associated with a tone-emitting otoscope) paired with a higher false-positive rate (associated with a survey). However, novel mobile app-based point of care hearing screening modalities would likely reduce false positives and lower overall test costs.<sup>267</sup>

Affordability of HAs after a positive screen and diagnosis of HL remains a large barrier to increased adoption of HAs.<sup>223</sup> HAs are not covered under Medicare and receive limited coverage by other insurers, so persons with HL bear the majority of the several thousand-dollar cost of HAs. One recent proposed mitigation of this problem is the Over-the-Counter Hearing Aid Act, which allows persons with perceived mild-to-

moderate HL to purchase FDA-regulated over-the-counter HA devices without a medical exam or fitting by a specialist.<sup>268</sup> While the introduction of this new category of FDA-regulated hearing devices is projected to increase access and lower HA device cost, its overall impacts on the costs and effectiveness of hearing screening are less well understood. Future research would be valuable to clarify the impact on screening cost-effectiveness.

While we found acceptable ICERs with yearly hearing screening from age 55 years, targeted screening strategies might further improve its cost-effectiveness. For example, men experience HL at younger ages than women, and individuals in occupations with high noise exposure are at higher risk of HL.<sup>4,269</sup> Screening at earlier ages may be warranted in such populations. Additionally, there are large disparities in hearing healthcare uptake by race, ethnicity, socioeconomic position, and rurality.<sup>227,228</sup> Focusing on providing access and linkage to care in these populations might yield larger societal benefit from a health equity perspective. Future research should investigate the differential impacts of hearing screening in selected populations.

Our analysis has several limitations. We made simplifying assumptions in our model structure and input data; however, we documented these assumptions and tested them in sensitivity analysis. Screening effectiveness was a key uncertain parameter, but we used the best available evidence to inform our basecase input and varied it in sensitivity analysis. Second, we assumed that the risk ratio of HA uptake due to

screening (hearing screening effectiveness) remained constant throughout the lifetime and did not change based on screening history or severity of HL. The true impact of repeated screening on persons with HL is unknown. To address this lack of information, we varied screening effectiveness extensively in sensitivity analysis. Third, we only considered uptake of HAs or downstream cochlear implants as benefits of adult hearing screening. However, there are possible benefits to screening beyond provision of technology, including acknowledgement of a suspected health issue and treatment approaches not based on use of HAs.<sup>270</sup> Additionally, there may be benefits to passing a hearing screen, such as peace of mind, that we did not consider. Fourth, we conservatively excluded potential benefits of hearing healthcare on physical and cognitive health and healthcare costs. Lastly, due to data limitations we did not include societal costs such as improved workforce participation due to HL and its treatment. Assuming that early treatment of HL improves workforce participation, the cost-effectiveness of hearing screening would improve.<sup>271</sup>

To conclude, we project annual hearing screening in US adults beginning at age 55 to be cost-effective. While future research might inform more certain parameters such as screening effectiveness, our findings were robust over a wide range of assumptions of screening effectiveness. Delaying hearing screening implementation in the hopes of perfect evidence will only further increase the wide hearing healthcare diagnosis and treatment gap and perpetuate long-standing inequities in hearing healthcare. The

inclusion of hearing in health assessments of older adults is imperative to their health and well-being, and we demonstrate here that it too is likely a good use of resources.

## **5. Adult Hearing Screening in the United States: The Value of Future Research**

### ***5.1 Introduction***

Hearing loss is the fourth leading cause of disability worldwide and over 50% of US adults ages 70 and over have clinically meaningful hearing loss.<sup>1,4</sup> While effective treatments for hearing loss are available, most US adults do not have their hearing tested and are unable to access these treatments. Hearing screening programs have been shown to increase hearing loss diagnosis and treatment uptake.<sup>10,239,240,272</sup> However, there are uncertainties around the optimal age of screening initiation, the generalizability of trial outcomes beyond predominately veteran populations, and the lack of randomized control trial evidence linking hearing screening to downstream quality of life improvements.<sup>23</sup> Future research studies may reduce the hearing screening health policy decision uncertainty, but their contribution must be weighed against the costs of conducting such studies.

Value of Information analysis (VOI) is a method to project the expected monetary value of a research project given its contributions to a decision problem.<sup>217</sup> VOI estimates the reduction in the probability of making a “wrong decision” after completion of the research project (and reduction of decision uncertainty), multiplied by the consequences of that wrong decision.<sup>217,273</sup> This value can then be compared to the

projected cost of a research project to give an upper bound on the dollar amount that should be allocated to a research project at a given willingness-to-pay (WTP).

Our objective was to estimate the potential economic value of future research reducing uncertainties in the evidence around adult hearing screening in the US. We extended a previously published model-based cost-effectiveness analysis of adult hearing screening programs in the US to perform VOI.<sup>245</sup> Decisionmakers can use these results, comparing to the projected cost of a research study, to make investment decisions and maximize patient welfare.

## ***5.2 Methods***

### **5.2.1 Analytic Overview**

For this analysis, we used the Decision model of the Burden of Hearing loss Across the Lifespan (DeciBHAL-US), parameterized with model inputs from a recent cost-effectiveness analysis of adult hearing screening in the US.<sup>245</sup> We first assigned distributions to uncertain model inputs from the prior analysis to perform probabilistic uncertainty analysis (PUA). We then calculated the expected value of perfect information (EVPI) and expected value of partial perfect information (EVPPI) by projecting the decision uncertainty reductions given reductions in model input uncertainty. We followed the Professional Society for Health Economics and Outcomes Research (ISPOR) best practices for VOI and the Second Panel on Cost-Effectiveness in

Health and Medicine.<sup>151,274</sup> We used a WTP of \$100,000/quality-adjusted life-year (QALY) and vary this value in sensitivity analysis.<sup>246,247</sup>

## **5.2.2 Model Description**

DeciBHAL-US is a microsimulation model of hearing loss natural history, diagnosis, and treatment that has been validated in the US setting.<sup>245</sup> Simulated males and females experience yearly age-specific probabilities of acquiring hearing loss (HL), either sensorineural HL or conductive HL, worsening of their HL, and receiving or discontinuing treatment (Table 7). We included hearing aids and cochlear implants as treatments for all types of hearing loss. DeciBHAL-US collects patient outcomes in terms of quality-adjusted life-years, based on hearing loss severity and treatment status, and costs in 2020 USD from a health systems perspective for each hearing simulated strategy.

## **5.2.3 Simulated Screening Schedules**

We simulated several screening strategies that varied in age at initiation, ages 45, 55, 65, and 75 years, and frequency (either every 1 or 5 years). The effects of simulated hearing screening were incorporated as a multiplier on hearing aid uptake during the year of screening. This multiplier was based on clinical trials of hearing screening as detailed later.

## 5.2.4 Probabilistic Uncertainty Analysis

We assigned distributions to five uncertain model parameters identified as most influential in deterministic sensitivity analysis. These parameters included: the utility benefit of hearing aids, screening effectiveness, screening test false positive rate, audiology diagnostic test cost, and hearing aid device cost (Table 7). We then ran 1,000 iterations of the simulation, each iteration drawing from specified distributions to inform that input.<sup>275</sup> In this way, we are able to estimate the effect of uncertainty for these five parameters assigned distributions simultaneously. Simulating all potential screening schedules and comparing incrementally, we compiled the incremental cost-effectiveness ratios (ICERs) from each iteration. We generated a cost-effectiveness acceptability curve (CEAC) by comparing each screening schedule's ICER to varying WTP values and determining the optimal strategy for that simulation iteration. The optimal strategy was defined as the most effective non-dominated strategy that fell below the defined WTP.

## 5.2.5 Value of Information Analysis

We followed previously published guidelines and methods to conduct our VOI analysis.<sup>217,274,276</sup> EVPI is the monetary consequence of making a “wrong” decision based on current knowledge compared to the optimal decision made with perfect knowledge. To project the EVPI, or the value of reducing all input parameter uncertainty, we

calculated the net marginal benefit of each strategy for every iteration of the probabilistic uncertainty analysis. The net monetary benefit is defined as the product of the expected effectiveness (QALYs) and WTP, less the expected costs. The optimal strategy is identified under each probabilistic uncertainty analysis iteration as the strategy with the highest positive net monetary benefit. We compared the net monetary benefit of the optimal strategy under each PUA to that of the expected optimal strategy (produced using the mean of each given distribution). The sum of the differences between the maximum net marginal benefit of each PUA iteration (decision with perfect information) and the expected average net monetary benefit is equivalent to the EVPI. Projected to the population level, the EVPI represents an estimated upper bound on the dollar amount of justifiable research investments. When the projected cost of a research study is less than the EVPI (or EVPPI), this study is likely a good use of research dollars.

To estimate EVPPI for screening effectiveness, or the maximum monetary benefit of a hearing screening trial that eliminates all uncertainty around the effectiveness of hearing screening on hearing aid uptake, we ran outer and inner loop simulations. In the inner loop simulation, DeciBHAL drew from four parameter distributions, analogous to the PUA. For each PUA inner loop iteration, DeciBHAL drew from the defined screening effectiveness distribution as the outer loop. This allowed for computation of the difference between the net monetary benefit of each outer loop iteration compared to the expected net monetary benefit to calculate the EVPPI in a similar manner to EVPI.

The resulting EVPPI is interpreted as the maximum monetary value of acquiring perfect information around the effectiveness of hearing screening – or the upper bound of the cost of a hearing screening trial. In our simulation, we ran 200 iterations of the inner loop and 50 iterations of the outer loop. To calculate the population EVPI and EVPPI, we multiplied the per-person EVPI and EVPPI by the estimated number of people ages 40 years and older in the US who currently have bilateral hearing loss and are not treated (prevalent population) and the expected number of people expected to acquire hearing loss over the next five years (incident population; incorporating a 3% discount factor).<sup>4,5,274,277</sup>

## 5.2.6 Clinical Input Parameters

Simulated persons began at age 40 years without HL and experience yearly probabilities of bilateral sensorineural HL (Table 7).<sup>4,181-184</sup> Yearly probabilities of conductive hearing loss were also incorporated.<sup>188-190,192,193,202,206</sup> Worsening of sensorineural HL was incorporated as a yearly decibel (dB) increase in PTA(mean=1.05dB/year; SD=0.4).<sup>187</sup> After acquiring HL of any type, simulated persons have age- and severity-specific probabilities of HL diagnosis and hearing aid uptake (0.5-8%).<sup>5,9</sup> Hearing aid discontinuation varies along with time since acquisition (13% in year 1 to 4% in year 10).<sup>197,198</sup> Hearing aid users with severe and profound HL have a 1.3% yearly probability of cochlear implantation.<sup>199,210</sup> Health state utilities were

incorporated from the literature, and the utility benefits of hearing aids (+0.11) and cochlear implants (+0.17) were from a recent systematic review.<sup>8,252,259</sup> In PUA, the utility benefit of hearing aids was assigned a beta distribution, using 95% confidence intervals 0.07-0.14.

We included screening effectiveness as the inverse variance weighted average of two trials of hearing screening (1.62).<sup>10,240</sup> We assigned a normal distribution to this parameter for PUA using the 95% confidence intervals generated by a random effects model. We used a false positive rate of 24%, which was used to calculate costs of screening, and assigned a beta distribution.<sup>23</sup>

## **5.2.7 Economic Input Parameters**

The costs of HL diagnosis and treatment included audiology diagnostic testing (\$295) and hearing aid devices (\$3,890).<sup>13,254</sup> Both parameters were assigned gamma distributions, assuming variance equal to the mean as is standard in PUA when variance is not reported for cost parameters.<sup>276</sup> Hearing aid device replacement every 5 years and battery costs were included as recurring cost. Cochlear implant costs were \$53,380 for implantation, with recurring maintenance and therapy costs of \$1,240-1,400/year.<sup>208,254,258</sup> The costs of screening were applied to persons without and with hearing loss. The screening test cost was \$2.<sup>253</sup> For persons without hearing loss, 43% of persons receiving a false positive screen acquired a diagnostic test.<sup>23,240,253,254</sup> For persons with hearing loss,

51% of persons receiving a true positive screen were assumed to pursue an audiology diagnostic test but not acquire hearing aids.<sup>240,253,254</sup>

## **5.3 Results**

### **5.3.1 Expected Cost-Effectiveness Results**

The expected discounted lifetime QALYs for current detection (CD) was 18.111, and ranged from 18.122-18.133 QALYs for the yearly screening strategies. Expected discounted lifetime costs were \$1,180 for CD, and ranges from \$1,580-2,480 for the yearly screening strategies. Yearly screening beginning at ages 75, 65, and 55 years all were cost-effective, with ICERs of \$21,600/QALY, \$45,600/QALY, and \$80,200/QALY. The ICERs for yearly screening beginning at age 45 years was \$231,700/QALY.

### **5.3.2 Probabilistic Uncertainty Analysis**

Assigning distributions to key uncertain parameters, we ran 1,000 model iterations of each screening schedule to identify the optimal strategy. At a base-case WTP of \$100,000/QALY, yearly screening beginning at age 55 years was the most effective non-dominated strategy under the WTP (optimal strategy) in 38% of the simulations (Figure 10). Yearly screening beginning at age 45 was optimal in 30% of simulations, yearly screening beginning at age 65 in 16%, CD in 11%, and yearly screening beginning at age 75 years in 6%. At lower WTPs, assuming payers are unwilling to pay >\$50,000/QALY,

CD was more frequently the optimal strategy. At WTPs higher than \$100,000/QALY, yearly screening beginning at age 45 years was frequently the optimal strategy (Figure 10).

Table 7: Selected model inputs for the value of information analysis.

Clinical input parameters	Value		Distribution	Reference
<b>Bilateral SNHL probability, yearly, %</b>	Males	Females		4,182-184
Ages 40-45y	0.76	0.06	-	
Ages 46-55y	1.22	0.36	-	
Ages 56-65y	2.33	1.25	-	
Ages 66-75y	5.39	3.83	-	
Ages 76+y	10.42	9.17	-	
<b>SNHL Progression, PTA decline in dB, mean (SD)</b>				187
Ages 35-65y	1.05 (0.4)		-	
Ages 65+, PTA <40 dB HL	1.37 (0.4)		-	
<b>Yearly probability of HA uptake, %*</b>	PTA < 40dB	PTA ≥ 40 dB		
Ages 40-55y	0.54	2.35	-	5,9
Age 65y	0.51	4.60	-	
Age 75y	0.60	8.14	-	
Age 85y	0.71	7.20	-	
<b>Yearly probability of HA d/c, ages 18+, %*</b>				197,198
1 year after use	12.9		-	
10+ years after use	3.50		-	
<b>Yearly probability of CI implantation, %</b>				
Adults with severe+ HL with HAs, %	1.3		-	199

<b>Clinical input parameters, continued</b>	<b>Value</b>	<b>Distribution</b>	<b>Reference</b>
<b>Health state utility values</b>			4,182-184
No hearing loss	0.84	-	
Mild hearing loss (PTA 25-34 dB HL)	0.71	-	
Mild-moderate hearing loss	0.68	-	
Moderate hearing loss	0.65	-	
Moderate-severe hearing loss	0.58	-	
Severe hearing loss	0.54	-	
Profound hearing loss	0.53	-	
Utility benefit of hearing aids	+0.11	Beta; alpha=33.61, beta=285.93	
Utility benefit of cochlear implants	+0.16	-	
Screening Effectiveness, multiplier on HA uptake	1.62	Normal; mean=1.6, SD=0.4	
Screening test false positive rate	14%	Beta, alpha=93.54, beta=29.70	
<b>Economic input parameters</b>	<b>Value (2020 USD)</b>	<b>Distribution</b>	<b>Reference</b>
Screening test cost	2	-	253
Audiology diagnostic test cost	295	Beta; alpha=1, beta=295	254
Hearing aid device(s) cost	3,890	Gamma; shape=1, scale=3890	13
Yearly Hearing aid recurring cost	1,090	Varied along with device cost	13,254
Cochlear implantation cost	54,380	-	
Yearly recurring costs, cochlear implantation	1,260-1,400	-	208,254,258

\*Linear interpolation was used between ages not displayed.

**Abbreviations:** CI: cochlear implant; dB: decibel; d/c: discontinuation; HA: hearing aid; HL: hearing level; PTA: pure tone average; SD: standard deviation; SNHL: sensorineural hearing loss.

### **5.3.3 Expected Value of Perfect Information**

At the basecase WTP of \$100,000/QALY, the per-person value of reducing all uncertainty in the hearing screening decision problem was \$176 (Table 8A). Extending this value to all US adults ages 40+ with untreated hearing loss, as well as those expected to acquire hearing loss over the next 5 years, the population EVPI was \$9.6 billion. This result is the estimated upper bound of research funding for the hearing screening problem. Varying WTP assumptions, the population EVPI ranged from \$8.2-\$12.6 billion.

### **5.3.4 Expected Value of Partial Perfect Information**

We projected the value of reducing all uncertainty on the hearing screening effectiveness parameter using EVPPI analysis. At the basecase WTP of \$100,000/QALY, the per-person EVPPI for screening effectiveness was \$45 (Table 8B). Extended to the current and future population affected by this decision, the population EVPPI was \$2.4 billion. This result suggests that no more than \$2.4 billion should be spent on a hearing screening trial.

**Table 8: Expected value of perfect information and expected value of partial perfect information for screening effectiveness across varying willingness to pay thresholds.**

<b>A. Willingness to Pay (\$/QALY)</b>	<b>Expected value of perfect information</b>	<b>Population expected value of perfect information (2020 USD, billions)</b>
\$50,000	\$234	\$12.641
\$100,000	\$176	\$9.555
\$150,000	\$152	\$8.244
\$200,000	\$167	\$9.020

<b>B. Willingness to Pay (\$/QALY)</b>	<b>Expected value of partial perfect information for screening effectiveness</b>	<b>Population expected value of partial perfect information for screening effectiveness (2020 USD, billions)</b>
\$50,000	\$23	\$1.270
\$100,000	\$45	\$2.434
\$150,000	\$38	\$2.038
\$200,000	\$58	\$3.148

Abbreviations: QALY: quality-adjusted life-year.

All costs are presented in 2020 USD.

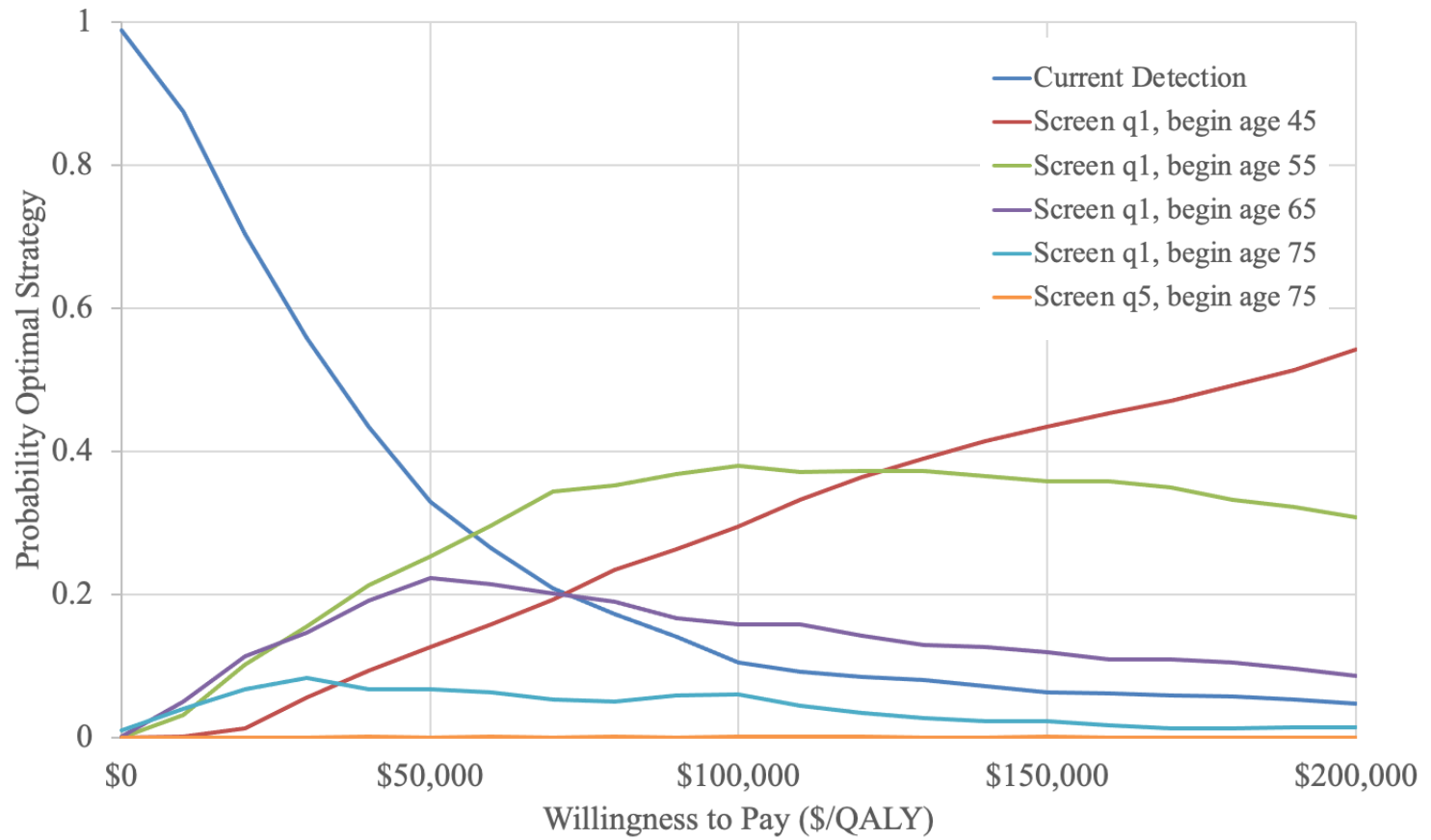


Figure 10: Cost-effectiveness acceptability curve.

## ***5.4 Discussion***

Our stochastic modeling analysis demonstrated large uncertainties in the optimal hearing screening schedule for US adults. At the US standard WTP, yearly screening beginning at age 55 years was most frequently the optimal strategy, although initiation at ages 45, and 65 years and no screening (CD) were each the optimal strategies in >10% of simulations. This high level of decision uncertainty due to imperfect current information, combined with the significant prevalence of untreated hearing loss, led to large EVPI estimates that ranged from \$8.2-\$12.6 billion. Considering just eliminating the uncertainty around the effectiveness of hearing screening, the population EVPPI was \$2.4 billion. This monetary value might be compared to the cost of future trials to inform hearing screening effectiveness – we project research efforts that clarify the effectiveness of hearing screening costing less than \$2.4 billion to be a good use of resources.

Comparing our estimated EVPPI of a hearing screening trial to costs of recently completed trials in hearing healthcare, it is imminently possible that further research be conducted to determine the effects of adult hearing screening on hearing aid uptake. For instance, the NIH-reported costs of the Aging, Cognition, and Hearing Evaluation in Elders (ACHIEVE) randomized trial totaled \$16.5 million.<sup>278</sup> This trial sought to evaluate the effect of hearing intervention vs. aging education control on incident dementia, recruiting 850 patients with a 3-year follow-up.<sup>20</sup> A hearing screening trial might be conducted over an even shorter timeline, and for much less than the EVPPI estimate of

\$2.4 billion. Further, our total EVPI suggests that research around hearing healthcare may be underfunded in the US. The entire National Institute on Deafness and Communication Disorders 2021 budget was \$446 million, substantially lower than our adult hearing screening research value of \$8.2-\$12.6 billion.<sup>279</sup> Given the large clinical and economic consequences of the adult hearing screening decision, large funding and research effort into identifying the optimal decision is warranted.

While our results give an upper bound on the monetary value of perfect and partial perfect information for adult hearing screening, they cannot estimate the value of a particular study or study design. Extended VOI methods, such as the expected value of sample information, might be implemented in future research to better understand the value of an imperfect research study that only partially clarifies an uncertain parameter.<sup>280</sup> Further, expected value of sample information methods can inform trial design and sample size calculation, and account for imperfect implementation.<sup>281</sup> Although computational power has been a limiting factor in calculating expected value of sample information, novel methods might allow for more efficient estimation.<sup>282</sup>

Our analysis is strong in that it incorporates the best available evidence to estimate the decision uncertainty around adult hearing screening in the US and is the first estimate of the value of future research in US adult hearing screening. However, this study has several limitations. First, our model includes simplifying assumptions around hearing loss natural history, treatment uptake, and screening implementation.

We detail and justify these assumptions here and elsewhere.<sup>245</sup> Second, given computational limitations, we did not assign distributions to every model parameter. Instead, we identified the most influential parameters in deterministic analysis, as well as the most uncertain parameters from a clinical and policy perspective, to explore in PUA. Third, we varied the false positive rate across its plausible range but did not simultaneously vary screening sensitivity. This was because we did not explicitly incorporate sensitivity in our calculations, but rather included screening effectiveness as downstream hearing aid uptake. Future analyses might better explore the sensitivity and specificity of specific hearing screening modalities. Lastly, we only estimated EVPPI for the screening effectiveness parameter. We selected this parameter for EVPPI analysis based on expert opinion on the most uncertain parameter in the general population and most significant research gap.<sup>23</sup>

In conclusion, our model-based analysis projects high potential value of future research on adult hearing screening, and in particular the effectiveness of hearing screening. The high degree of uncertainty around the optimal age of hearing screening initiation, paired with the significant burden of hearing loss in the US, justifies research investment. Future research projects that resolve uncertain elements of the decision problem may clarify the best hearing screening decision for the millions of US adults with hearing loss.

## 6. Conclusions and Future Directions

The combined results of this dissertation have significant clinical and policy implications. The evidence-based modeling analyses demonstrate the cost-effectiveness of screening older US adults for hearing loss yearly beginning at age 55. This finding may help bring clarity to current USPSTF recommendations that leave the hearing screening decision up to individual patient-clinician decision making. The findings support, from a cost-effectiveness perspective, clinical guidelines that recommend screening older adults for hearing loss. While the USPSTF usually requires a randomized clinical trial demonstrating health benefits of preventative services, our decision modeling approach shows that across a wide range of hearing screening effectiveness assumptions screening adults for hearing loss yearly at age 55 is cost-effective. Decisions to screen or to not screen for hearing loss are being made daily in the US, and we show that given the current evidence hearing screening is likely effective and cost-effective. Our results further inform conversations around the value assessment of hearing healthcare interventions and may be used in clinical decision support tools weighing costs with potential benefits. Lastly, consumer education around the burden of hearing loss in the US, the various treatment options, and their value, might reduce barriers to screening and appropriate treatment and mitigate stigma.

Importantly, hearing aids are poorly covered under most insurance and Medicare explicitly excludes hearing aid coverage in its statutes. Our work shows the

large potential health gains resulting from identifying persons with hearing loss and providing them with hearing aids and hearing healthcare. As cost of hearing aids is often prohibitive for patients in the US, policy changes that cover or partially cover the cost of hearing aids would be beneficial to patients and cost-effective by US standards. While reforms to Medicare regulations to cover hearing aids was considered in 2021, they were not enacted. Our work may be used to inform future debates around the value of hearing healthcare provision in the US. Further, our work potentially supports additional research and medical technology innovation to enhance the value of hearing aids, and increase utilization and sustainable uptake.

While the base-case, or best-guess, model pointed to yearly screening beginning at age 55 years as the decision strategy, when all model parameter uncertainty was considered the optimal age for screening initiation was uncertain. Through value of information analysis, I showed that large investments are warranted to help reduce this decision uncertainty. Indeed, the expected value of partial perfect information for hearing screening was \$2.4 billion. Compared to other randomized trials in hearing healthcare, this is a large sum and suggests that future research funding for a hearing screening trial is likely a good use of resources.

The research outcomes from Chapter Three provide one of the first quantitative decision modeling frameworks for US adult hearing screening. The framework informed research output in subsequent chapters of the current dissertation, but also may serve as

a basis for future research questions regarding adult hearing health. There are ongoing efforts to expand this model to low- and middle-income settings to better inform global hearing healthcare and resource prioritization. Using similar methods as those in Chapter Four, we seek to use DeciBHAL to inform global cost-effectiveness analyses for the Lancet Commission on Hearing Loss.<sup>1,12</sup> As a part of these efforts, we seek to make a version of DeciBHAL available to decisionmakers in an online tool. This will require adapting the current modeling framework to allow for end-user imputation of inputs relevant to their decision problem. Lastly, there are ongoing efforts clarifying the impacts of hearing loss and its treatment on employment status, absenteeism, and education attainment to better inform a societal perspective analysis of hearing healthcare.

The association between hearing loss and other health outcomes, such as falls risk and dementia, is well understood and future DeciBHAL analyses might account for any potential reduction in these spillover health effects due to the prevention or treatment of hearing loss. Hearing loss is the leading preventable cause of dementia worldwide, with a population attributable fraction of 9%, so the ability to assess the impact of hearing loss prevention on dementia incidence will be important to future analyses. With regard to the hearing screening question, to the extent that hearing loss treatment reduces falls or dementia risk, hearing screening would become even more economically efficient.

There are additionally well-documented disparities in hearing healthcare and future DeciBHAL analyses might further stratify hearing loss natural history and treatment outcomes by race, ethnicity, socioeconomic status, or rurality. This stratification might allow for the assessment of targeted hearing screening strategies, or other hearing healthcare interventions, to reduce health inequities due to systemic racism and classism. Novel methods to incorporate the evaluation of health equity impacts of cost-effectiveness analysis, such as equity impact and equity trade-off analysis, might better illuminate the potential effects of hearing intervention on health equity.<sup>283</sup>

The significant burden of unaddressed hearing loss in the United States presents a large opportunity for implementation of cost-effective interventions to prevent, diagnose, and treat hearing loss across the lifespan. Research outcomes within this dissertation provide quantitative evidence to hearing health clinical and policy decisionmakers to inform optimal hearing screening and treatment strategies for older adults in the United States. Maximizing patient welfare through selection of cost-effective hearing public health interventions is an important step towards eliminating hearing loss as a barrier to human communication and fulfillment.

## Appendix A. Lancet Commission on Hearing Loss Commissioner Roster List.

Table A.1: Lancet Commission on Hearing Loss Commissioner roster list.

Name	Title	Affiliation
Blake Wilson	Commission Chair	Duke University
Debara Tucci	Commission Co-Chair	National Institutes of Health
Bolajoko Olusanya	Commission Co-Chair	Centre for Healthy Start Initiative
Shelly Chadha	Commissioner Co-Chair	World Health Organization
Gillian Sanders Schmidler	Commissioner	Duke University
Howard Francis	Advisory Board Member	Duke University
Osondu Ogbuoji	Commissioner	Duke University
Gerry O'Donoghue	Commissioner	University of Nottingham
Anne Schilder	Commissioner	University College London
Catherine McMahon	Commissioner	Macquarie University
Enis Baris	Commissioner	The World Bank
Eric Finkelstein	Commissioner	Duke NUS Medical School
Fan-Gang Zeng	Commissioner	University of California, Irvine
Frank Lin	Commissioner	Johns Hopkins
George Tavartkiladze	Commissioner	National Research Centre for Audiology

Name	Title	Affiliation
		and Hearing Rehabilitation
Judy Dubno	Commissioner	Medical University of South Carolina
Ms. Katherine Bouton	Commissioner	Hearing Loss Association of America
Muhammad Pate	Commissioner	World Bank
Mark McClellan	Commissioner	Duke
Patricia Castellanos de Munoz	Commissioner	CEDAF Hearing Center
Ricardo Ferreira Bento	Commissioner	Medicine School University of Sao Paulo
Ronna Hertzano	Commissioner	University of Maryland
Susan Emmett	Commissioner	Duke
Zulfiqar Bhutta	Commissioner	University of Toronto Aga Khan University
Isaac Macharia	Commissioner	University of Nairobi
Suneela Garg	Commissioner	Maulana Azad Medical College & Associated Hospitals New Delhi
Carolina Der	Commissioner	University of Chile
Charlotte Chiong	Commissioner	University of the Philippines
Mira Johri	Commissioner	University of Montreal
Janet Bettger	Commissioner	Duke University
Shiming Yang	Commissioner	Chinese PLA General

## Appendix B. Search Strategy for the Systematic Review.

### Database: MEDLINE (via PubMed)

Search date: 6/14/2020

Note: set sort order to Most Recent

Table B.1: MEDLINE search strategy.

#	Terms	Results
#1 <i>Hearing loss</i>	"Hearing Loss"[Mesh] OR "hearing"[tiab]	128,921
#2 <i>Cost effectiveness</i>	"Costs and Cost Analysis"[Mesh] OR "Cost-Benefit Analysis"[Mesh] OR "cost-benefit"[tiab] OR "cost-effectiveness"[tiab] OR "cost utility"[tiab] OR "economic evaluation"[tiab] OR "economic evaluations"[tiab] OR "economic model"[tiab] OR "economic models"[tiab]	271,991
#3 (combining)	#1 AND #2	919
#4 (narrowing)	#3 AND English[lang]	856
#5 (narrowing)	#4 NOT (Editorial[ptyp] OR Letter[ptyp] OR Case Reports[ptyp] OR Comment[ptyp]) NOT (animals[mh] NOT humans[mh])	806

### Database: EMBASE (via Elsevier)

Search date: 6/14/2020

Note: Search from the Results page

Table B.2: EMBASE search strategy.

#	Terms	Results
#1 <i>Hearing loss</i>	'hearing impairment'/exp OR hearing:ti,ab	188,233
#2	'cost benefit analysis'/exp OR 'cost effectiveness	260,154

<i>Cost effectiveness</i>	analysis'/exp OR 'cost utility analysis'/exp OR 'economic evaluation'/de OR 'cost-benefit':ti,ab OR 'cost-effectiveness':ti,ab OR 'cost utility':ti,ab OR 'economic evaluation':ti,ab OR 'economic evaluations':ti,ab OR 'economic model':ti,ab OR 'economic models':ti,ab	
#3 (combining)	#1 AND #2	1,212
#4 (narrowing)	#3 AND [english]/lim AND [humans]/lim	1,084
#5 (narrowing)	#4 NOT ('case report'/exp OR 'case study'/exp OR 'editorial'/exp OR [editorial]/lim OR 'letter'/exp OR [letter]/lim OR 'note'/exp OR [note]/lim OR [conference abstract]/lim OR 'conference abstract'/exp OR 'conference abstract'/it)	882

**Database: Cochrane Library (via Wiley)**

Search date: 6/14/2020

Note: search from Advanced Search < Search Manager

**Table B.3: Cochrane Library search strategy.**

#	Terms	Results
#1 <i>Hearing loss</i>	[mh "Hearing Loss"] OR hearing:ti,ab	5611
#2 <i>Cost effectiveness</i>	[mh "Costs and Cost Analysis"] OR [mh "Cost-Benefit Analysis"] OR cost-benefit:ti,ab OR cost-effectiveness:ti,ab OR "cost utility":ti,ab OR "economic evaluation":ti,ab OR "economic evaluations":ti,ab OR "economic model":ti,ab OR "economic models":ti,ab	25,215
#3 (combining)	#1 AND #2	97

**Database: Global Index Medicus**

*Produced by the World Health Organization, this resource offers the ability to search the literature in regional medical indices, including AIM (AFRO), LILACS (AMRO/PAHO), IMEMR (EMRO), IMSEAR (SEARO), and WPRIM (WPRO).*

Search date: 6/14/2020

*Note: Search from Advanced Search*

**Table B.4: Global Index Medicus search strategy.**

#	Terms	Results
#1	tw:(hearing) AND (tw:(cost OR costs OR cost-effectiveness OR cost-benefit OR cost-utility))	137
#2	English Filter	80

## Appendix C. Population, Intervention, Comparison, Outcome, Time, and Study Design Table of the Inclusion Criteria for the Systematic Review.

Table C.1: Population, Intervention, Comparison, Outcome, Time, and Study Design table of the inclusion criteria for the systematic review.

	Inclusion Criteria	Exclusion Criteria
<b>Population or problem of interest</b>	Persons with hearing loss  Conditions that affect hearing loss (i.e., bacterial meningitis, etc.)	Persons without hearing loss
<b>Interventions / prognostic factors / diagnostic test / exposure of interest</b>	Any diagnostic or therapeutic intervention related to hearing loss	Interventions unrelated to hearing loss
<b>Comparison (if any)</b>	Any comparison	-
<b>Outcome</b>	Study must consider costs and clinical benefits	Studies that do not consider costs and clinical benefits
<b>Time</b>	Any	-
<b>Study Types</b>	Original research articles  Cost-effectiveness analyses that utilize a decision model	Editorials, case reports, letters, comments  Trial-based cost-effectiveness analyses that do not use a decision model  Cost-benefit analyses that do not report clinical outcomes

## Appendix D. Complete List of Data Points Extracted for the Systematic Review.

Table D.1: Complete list of data points extracted for the systematic review.

Variable	Definition	Data Collection
<b>Article Type</b>	-	CEA with decision model Systematic Review
<b>Setting</b>	What was the primary setting the study was performed?	Africa Asia Australia/NZ Canada Latin America Middle East South America UK/Europe United States Other or unsure (list country here)
<b>Intervention/Condition</b>	What type of intervention or condition was analyzed? (select all that apply)	Cochlear Implants Neonatal Screening Child Screening Occupational Exposure Otitis Media with Effusion Vaccine Adult Screening Hearing Aids ASNHL MRI Hearing loss general Medulloblastoma Drug Reactions Neonatal CMV Schwannoma Otosclerosis

<b>Variable</b>	<b>Definition</b>	<b>Data Collection</b>
		Implantable Hearing Aids Other or Unsure (list here):
<b>Model Type</b>	What type of decision model was used?	Decision Tree Markov Diagram Probabilistic Net-Cost Other/Unclear (list other model here)
<b>Perspective</b>	What was the perspective of the model?	Healthcare Payer Healthcare System Patient Societal Modified Societal Not Clear Other (list here):
<b>Statement of Perspective</b>	Was the perspective explicit or inferred?	Explicit Inferred
<b>Population</b>	What was the population?	Pediatric (<18) Adult (18+) Subgroup (enter here):

<b>Variable</b>	<b>Definition</b>	<b>Data Collection</b>
<b>Hearing Loss Type</b>	What was the hearing loss type?	Unilateral sensorineural Bilateral sensorineural Sensorineural (not reported either unilateral or bilateral) Conductive Mixed Unclear Other (enter here):
<b>Comparators</b>	Enter each comparator in each field	Arm 1: Arm 2: Arm 3: Etc.
<b>Health Outcome Measurement</b>	What was the health outcome measurement of the model?	QALY DALY Life-years Other (enter here):
<b>Definition of Hearing Loss</b>	What was the definition of hearing loss in the model?	Enter here:
<b>Time Horizon</b>	What was the time horizon of the model?	Lifetime Other: reported in years
<b>Currency/Year</b>	What was the currency/year of the model?	Year/Currency
<b>Basecase ICER of Intervention</b>	What are the “Abstract-worthy” cost-effectiveness results?	Enter here:
<b>Model Validation</b>	How was the model validated?	Enter here:
<b>Method of</b>	What was the	One-way deterministic

<b>Variable</b>	<b>Definition</b>	<b>Data Collection</b>
<b>Characterizing Uncertainty</b>	method of the model?	Multi-way deterministic Probabilistic Unclear None Other (list here):
<b>Funding</b>	What was the funding source?	No funding Government Non-Government/Non-Industry Industry Unclear Other (enter here):
<b>Disclosure Statement</b>	Was there a disclosure statement?	Yes No

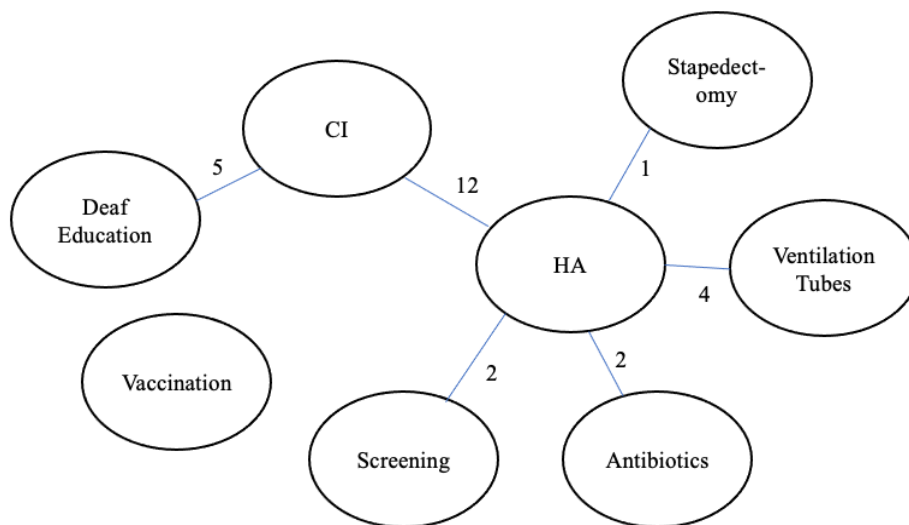
## Appendix E. Summary of the Quality Rating Measure for the Systematic Review.

Table E.1: Summary of the quality rating measure for the systematic review.

Criterion Short Name	Criterion Description	Weight
Study Objective	Was the study objective presented in a clear, specific, and measurable manner?	7
Perspective	Were the perspective of the analysis (societal, third-party payer, etc.) and reasons for its selection stated?	4
Source of variable estimates	Were variable estimates used in the analysis from the best available source (i.e., Randomized Control Trial-Best, Expert Opinion-Worst)?	8
Subgroup	If estimates came from a subgroup analysis, were the groups prespecified at the beginning of the study?	1
Uncertainty	Was uncertainty handled by: 1) statistical analysis to address random events; 2) sensitivity analysis to cover a range of assumptions?	9
Incremental analysis	Was incremental analysis performed between alternatives for resources and costs?	6
Data abstraction methodology	Was the methodology for data abstraction (including value health states and other benefits) stated?	5
Time horizon	Did the analytic horizon allow time for all relevant and important outcomes? Were benefits and costs that went beyond 1 year discounted (3-5%) and justification given for the discount rate?	7
Cost measurement	Was the measurement of costs appropriate and the methodology for the estimation of quantities and unit costs clearly described?	8

Primary outcome measures	Were the primary outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	6
Health outcomes measures	Were the health outcomes measures/scales valid and reliable? If previously tested valid and reliable measures were not available, was justification given for the measures/scales used?	7
Display of economic model	Were the economic model (including structure), study methods and analysis, and the components of the numerator and denominator displayed in a clear transparent manner?	8
Statement and justification of choices	Were the choice of economic mode, main assumptions and limitations of the study stated and justified?	7
Direction and magnitude of potential biases	Did the author(s) explicitly discuss direction and magnitude of potential biases?	6
Conclusions	Were the conclusions/recommendations of the study justified and based on the study results?	8
Disclosure of funding	Was there a statement disclosing the source of funding for the study?	3

## Appendix F. Intervention Comparisons Made Among Included Studies in the Systematic Review.



**Figure F.1: Intervention comparisons made among included studies in the systematic review.**

In this Figure, we compiled the number of studies that had comparisons across intervention categories. In this figure, we included studies that considered the four most common interventions: hearing screening, cochlear implants, hearing aids, and vaccination. CI: cochlear implantation, HA: hearing aid.

## Appendix G. Main Cost-Effectiveness Findings from Included Studies in the Systematic Review.

**Table G.1: Main cost-effectiveness findings from included studies in the systematic review.**

Bibliography	Main Cost-Effectiveness Findings
Abrams, H., Chisolm, T. H., McArdle, R. A. cost-utility analysis of adult group audiologic rehabilitation: are the benefits worth the cost? <i>J Rehabil Res Dev.</i> 2002. 39:549-58	HA treatment cost \$60.00/QALY gained compared to no treatment, while HA + audiologic rehabilitation cost only \$31.91/QALY gained compared to no treatment.
Baltussen, R., Smith, A. Cost-effectiveness of selected interventions for hearing impairment in Africa and Asia: A mathematical modelling approach. <i>International Journal of Audiology.</i> 2009. 48:144-158	Findings showed that in both regions, screening strategies for hearing impairment and delivery of hearing aids cost between I\$1000/DALY and I\$1600/DALY, with passive screening being the most efficient intervention. Active screening at schools and in the community were somewhat less cost-effective. In the treatment of chronic otitis media, aural toilet in combination with topical antibiotics costs was more efficient than aural toilet alone, and cost between I\$11 and I\$59/DALY in both regions. The treatment of meningitis with ceftriaxone cost between I\$55 and I\$217/DALY at low coverage levels, in both regions.
Baltussen, R. Smith, A. Cost effectiveness of strategies to combat vision and hearing loss in sub-Saharan Africa and South East Asia: mathematical modelling study. <i>Bmj.</i> 2012. 344:e615	The cost per DALY averted was < I\$285 for all hearing loss interventions.
Bamford, J. Fortnum, H., Bristow, K., Smith, J., Vamvakas, G., Davies, L., Taylor, R., Watkin, P., Fonseca, S., Davis, A., Hind, S. Current practice, accuracy, effectiveness and cost-effectiveness of the school entry hearing screen. <i>Health Technol Assess.</i> 2007. 11:1-168, iii-iv	Universal school entry screening based on pure-tone sweep tests was associated with higher costs and slightly higher QALYs compared with no screen and other screen alternatives; ICER = £2500/QALY gained. The range of expected costs, QALYs, and net benefits was broad.
Berman, S., Roark, R., Luckey., D. Theoretical cost effectiveness of management options for children with persisting middle ear effusions. <i>Pediatrics.</i> 1994. 93:353-63	Most cost-effective intervention combination is corticosteroid plus an antibiotic at visit 1 followed by second antibiotic in non-responders at visit 2 and referral for ventilating tubes in non-responders at visit 3.
Beswick, R., David, M., Higashi, H., Thomas, D., Nourse, C., Koh, G., Koorts, P., Jardine, L. A., Clark, J. E. Integration of congenital cytomegalovirus screening	The cost comparison suggests the cost implementation of cCMV screening (and subsequent potential treatment benefits and management over time), compared to non-screening (and subsequent

within a newborn hearing screening programme. <i>Journal of Paediatrics and Child Health</i> . 2019. 55:1381-1388	management), to be negligible.
Bichey, B. G., Hoversland, J. M., Wynne, M. K., Miyamoto, R. T. Changes in quality of life and the cost-utility associated with cochlear implantation in patients with large vestibular aqueduct syndrome. <i>Otol Neurotol</i> . 2002. 23:323-7	Cochlear implantation vs hearing aid had an ICER of \$12,774/QALY.
Bichey, B. G., Miyamoto, R. T. Outcomes in bilateral cochlear implantation. <i>Otolaryngol Head Neck Surg</i> . 2008. 138:655-61	Results indicated a 0.48 mean gain in health utility after bilateral cochlear implantation and a discounted cost of \$24,859/QALY in this cohort of patients.
Boas, G., Van Der Stel, H., Peters, H., Joore, M., Anteunis, L. Dynamic modeling in medical technology assessment: Fitting hearing aids in the Netherlands. <i>International Journal of Technology Assessment in Health Care</i> . 2001. 17:618-625	In the age group of 60–64 years old, the costs per QALY ratios of the Fitting HA Program and the Post-purchase Counseling HA Program amounted to €21,154 and €18,046/QALY, respectively.
Bond, M., Mealing, S., Anderson, R., Elston, J., Weiner, G., Taylor, R. S., Hoyle, M., Liu, Z., Price, A., Stein, K. The effectiveness and cost-effectiveness of cochlear implants for severe to profound deafness in children and adults: a systematic review and economic model. <i>Health Technol Assess</i> . 2009. 13:1-330	In prelingually deaf children, the ICER for u/l CI was £13,413/QALY, £40,410/QALY for simultaneous b/l CI, and 54,098/QALY for sequential b/l CI.  In post-lingually deaf adults, the ICER for u/l CI was £14,163, for simultaneous b/l CI was £49,559, and for sequential b/l CI was £60,301/QALY.
Bos, J. M., Rumke, H. C., Welte, R., Spanjaard, L., van Alphen, L., Postma, M. J. Combination vaccine against invasive meningococcal B and pneumococcal infections: potential epidemiological and economic impact in the Netherlands. <i>Pharmacoeconomics</i> . 2006. 24:141-53	Base-case cost-effectiveness (vaccine price €40) was €17,700/QALY. The model was most sensitive to changes in incidence, vaccine price, and duration of protective efficacy.
Bos, Jasper M, Rümke, Hans, Welte, R, Postma, MJ. Epidemiologic impact and cost-effectiveness of universal infant vaccination with a 7-valent conjugated pneumococcal vaccine in the Netherlands. <i>Clinical therapeutics</i> . 2003. 25:2614-2630	With a vaccine price of €40 per dose, the base-case cost-effectiveness ratio would be €71,250/QALY.
Boshuizen, H. C., van der Lem, G. J., Kauffman-de Boer, M. A., van Zanten, G. A., Oudesluys-Murphy, A. M., Verkerk, P. H. Costs of different strategies for neonatal hearing screening: a modelling approach. <i>Arch Dis Child Fetal Neonatal Ed</i> . 2001. 85:F177-81	Costs of a three-stage screening process in child health clinics were €39.0 (95% confidence interval 20.0 to 57.0) per child detected with automated auditory brainstem response compared with €25.0 (14.4 to 35.6) per child detected with otoacoustic emissions.
Brown, J. Screening infants for hearing loss--an economic evaluation. <i>J Epidemiol Community Health</i> . 1992. 46:350-6	Cost per unit output: - £20.57 for the conventional screening - £11.23 for Alternative policy 1

	<p>- £11.23 for Alternative policy 2  - £11.13 for Alternative policy 3  - £11.27 for No screening</p>
<p>Bruce, I., Harman, N., Williamson, P., Tierney, S., Callery, P., Mohiuddin, S., Payne, K., Fenwick, E., Kirkham, J., O'Brien, K. The management of Otitis Media with Effusion in children with cleft palate (mOMent): a feasibility study and economic evaluation. <i>Health Technol Assess.</i> 2015. 19:1-374</p>	<p>VTs vs. do nothing had an ICER of £9,065 per QALY gained. Other strategies are dominated.</p>
<p>Burke, M. J., Shenton, R. C., Taylor, M. J. The economics of screening infants at risk of hearing impairment: an international analysis. <i>Int J Pediatr Otorhinolaryngol.</i> 2012. 76:212-8</p>	<p>Universal screening vs. selective screening had an ICER per case detected of £36,181 (\$58,497), and INR 157,084 (\$9,863) for the UK and India, respectively. One-stage vs. two-stage universal screening had an ICER per case detected of £120,972 (\$195,586), and INR 926,675 (\$58,183) for the UK and India, respectively.</p>
<p>Butler, James RG, McIntyre, Peter, MacIntyre, C Raina, Gilmour, Robin, Howarth, Ann L, Sander, Beate. The cost-effectiveness of pneumococcal conjugate vaccination in Australia. <i>Vaccine.</i> 2004. 22:1138-1149</p>	<p>The discounted cost per death avoided is \$5.0 million, \$230,130 per life-year saved, and \$121,100 per DALY averted, giving a break-even vaccine price of \$15.40 per dose.</p>
<p>Carter, R., Hailey, D. Economic evaluation of the cochlear implant. <i>Int J Technol Assess Health Care.</i> 1999. 15:520-30</p>	<p>Costs in AUD per QALY (15-year assessment) ranged from \$5,070–\$11,100 for children, \$11,790–\$38,150 for profoundly deaf adults, and \$14,410– \$41,000 for partially deaf adults.</p>
<p>Chao, T. K., Chen, T. H. Cost-effectiveness of hearing aids in the hearing-impaired elderly: a probabilistic approach. <i>Otol Neurotol.</i> 2008. 29:776-83</p>	<p>HA ICERs for women and men were US \$13,615/QALY (Euro 10,826) and \$9,702/QALY (Euro 7,715), respectively</p>
<p>Chen, J. M., Amoodi, H., Mittmann, N. Cost-utility analysis of bilateral cochlear implantation in adults: a health economic assessment from the perspective of a publicly funded program. <i>Laryngoscope.</i> 2014. 124:1452-8</p>	<p>The ICER for bilateral CI compared to no intervention was \$14,658/QALY. The ICUR was \$55,020/QALY comparing unilateral to bilateral CI.</p>
<p>Cheng, A. K., Rubin, H. R., Powe, N. R., Mellon, N. K., Francis, H. W., Niparko, J. K. Cost-utility analysis of the cochlear implant in children. <i>Jama.</i> 2000. 284:850-6</p>	<p>The CI ICER was \$9,029/QALY using the TTO, \$7,500/QALY using the VAS, and \$5,197/QALY using the HUI. CI was cost-saving when educational impact was included.</p>
<p>Cheng, L. J., Soon, S. S., Wu, D. B., Ju, H., Ng, K. Cost-effectiveness analysis of bilateral cochlear implants for children with severe-to-profound sensorineural hearing loss in both ears in Singapore. <i>PLoS One.</i> 2019. 14:e0220439</p>	<p>Simultaneous bilateral cochlear implant compared to bimodal hearing had an ICER of \$60,607/ QALY. Sequential bilateral cochlear implantation compared to bimodal had an ICER of \$81,782/QALY.</p>

Chiou, S. T., Lung, H. L., Chen, L. S., Yen, A. M., Fann, J. C., Chiu, S. Y., Chen, H. H. Economic evaluation of long-term impacts of universal newborn hearing screening. <i>Int J Audiol.</i> 2017. 56:46-52	At willingness to pay of \$20,000, aABR had a 90% probability of being cost-effective against TEOAE.
Claes, Christa, von der Schulenburg, Johann-Matthias Graf. Cost effectiveness of pneumococcal vaccination for infants and children with the conjugate vaccine PnC-7 in Germany. <i>Pharmacoeconomics.</i> 2003. 21:587-600	Conjugate pneumococcal vaccine will result in and ICER of €72,866/life-year saved in Germany.
Clegg, A. J., Loveman, E., Gospodarevskaya, E., Harris, P., Bird, A., Bryant, J., Scott, D. A., Davidson, P., Little, P., Coppin, R. The safety and effectiveness of different methods of earwax removal: a systematic review and economic evaluation. <i>Health Technol Assess.</i> 2010. 14:1-192	ICER of softeners followed by self-irrigation is £24,450/QALY. ICER of softeners followed by irrigation at primary care is £32,136/QALY. ICERS are both compared to no treatment.
Colquitt, J. L., Jones, J., Harris, P., Loveman, E., Bird, A., Clegg, A. J., Baguley, D. M., Proops, D. W., Mitchell, T. E., Sheehan, P. Z., Welch, K. Bone-anchored hearing aids (BAHAs) for people who are bilaterally deaf: a systematic review and economic evaluation. <i>Health Technol Assess.</i> 2011. 15:1-200, iii-iv	Incremental cost per QALY gained was between £55,642 and £119,367 for children and between £46,628 and £100,029 for adults for BAHAs compared with BCHA.
Crowson, M. G., Rocke, D. J., Hoang, J. K., Weissman, J. L., Kaylie, D. M. Cost-effectiveness analysis of a non-contrast screening MRI protocol for vestibular schwannoma in patients with asymmetric sensorineural hearing loss. <i>Neuroradiology.</i> 2017. 59:727-736	Screening MRI was dominant.
Daniels, R. L., Shelton, C., Harnsberger, H. R. Ultra-high resolution nonenhanced fast spin echo magnetic resonance imaging: cost-effective screening for acoustic neuroma in patients with sudden sensorineural hearing loss. <i>Otolaryngol Head Neck Surg.</i> 1998. 119:364-9	The cost per tumor found was \$26,087 for traditional protocol and \$12,035 for FSE-MRI.
Dempsey, A. F., Pangborn, H. M., Prosser, L. A. Cost-effectiveness of routine vaccination of adolescent females against cytomegalovirus. <i>Vaccine.</i> 2012. 30:4060-6	Base case: Vaccination is dominant  Does not report CEA findings.
Dorji, K., Phuntsho, S., Pempa, Kumluang, S., Khuntha, S., Kulpeng, W., Rajbhandari, S., Teerawattananon, Y. Towards the introduction of pneumococcal conjugate vaccines in Bhutan: A cost-utility analysis to	In Bhutan, PCV13 produced an ICER of US \$92 compared with PCV10.

determine the optimal policy option. Vaccine. 2018. 36:1757-1765	
Emmett, S. D., Tucci, D. L., Smith, M., Macharia, I. M., Ndegwa, S. N., Nakku, D., Mukara, K. B., Ibekwe, T. S., Mulwafu, W., Gong, W., Francis, H. W., Saunders, J. E. GDP Matters: Cost Effectiveness of Cochlear Implantation and Deaf Education in Sub-Saharan Africa. Otol Neurotol. 2015. 36:1357-65	CI was CE in South Africa and Nigeria: CER/GDP was 1.03 and 2.05. Deaf education was CE in South Africa, Nigeria, Kenya, Rwanda, Uganda, Malawi with CER/GDP ranging from 0.55-1.56.
Emmett, S. D., Tucci, D. L., Bento, R. F., Garcia, J. M., Juman, S., Chiossone-Kerdel, J. A., Liu, T. J., de Munoz, P. C., Ullauri, A., Letort, J. J., Mansilla, T., Urquijo, D. P., Aparicio, M. L., Gong, W., Francis, H. W., Saunders, J. E. Moving Beyond GDP: Cost Effectiveness of Cochlear Implantation and Deaf Education in Latin America. Otol Neurotol. 2016. 37:1040-8	Deaf education was very cost effective in all countries (CER/GDP 0.07 – 0.93). CI was cost effective in all countries (CER/GDP 0.69 – 2.96).
Emmett, S. D., Sudoko, C. K., Tucci, D. L., Gong, W., Saunders, J. E., Akhtar, N., Bhutta, M. F., Touch, S., Pradhananga, R. B., Mukhtar, N., Martinez, N., Martinez, F. D., Ramos, H., Kameswaran, M., Kumar, R. N. S., Soekin, S., Prepageran, N. Expanding Access: Cost-effectiveness of Cochlear Implantation and Deaf Education in Asia. Otolaryngol Head Neck Surg. 2019. 161:672-682	Deaf education was cost-effective in all countries except Nepal (CER/GDP, 3.59). CI was cost-effective in all countries except Nepal (CER/GDP, 6.38) and Pakistan (CER/GDP, 3.14).
Ess, Silvia M, Schaad, Urs B, Gervaix, Alain, Pinösch, Seline, Szucs, Thomas D. Cost-effectiveness of a pneumococcal conjugate immunisation program for infants in Switzerland. Vaccine. 2003. 21:3273-3281	Pneumococcal vaccination has a cost-utility ratio of 35,700 CHF (approximately 26,300 USD) per QALY from the societal perspective and 39,300 CHF (28,900 USD) per QALY from the sickness funds' perspective.
Fang, T. Y., Cheng, L. J., Wu, D. B., Wang, P. C. Cost-effective analysis of unilateral cochlear implantation under the Taiwan national healthcare insurance. Int J Audiol. 2019. 1-6	The ICER for bimodal was \$6,487/QALY.
Fortnum, H., O'Neill, C., Taylor, R., Lenthall, R., Nikolopoulos, T., Lightfoot, G., O'Donoghue, G., Mason, S., Baguley, D., Jones, H., Mulvaney, C. The role of magnetic resonance imaging in the identification of suspected acoustic neuroma: a systematic review of clinical and cost effectiveness and natural history. Health Technol Assess. 2009. 13:iii-iv, ix-xi, 1-154	In the base-case, contrast-enhanced MR imaging cost an additional £71.79 per patient.
Fortnum, H., Leighton, P., Smith, M. D.,	The most cost-effective strategy for a child with

<p>Brown, L., Jones, M., Benton, C., Marder, E., Marshall, A., Sutton, K. Assessment of the feasibility and clinical value of further research to evaluate the management options for children with Down syndrome and otitis media with effusion: a feasibility study. <i>Health Technol Assess.</i> 2014. 18:1-147, v-vi</p>	<p>Down syndrome experiencing OME-induced hearing loss was watchful waiting, followed by symptom management using HAs.</p>
<p>Fortnum, H., Ukoumunne, O. C., Hyde, C., Taylor, R. S., Ozolins, M., Errington, S., Zhelev, Z., Pritchard, C., Benton, C., Moody, J., Cocking, L., Watson, J., Roberts, S. A programme of studies including assessment of diagnostic accuracy of school hearing screening tests and a cost-effectiveness model of school entry hearing screening programmes. <i>Health Technol Assess.</i> 2016. 20:1-178</p>	<p>No screening was dominant over screening. Screening using pure-tone screening was dominant over screening using the HearCheck screener.</p>
<p>Foteff, C., Kennedy, S., Milton, A. H., Deger, M., Payk, F., Sanderson, G. Cost-Utility Analysis of Cochlear Implantation in Australian Adults. <i>Otol Neurotol.</i> 2016. 37:454-61</p>	<p>Compared with bilateral hearing aids, the incremental cost-utility ratio for the CI treatment population was AUD 11,160/QALY.</p>
<p>Foteff, C., Kennedy, S., Milton, A. H., Deger, M., Payk, F., Sanderson, G. Economic Evaluation of Treatments for Pediatric Bilateral Severe to Profound Sensorineural Hearing Loss: An Australian Perspective. <i>Otol Neurotol.</i> 2016. 37:462-9</p>	<p>The ICER for unilateral CI compared with HAs was AUD 21,947/QALY. Weighted combined CI compared with HAs had an ICER of AUD 31,238/ QALY.</p>
<p>Francis, H. W., Chee, N., Yeagle, J., Cheng, A., Niparko, J. K. Impact of cochlear implants on the functional health status of older adults. <i>Laryngoscope.</i> 2002. 112:1482-8</p>	<p>CI in older adults had a cost-utility of \$9,530/QALY.</p>
<p>Gantt, S., Dionne, F., Kozak, F. K., Goshen, O., Goldfarb, D. M., Park, A. H., Boppana, S. B., Fowler, K. Cost-effectiveness of Universal and Targeted Newborn Screening for Congenital Cytomegalovirus Infection. <i>JAMA Pediatr.</i> 2016. 170:1173-1180</p>	<p>The cost of identifying 1 case of hearing loss due to cCMV ranged from \$27,460 - \$90,038 for universal screening, and \$975 - \$3,916 for targeted screening.</p>
<p>Garcia, S. L., Smith, K. J., Palmer, C. Cost-Effectiveness Analysis of a Military Hearing Conservation Program. <i>Mil Med.</i> 2018. 183:e547-e553</p>	<p>The ICER of a hearing conservation program was \$10,657 per case of hearing loss prevented.</p>
<p>Gillard, D. M., Harris, J. P. Cost-effectiveness of Stapedectomy vs Hearing Aids in the Treatment of Otosclerosis. <i>JAMA Otolaryngol Head Neck Surg.</i> 2019.</p>	<p>In otosclerosis, stapedectomy had an ICER of \$3,918.43/QALY compared to hearing aids.</p>

<p>Grill, E., Uus, K., Hessel, F., Davies, L., Taylor, R. S., Wasem, J., Bamford, J. Neonatal hearing screening: modelling cost and effectiveness of hospital- and community-based screening. <i>BMC Health Serv Res.</i> 2006. 6:14</p>	<p>Both hospital and community programs yielded 794 quality weighted detected child months (QCM) at the age of 6 months with total costs of £3,690,000 per 100,000 screened children in the hospital and £3,340,000 in the community.</p>
<p>Grutters, J. P., Joore, M. A., Van Der Horst, F., Stokroos, R. J., Anteunis, L. J. Decision-analytic modeling to assist decision making in organizational innovation: the case of shared care in hearing aid provision. <i>Health Serv Res.</i> 2008. 43:1662-73</p>	<p>Follow-up format resulted in €10,972 saved/QALY lost.</p>
<p>Heidari, S., Manesh, A. O., Rajabi, F., Moradi-Joo, M. Cost-effectiveness analysis of automated auditory brainstem response and otoacoustic emission in universal neonatal hearing screening. <i>Iranian Journal of Pediatrics.</i> 2017. 27</p>	<p>Over 1 year, the AABR device cost \$103,400 less than the OAE device, and detected 800 more cases than the OAE device.</p>
<p>Hessel, F., Grill, E., Schnell-Inderst, P., Siebert, U., Kunze, S., Nickisch, A., von Voss, H., Wasem, J. Economic evaluation of newborn hearing screening: modelling costs and outcomes. <i>Ger Med Sci.</i> 2003. 1:Doc09</p>	<p>Cost per case detected:  Universal screening = €13,395  Risk screening = €6,715  No screening = €4,125</p>
<p>Hirano, E., Fuji, H., Onoe, T., Kumar, V., Shirato, H., Kawabuchi, K. Cost-effectiveness analysis of cochlear dose reduction by proton beam therapy for medulloblastoma in childhood. <i>J Radiat Res.</i> 2014. 55:320-7</p>	<p>The ICERs for proton therapy vs. x-ray therapy using EQ-5D, HUI3, and SF-6D QoL measures were \$21,716/QALY, \$11,773/QALY, and \$20,150/QALY, respectively.</p>
<p>Hojjat, H., Svider, P. F., Davoodian, P., Hong, R. S., Folbe, A. J., Eloy, J. A., A. Shkoukani M. To image or not to image? A cost-effectiveness analysis of MRI for patients with asymmetric sensorineural hearing loss. <i>Laryngoscope.</i> 2017. 127:939-944</p>	<p>ICERs of pursuing gadolinium T1-weighted magnetic resonance imaging (GdT1W) and T2 weighted magnetic resonance imaging (T2MR) were \$27,660 and \$15,943, respectively.</p>
<p>Huang, L. H., Zhang, L., Tobe, R. Y., Qi, F. H., Sun, L., Teng, Y., Ke, Q. L., Mai, F., Zhang, X. F., Zhang, M., Yang, R. L., Tu, L., Li, H. H., Gu, Y. Q., Xu, S. N., Yue, X. Y., Li, X. D., Qi, B. E., Cheng, X. H., Tang, W., Xu, L. Z., Han, D. M.. Cost-effectiveness analysis of neonatal hearing screening program in China: should universal screening be prioritized? <i>BMC Health Serv Res.</i> 2012. 12:97</p>	<p>Targeted strategy tended to be cost-effective in Guangxi, Jiangxi, Henan, Guangdong, Zhejiang, Hebei, Shandong, and Beijing from the level of 9%, 9%, 8%, 4%, 3%, 7%, 5%, and 2%, respectively; while universal strategy trended to be cost-effective in those provinces from the level of 70%, 70%, 48%, 10%, 8%, 28%, 15%, 4%, respectively.</p>
<p>Hutton, J., Politi, C., Seeger, T. Cost-effectiveness of cochlear implantation of children. A preliminary model for the UK.</p>	<p>CI in children had an ICER of £16,214/QALY.</p>

Adv Otorhinolaryngol. 1995. 50:201-6	
Izquierdo, G., Torres, J. P., Santolaya, M. E., Valenzuela, M. T., Vega, J., Chomali, M. Cost-effectiveness analysis of a multicomponent meningococcal serogroup B vaccine in hypothetical epidemic situation in a middle-income country. Human Vaccines and Immunotherapeutics. 2015. 11:875-883	In Chile, the 4CMenB mass vaccination strategy would avoid 215 cases, 61 sequelae, and 16 deaths per year. It would be CE at a dose cost <\$18.
Joore, M. A., Van Der Stel, H., Peters, H. J., Boas, G. M., Anteunis, L. J. The cost-effectiveness of hearing-aid fitting in the Netherlands. Arch Otolaryngol Head Neck Surg. 2003. 129:297-304	The ICER for hearing aid fitting was €15,807/QALY (US \$17,072/QALY).
Kemper, A. R., Downs, S. M. A cost-effectiveness analysis of newborn hearing screening strategies. Arch Pediatr Adolesc Med. 2000. 154:484-8	For every 100,000 newborns screened, universal screening detected 86 of 110 cases of congenital hearing loss, at a cost of \$11,650 per case identified. Targeted screening identified 51 of 110 cases, at \$3,120 per case identified.
Keren, R., Helfand, M., Homer, C., McPhillips, H., Lieu, T. A. Projected cost-effectiveness of statewide universal newborn hearing screening. Pediatrics. 2002. 110:855-64	The ICER for selective screening vs. no screening was \$16,400 per additional infant whose deafness was diagnosed by 6 months of age. The ICER for universal screening vs. selective screening was \$44,000 per additional infant whose deafness was diagnosed by 6 months of age.
Kezirian, E. J., White, K. R., Yueh, B., Sullivan, S. D. Cost and cost-effectiveness of universal screening for hearing loss in newborns. Otolaryngol Head Neck Surg. 2001. 124:359-67	Cost per infant with HL identified: 1- S-ABR/S-ABR = \$8,112 2- S-ABR/None = \$9,470 3- OAE/OAE= \$5,113 4- OAE then S-ABR/None= \$7,996.
Kitano, T., Onaka, M., Ishihara, M., Nishiyama, A., Hashimoto, N., Yoshida, S. Static model simulation for routine mumps vaccination in Japan: With a result of mumps-related complications in a Japanese community hospital. Clinical and Experimental Vaccine Research. 2017. 6:120-127	Routine mumps vaccination in Japan is CE, with cost-benefit ratios ranging from 3.69-6.84.
Kosaner Kliess, M., Kluibenschaedl, M., Zoehrer, R., Schlick, B., Scandurra, F., Urban, M. Cost-Utility of Partially Implantable Active Middle Ear Implants for Sensorineural Hearing Loss: A Decision Analysis. Value Health. 2017. 20:1092-1099	Active middle ear implants had an ICUR of AUD 9,913.72/QALY.
Kruyt, I. J., Bours, M. R. W., Rovers, M. M., Hol, M. K. S., Rongen, J. Economic Evaluation of Percutaneous Titanium Implants for Bone Conduction Hearing: A	Next generation implant is up to €506 more beneficial per patient over 10 years.

Cost-benefit Analysis. Otol Neurotol. 2020. 41:580-588	
Kuznik, A., Iliyasa, G., Lamorde, M., Mahmud, M., Musa, B. M., Nashabaru, I., Obaro, S., Mohammed, I., Habib, A. G.. Cost-effectiveness of expanding childhood routine immunization against Neisseria meningitidis serogroups C, W and Y with a quadrivalent conjugate vaccine in the African meningitis belt. PLoS ONE. 2017. 12:#pages#	At an incidence rate of 50 per 100,000/year, routine conjugate vaccination is highly cost-effective in 14 out of 26 countries with a cost/DALY averted ranging from US\$555-US\$787.
Langer, A., Brockow, I., Nennstiel-Ratzel, U., Menn, P. The cost-effectiveness of tracking newborns with bilateral hearing impairment in Bavaria: a decision-analytic model. BMC Health Serv Res. 2012. 12:418	The ICER of tracking vs. no tracking was €1,697 per additional case of bilateral hearing impairment detected.
Laske, R. D., Dreyfuss, M., Stulman, A., Veraguth, D., Huber, A. M., Roosli, C. Age Dependent Cost-Effectiveness of Cochlear Implantation in Adults. Is There an Age-Related Cut-off? Otol Neurotol. 2019. 40:892-899	Unilateral CI was CE compared to HA in women up to age 91 and men 89. Sequential CI compared to HA was CE for up to 87 in women and 85 for men. Sequential CI was CE compared to unilateral CI up to age 80 in women and 78 in men.
Le, P., Rothberg, M. B. Cost-effectiveness of herpes zoster vaccine for persons aged 50 years. Annals of Internal Medicine. 2015. 163:489-497	The ICER for herpes zoster vaccine versus no vaccine was \$323,456 per QALY.
Lea, A. R., Hailey, D. M. The cochlear implant. A technology for the profoundly deaf. Med Prog Technol. 1995. 21:47-52	CI had an ICER of \$14,000/QALY in children and \$22,000/QALY in adults.
Leeds, I. L., Namasivayam, V., Bamogo, A., Sankhla, P., Thayer, W. M. Cost Effectiveness of Meningococcal Serogroup B Vaccination in College-Aged Young Adults. American Journal of Preventive Medicine. 2019. 56:196-204	Universal meningococcus vaccination was not CE in the US.
Lieu, T. A., Ray, G. T., Black, S. B., Butler, J. C., Klein, J. O., Brelman, R. F., Miller, M. A., Shinefield, H. R.. Projected cost-effectiveness of pneumococcal conjugate vaccination of healthy infants and young children. Journal of the American Medical Association. 2000. 283:1460-1468	At the manufacturer's list price of \$58 per dose, infant vaccination would cost society \$80,000 per life-year saved or \$160 per otitis media episode prevented (other estimated costs would be \$3,200 per pneumonia case prevented, \$15,000 for bacteremia and \$280,000 for meningitis).
Linssen, A. M., Anteunis, L. J., Joore, M. A. The Cost-Effectiveness of Different Hearing Screening Strategies for 50- to 70-Year-Old Adults: A Markov Model. Value Health. 2015. 18:560-9	Incremental costs of the screening strategies compared with no screening ranged from €4 to €59. Incremental QALYs ranged from 0.0003 to 0.0104. The ICERs of all the screening strategies compared with the current practice were below €20,000/QALY gained.

<p>Liu, C. F., Collins, M. P., Souza, P. E., Yueh, B. Long-term cost-effectiveness of screening strategies for hearing loss. <i>J Rehabil Res Dev.</i> 2011. 48:235-43</p>	<p>The tone-emitting otoscope was the most cost-effective strategy, with a significant increase in hearing aid use 1 year after screening (2.8%) and an ICER of \$1,439.00 per additional hearing aid user compared with the control group.</p>
<p>Lundkvist, J., Ekman, M., Ericsson, S. R., Jonsson, B., Glimelius, B. Cost-effectiveness of proton radiation in the treatment of childhood medulloblastoma. <i>Cancer.</i> 2005. 103:793-801</p>	<p>Proton therapy was associated with €23,600 in cost savings and 0.68 additional quality-adjusted life-years per patient.</p>
<p>McIntosh, E David G, Conway, Peter, Willingham, Julie, Lloyd, Adam. The cost-burden of paediatric pneumococcal disease in the UK and the potential cost-effectiveness of prevention using 7-valent pneumococcal conjugate vaccine. <i>Vaccine.</i> 2003. 21:2564-2572</p>	<p>NHS cost per life year gained was estimated at £31,512, close to the limit at which PCV would be considered cost-effective</p>
<p>Melegaro, Alessia, Edmunds, WJ. Cost-effectiveness analysis of pneumococcal conjugate vaccination in England and Wales. <i>Vaccine.</i> 2004. 22:4203-4214</p>	<p>Under base-case assumptions (no herd immunity and no serotype replacement) the program is not expected to be cost-effective from the NHS perspective at the current price of the vaccine (assumed £30 per dose, three-dose program)</p>
<p>Merlin, T, Hedayati, H, Sullivan, T, Buckley, E, Newton, S, Hodgkinson, B, Bywood, P, Jenner, F, Moss, J, Hiller, JE. Universal neonatal hearing screening. MSAC reference 17 Assessment report. Canberra: MSAC. 2007.</p>	<p>In the short term, the decision analytic model presented in this report predicted that implementing a two-stage automated auditory brainstem response (AABR) universal neonatal hearing screening (UNHS) program for a cohort of 250,000 newborns would identify an extra 607 infants with unilateral or bilateral hearing impairment by the age of 6 months compared to no formal screening program, at an incremental cost of \$6–\$11 million. Where a targeted screening program is already in place, expanding to a universal screening program would identify 319 more infants, at an incremental cost of \$4–\$8 million.</p>
<p>Mohiuddin, S., Schilder, A., Bruce, I. Economic evaluation of surgical insertion of ventilation tubes for the management of persistent bilateral otitis media with effusion in children. <i>BMC Health Serv Res.</i> 2014. 14:253</p>	<p>The ICER for VTs strategy compared with the HAs strategy was £5,086/QALY gained.</p>
<p>Mohiuddin, S., Payne, K., Fenwick, E., O'Brien, K., Bruce, I. A model-based cost-effectiveness analysis of a grommets-led care pathway for children with cleft palate affected by otitis media with effusion. <i>Eur J Health Econ.</i> 2015. 16:573-87</p>	<p>The ICER of Grommets strategy vs. do-nothing was £9,065/QALY gained. Hearing-aids strategy was extendedly dominated by the grommets strategy.</p>
<p>Monksfield, P., Jowett, S., Reid, A., Proops, D. Cost-effectiveness analysis of the bone-anchored hearing device. <i>Otol Neurotol.</i></p>	<p>BAHD had an ICER of £17,610 (US \$26,415) per QALY gained.</p>

2011. 32:1192-7	
Montes, F., Penaranda, A., Correa, S., Penaranda, D., Garcia, J. M., Aparicio, M. L., Varela, A. R., Castillo, M. Cochlear Implants Versus Hearing Aids in a Middle-Income Country: Costs, Productivity, and Quality of Life. <i>Otol Neurotol.</i> 2017. 38:e26-e33	The ICER for CI was \$15,169/QALY, and for HA was \$15,430/QALY.
Moradi-Lakeh, M., Shakerian, S., Esteghamati, A. Immunization against Haemophilus Influenzae type B in Iran; cost-utility and cost-benefit analyses. <i>International Journal of Preventive Medicine.</i> 2012. 3:332-340	Routine vaccination of the 2008 birth cohort would prevent 4,079 DALYs at a cost per DALY averted of US\$4,535.
Morris, A. E., Lutman, M. E., Cook, A. J., Turner, D. An economic evaluation of screening 60- to 70-year-old adults for hearing loss. <i>J Public Health (Oxf).</i> 2013. 35:139-46	The ICER of one-stage screening for 35 dB HL from 60 years vs. GP referrals was £1,461. Two-stage screening was eliminated by extended dominance.
Morris, A. An Economic Model of Adult Hearing Screening. <i>Audiol Res.</i> 2011. 1:e16	The ICER of screening compared to general practitioner referral service ranged from £1,266 to £2,185.
Navas, Elisa, Salleras, L, Gisbert, Ramon, Dominguez, A, Timoner, E, Ibáñez, D, Prat, A. Cost-benefit and cost-effectiveness of the incorporation of the pneumococcal 7-valent conjugated vaccine in the routine vaccination schedule of Catalonia (Spain). <i>Vaccine.</i> 2005. 23:2342-2348	The cost per DALY gained was €44,307 from the societal perspective and €80,291 from the provider's perspective.
Newall, A. T., Reyes, J. F., McIntyre, P., Menzies, R., Beutels, P., Wood, J. G. Retrospective economic evaluation of childhood 7-valent pneumococcal conjugate vaccination in Australia: Uncertain herd impact on pneumonia critical. <i>Vaccine.</i> 2016. 34:320-327	The incremental cost-effectiveness ratio was ~ AUD \$161,000 per QALY gained when including only IPD-related outcomes. The cost-effectiveness of PCV7 remained in the range A\$88,000–\$122,000 when changes in various non-invasive disease states were included.
Nguyen, K. H., Smith, A. C., Armfield, N. R., Bensink, M., Scuffham, P. A. Cost-Effectiveness Analysis of a Mobile Ear Screening and Surveillance Service versus an Outreach Screening, Surveillance and Surgical Service for Indigenous Children in Australia. <i>PLoS One.</i> 2015. 10:e0138369	The ICER of MTESS (mobile telemedicine-enabled screening and surveillance) + Deadly Ears vs Deadly ears alone was AUD \$656/QALY gained
Ning, G., Yin, Z., Li, Y., Wang, H., Yang, W. Cost-effectiveness of the Haemophilus influenzae type b vaccine for infants in mainland China. <i>Hum Vaccin Immunother.</i> 2018. 14:36-44	The ICER was US \$13,640, and US \$59,122.9 per QALY gained using market prices and UNICEF prices, respectively.
Ontario Health Technology Assessment.	Bilateral CI ICER:

Bilateral Cochlear Implantation: A Health Technology Assessment. Ontario Health Technology Assessment Series. 2018. 18:1-139	Adult post-lingual: \$48,978/QALY Child prelingual: \$27,427/QALY Child post-lingual: \$30,386/QALY
Ontario Health Technology Assessment. Implantable Devices for Single-Sided Deafness and Conductive or Mixed Hearing Loss: A Health Technology Assessment. Ontario Health Technology Assessment Series. 2020. 20:1-165	Among people with single-sided deafness, cochlear implants may be cost-effective compared with no intervention, but bone-conduction implants are unlikely to be. Among people with conductive or mixed hearing loss, bone-conduction implants may be cost-effective compared with no intervention.
Perez-Martin, J., Artaso, M. A., Diez, F. J. Cost-effectiveness of pediatric bilateral cochlear implantation in Spain. <i>Laryngoscope</i> . 2017. 127:2866-2872	The ICER for simultaneous bilateral CI for 1 year old was €10,323/QALY. The ICER for sequential bilateral CI for 1 year old is €11,733/QALY.
Prager, D. A., Stone, D. A., Rose, D. N. Hearing loss screening in the neonatal intensive care unit: auditory brain stem response versus Crib-O-Gram; a cost-effectiveness analysis. <i>Ear Hear</i> . 1987. 8:213-6	Crib-O-Gram cost \$14,310 per case detected.
Prusa, A. R., Kasper, D. C., Sawers, L., Walter, E., Hayde, M., Stillwaggon, E. Congenital toxoplasmosis in Austria: Prenatal screening for prevention is cost-saving. <i>PLoS Negl Trop Dis</i> . 2017. 11:e0005648	The model calculated total lifetime costs of €103 per birth under prenatal screening as carried out in Austria, saving €323 per birth compared with No-Screening. Without screening and treatment, lifetime societal costs for all affected children would have been €35 million per year.
Pugh, S. J., Fletcher, M. A., Charos, A., Imekraz, L., Wasserman, M., Farkouh, R. Cost-Effectiveness of the Pneumococcal Conjugate Vaccine (10- or 13-Valent) Versus No Vaccination for a National Immunization Program in Tunisia or Algeria. <i>Infectious Diseases and Therapy</i> . 2019. 8:63-74	PCV10 was cost-effective in both Algeria at \$731/QALY and Tunisia at \$1355/QALY.
Qiu, J., Yu, C., Ariyaratne, T. V., Foteff, C., Ke, Z., Sun, Y., Zhang, L., Qin, F., Sanderson, G. Cost-Effectiveness of Pediatric Cochlear Implantation in Rural China. <i>Otol Neurotol</i> . 2017. 38:e75-e84	The ICER for the Payer + Patient perspective was 100,561 CNY/QALY (\$15,084/QALY). The ICER for the Payer perspective was 40,929 CNY/QALY (\$6,139/QALY). Both were below 3x Chinese GDP.
Rivera, Adovich S, Lam, Hilton Y, Chiong, Charlotte M, Reyes-Quintos, Maria Rina T, Ricalde, Rosario R. The cost-effectiveness and budget impact of a community-based universal newborn hearing screening program in the Philippines. <i>Acta Medica Philippina</i> . 2017.	Community-based universal newborn hearing screening was found to be cost saving.
Rob, B., Vinod, J. A., Monica, P., Balraj, A., Job, A., Norman, G., Joseph, A. Costs and health effects of screening and delivery of	The cost per DALY averted was around Rs 42,200 (US\$900) at secondary care level and Rs 33,900 (US\$720) at tertiary care level.

hearing aids in Tamil Nadu, India: an observational study. <i>BMC Public Health</i> . 2009. 9:135	
Salo, Heini, Sintonen, Harri, Pekka Nuorti, J, Linna, Miika, Nohynek, Hanna, Verho, Jouko, Kilpi, Terhi. Economic evaluation of pneumococcal conjugate vaccination in Finland. <i>Scandinavian journal of infectious diseases</i> . 2005. 37:821-832	In the base case, vaccination would cost society €134,986 per life year gained.
Saunders, J. E., Barrs, D. M., Gong, W., Wilson, B. S., Mojica, K., Tucci, D. L. Cost Effectiveness of Childhood Cochlear Implantation and Deaf Education in Nicaragua: A Disability Adjusted Life Year Model. <i>Otol Neurotol</i> . 2015. 36:1349-56	Costs per DALY averted were \$5,898 and \$5,529 for CI and deaf education, respectively.
Schopflocher D, Corabian P, Eng K, Lier D. The use of the automated auditory brainstem response and otoacoustic emissions tests for newborn hearing screening. <i>Institute for Health Economics: Alberta, Canada</i> . 2007.	1-stage AABR was more cost-effective than 1-stage AOA. 2-stage (AOA followed by AABR) cost \$7,574.78 additional to correctly identify one additional infant.
Schnippel, K., Firnhaber, C., Page-Shipp, L., Sinanovic, E. Impact of adverse drug reactions on the incremental cost-effectiveness of bedaquiline for drug-resistant tuberculosis. <i>Int J Tuberc Lung Dis</i> . 2018. 22:918-925	Including adverse drug reactions, bedaquiline vs. second-line injectable for multidrug-resistant and rifampicin-resistant tuberculosis is cost saving (\$96 per patient) and more effective (0.96 DALY averted).
Semenov, Y. R., Yeh, S. T., Seshamani, M., Wang, N. Y., Tobey, E. A., Eisenberg, L. S., Quittner, A. L., Frick, K. D., Niparko, J. K. Age-dependent cost-utility of pediatric cochlear implantation. <i>Ear Hear</i> . 2013. 34:402-12	CI led to net societal savings of \$31,252, \$10,217, and \$6,680 for ages <18 months, 18-36 months, 36 months.
Sharma, A., Viets, R., Parsons, M. S., Reis, M., Chrisinger, J., Wippold, F. J., 2nd. A two-tiered approach to MRI for hearing loss: incremental cost of a comprehensive MRI over high-resolution T2-weighted imaging. <i>AJR Am J Roentgenol</i> . 2014. 202:136-44	Conventional MRI had an ICER of \$258,664 per unit increase in effectiveness.
Simon, M. S., Weiss, D., Geevarughese, A., Kratz, M. M., Cutler, B., Gulick, R. M., Zucker, J. R., Varma, J. K., Schackman, B. R. Cost-Effectiveness of Meningococcal Vaccination among Men Who Have Sex with Men in New York City. <i>Journal of Acquired Immune Deficiency Syndromes</i> . 2016. 71:146-154	Compared with no vaccination, the targeted vaccination campaign averted an estimated 2.7 invasive meningococcal disease (IMD) cases, 1.0 IMD deaths, with an ICER of \$66,000/QALY when herd immunity was assumed.
Summerfield, A.Q., Marshall, D.H., Davis, A.C. Cochlear implantation: demand, costs,	The cost of gaining 1 QALY through multichannel implantation in adulthood was between £8,624-

and utility. <i>Ann Otol Rhinol Laryngol Suppl.</i> 1995. 166:245-8	25,871.
Summerfield, A. Q., Marshall, D. H., Archbold, S. Cost-effectiveness considerations in pediatric cochlear implantation. <i>Am J Otol.</i> 1997. 18:S166-8	CI had an ICER of £15,600/QALY.
Summerfield, A. Q., Marshall, D. H., Barton, G. R., Bloor, K. E. A cost-utility scenario analysis of bilateral cochlear implantation. <i>Arch Otolaryngol Head Neck Surg.</i> 2002. 128:1255-62	The ICERs were £16,774 for type 1: unilateral implantation vs no intervention, £27,401 for type 2: unilateral implantation vs management with hearing aids, £61,734 for simultaneous bilateral implantation vs unilateral implantation, and £68,916 for provision of an additional implant vs no additional intervention.
Summerfield, A. Q., Lovett, R. E., Bellenger, H., Batten, G. Estimates of the cost-effectiveness of pediatric bilateral cochlear implantation. <i>Ear Hear.</i> 2010. 31:611-24	The net benefit was positive, provided that £21,768 could be spent to gain a QALY.
Theriou, C., Fielden, C. A., Kitterick, P. T. The Cost-Effectiveness of Bimodal Stimulation Compared to Unilateral and Bilateral Cochlear Implant Use in Adults with Bilateral Severe to Profound Deafness. <i>Ear Hear.</i> 2019. 40:1425-1436	Bimodal had an ICER of £1,521/QALY in UK and \$8,192 in US. The value of further research was £4.8M at 20,000/QALY in UK and \$87.0M at \$50,000/QALY in US.
Tobe, R. G., Mori, R., Huang, L., Xu, L., Han, D., Shibuya, K. Cost-effectiveness analysis of a national neonatal hearing screening program in China: conditions for the scale-up. <i>PLoS One.</i> 2013. 8:e51990	OAE was the most cost-effective strategy at an average cost-effectiveness ratio of I\$13,100 (95% CI: 8,400–17,200) per DALY averted.
Turner, R. G. Comparison of four hearing screening protocols. <i>J Am Acad Audiol.</i> 1992. 3:200-7	NA
UK Cochlear Implant Group. Criteria of candidacy for unilateral cochlear implantation in post-lingually deafened adults II: cost-effectiveness analysis. <i>Ear Hear.</i> 2004. 25:336-60	Unilateral CI in post-lingually deafened adults had an ICER of €27,142/QALY.
Vallejo-Torres, L., Castilla, I., Couce, M. L., Pérez-Cerdá, C., Martín-Hernández, E., Pineda, M., Campistol, J., Arrospide, A., Morris, S., Serrano-Aguilar, P. Cost-effectiveness analysis of a national newborn screening program for biotinidase deficiency. <i>Pediatrics.</i> 2015. 136:e424-e432	Newborn biotinidase deficiency screening was CE at \$24,677/QALY in Spain.
Veenstra, D. L., Harris, J., Gibson, R. L., Rosenfeld, M., Burke, W., Watts, C. Pharmacogenomic testing to prevent aminoglycoside-induced hearing loss in cystic fibrosis patients: potential impact on clinical, patient, and economic outcomes.	Genetic testing had an ICER of \$79,300/QALY.

Genet Med. 2007. 9:695-704	
Williams, E. J., Gray, J., Luck, S., Atkinson, C., Embleton, N. D., Kadambari, S., Davis, A., Griffiths, P., Sharland, M., Berrington, J. E., Clark, J. E. First estimates of the potential cost and cost saving of protecting childhood hearing from damage caused by congenital CMV infection. Arch Dis Child Fetal Neonatal Ed. 2015. 100:F501-6	The cost per case of cCMV-related SNHL identified was £668. The cost per case of cCMV-related SNHL improved was £14,202.
Williamson, I., Benghe, S., Barton, S., Petrou, S., Letley, L., Fasey, N., Abangma, G., Dakin, H., Little, P. A double-blind randomised placebo-controlled trial of topical intranasal corticosteroids in 4- to 11-year-old children with persistent bilateral otitis media with effusion in primary care. Health Technol Assess. 2009. 13:1-144	Placebo dominated intranasal steroids.
Wong, B. Y., Hui, Y., Au, D., Wei, W. Economic evaluation of cochlear implantation. Adv Otorhinolaryngol. 2000. 57:377-81	The ICER for unilateral cochlear implantation was HK\$133,087/QALY in adults and HK\$183,100/QALY in children.
Wong, L. Y., Espinoza, F., Alvarez, K. M., Molter, D., Saunders, J. E. Otoacoustic Emissions in Rural Nicaragua: Cost Analysis and Implications for Newborn Hearing Screening. Otolaryngol Head Neck Surg. 2017. 156:877-885	OAE screening was cost-effective without treatment (CER/GDP=0.06-2.00) and with treatment (CER/GDP=0.58-2.52).
Wyatt, JR., Niparko, JK. Evaluating the cost-effectiveness of hearing rehabilitation. 1995. (Number 1)	The ICER for CI was \$9,325/QALY, with a range of \$7,988-\$11,201/QALY.
Wyatt, J. R., Niparko, J. K., Rothman, M. L., deLissovoy, G. Cost effectiveness of the multichannel cochlear implant. Am J Otol. 1995. 16:52-62 (Number 2)	The ICER for cochlear implantation was \$15,600/QALY.
Wyatt, J. R., Niparko, J. K., Rothman, M., deLissovoy, G. Cost utility of the multichannel cochlear implants in 258 profoundly deaf individuals. Laryngoscope. 1996. 106:816-21	The ICER for CI was \$15,928/QALY.

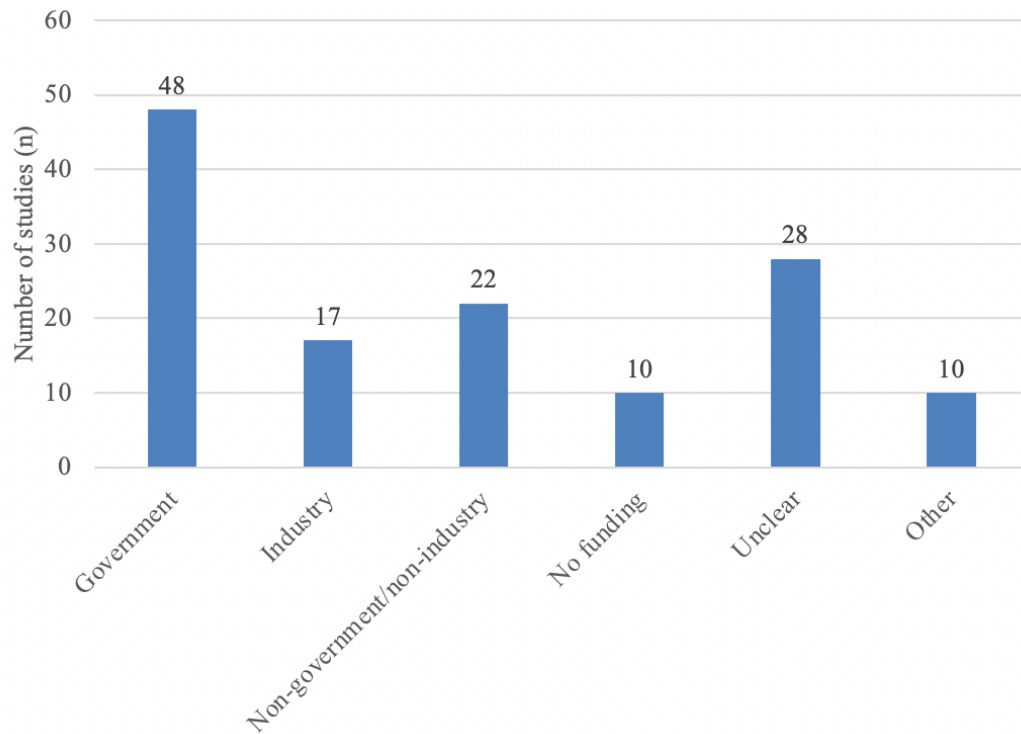
Currencies: AUD – Australian Dollar, HK – Hong Kong Dollar, CHF – Swiss

Franc, INR/Rs – Indian Rupee, USD – United States Dollar, GDP – Global Domestic

Product, £ – Pound, € – Euro, I\$ – International Dollars

Other Abbreviations: HL – hearing loss, SNHL – sensorineural hearing loss, BAHA – bone anchored hearing aid, BAHD – bone anchored hearing device, HA – hearing aid, HA – hearing aid, CI – cochlear implant, VTs – ventilation tubes, DN – do nothing, QALY – quality-adjusted life year, DALY – disability-adjusted life years, QoL – quality of life, (U)NHS – (universal) newborn hearing screening, OME – otitis media with effusion, cCMV – congenital cytomegalovirus, CE – cost-effectiveness, (I)CER – (incremental) cost-effectiveness ratio, ICUR – incremental cost-utility ratio, OEA – otoacoustic emission, TEOAE – Transient Evoked Otoacoustic Emissions, S-ABR – simulated auditory brain response, AABR – automated auditory brain response, HUI – health utilities index, TTO – Time Trade Off, SF-6D – Short Form Dimension Six.

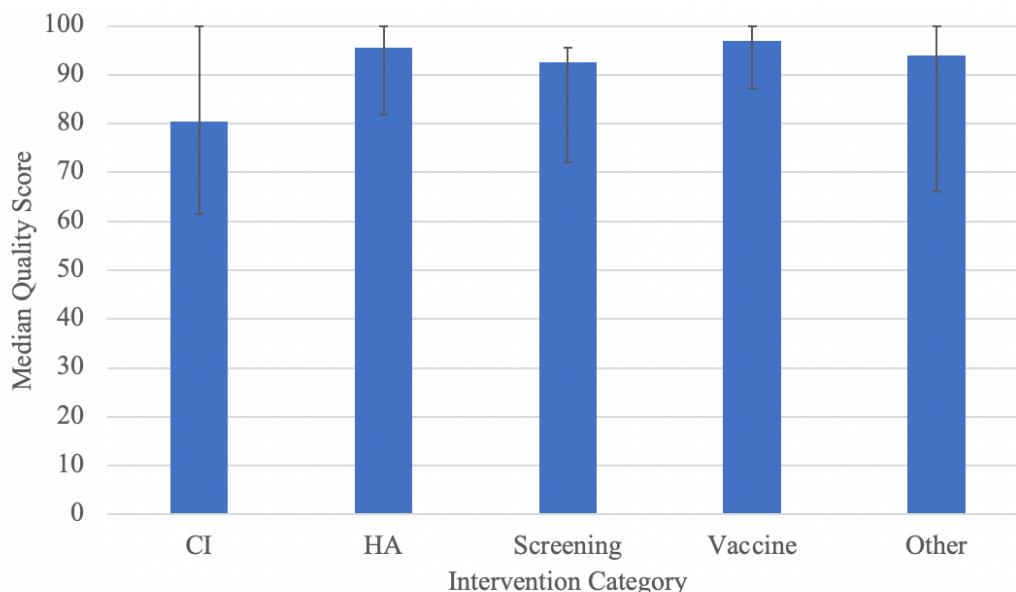
## Appendix H. Funding Sources for Included Studies in the Systematic Review.



**Figure H.1: Funding sources for included studies in the systematic review.**

Legend: This Figure indicates the number of studies that reported each type of funding. Note some studies had more than 1 funding source.

## Appendix I. Median Quality Scores by Intervention Category in the Systematic Review.



**Figure I.1: Median quality scores by intervention category in the systematic review.**

Legend: Figure I.1 indicates the median quality score for studies in each intervention category. Error bars indicate the interquartile range.

**Table I.1: The distribution of quality scores by intervention category.**

Quality Score Range	Intervention Category				
	CI	HA	Screening	Vaccine	Other
>90	41.2%	64.3%	54.3%	72.7%	55.2%
80-90	11.8%	17.9%	14.3%	13.6%	10.3%
70-80	11.8%	0.0%	8.6%	9.1%	3.4%
<70	35.3%	17.9%	22.9%	4.5%	31.0%

CI: cochlear implantation, HA: Hearing Aid.

## **Appendix J. AdViSHE Checklist for Model Development and Validation.**

### **AdViSHE**

#### Assessment of the Validation Status of Health-Economic decision models

AdViSHE is a questionnaire that modellers can complete to report on the efforts performed to improve the validation status of their health-economic (HE) decision model. It is not intended to replace validation by model users but rather to inform the direction of validation efforts and to provide a baseline for replication of the results. In addition to using it after a model is finished, the modellers can use AdViSHE to guide validation efforts during the modelling process.

The modellers are asked to comment on the validation efforts performed while building the underlying HE decision model and afterwards. Many of the questions simply refer to the model documentation. AdViSHE is divided into five parts, each covering an aspect of validation:

- Part A: Validation of the conceptual model (2 questions)
- Part B: Input data validation (2 questions)
- Part C: Validation of the computerized model (4 questions)
- Part D: Operational validation (4 questions)
- Part E: Other validation techniques (1 question)

No final validation score is calculated, as the assessment of the answers and the overall validation effort is left to the model users. It is assumed that the model has been built according to prevailing modelling and reporting guidelines. For instance, the model builders would presumably adhere to the ISPOR-SMDM<sup>+</sup> Modeling Good Research Practices (Caro et al., 2010) and/or CHEERS<sup>+</sup> Statement (Husereau et al., 2013). Some questions may not be applicable to a particular model. If this is the case, the model builder should take the opt-out option and provide a justification of why this item is not deemed applicable.

#### **Part A: Validation of the conceptual model (2 questions)**

Part A discusses techniques for validating the conceptual model. A conceptual model describes the underlying system (e.g., progression of disease) using a mathematical, logical, verbal, or graphical representation. Please indicate where the conceptual model and its underlying assumptions are described

**A1/ Face validity testing (conceptual model):** Have experts been asked to judge the appropriateness of the conceptual model?

If yes, please provide information on the following aspects:

- Who are these experts?
- What is your justification for considering them experts?
- To what extent do they agree that the conceptual model is appropriate?

If no, please indicate why not.

*The conceptual model was developed in conjunction with co-authors and other hearing healthcare experts on the Lancet Commission on Hearing Loss.*

Aspects to judge include: appropriateness to represent the underlying clinical process/disease (disease stages, physiological processes, etc.); and appropriateness for economic evaluation (comparators, perspective, costs covered, etc.).

**A2/ Cross validity testing (conceptual model):** Has this model been compared to other conceptual models found in the literature or clinical textbooks?

If yes, please indicate where this comparison is reported.

If no, please indicate why not.

## Part B: Input data validation (2 questions)

Part B discusses techniques to validate the data serving as input in the model. These techniques are applicable to all types of models commonly used in HE modelling.

Please indicate where the description and justification of the following aspects are given:

- search strategy;
- data sources, including descriptive statistics;
- reasons for inclusion of these data sources;
- reasons for exclusion of other available data sources;
- assumptions that have been made to assign values to parameters for which no data was available;
- distributions and parameters to represent uncertainty;
- data adjustments: mathematical transformations (e.g., logarithms, squares); treatment of outliers; treatment of missing data; data synthesis (indirect treatment comparison, network meta-analysis); calibration; etc.

*We performed targeted literature review to identify data informing model inputs and cite the literature incorporated into DeciBHAL-US throughout the Methods section. We reviewed our literature choices with hearing health experts on the Lancet Commission.*

*When necessary, we adjusted published data as described in the Methods and Technical Appendix.*

**B1/ Face validity testing (input data):** Have experts been asked to judge the appropriateness of the input data?

If yes, please provide information on the following aspects:

- Who are these experts?
- What is your justification for considering them experts?
- To what extent do they agree that appropriate data has been used?

If no, please indicate why not.

*We reviewed and refined our input data through recurrent video conferences with co-authors. We presented key components of our analysis to the Lancet Commission on Hearing Loss.*

Aspects to judge may include but are not limited to: potential for bias; generalizability to the target population; availability of alternative data sources; any adjustments made to the data.

**B2/ Model fit testing:** When input parameters are based on regression models, have statistical tests been performed?

If yes, please indicate where the description, the justification and the outcomes of these tests are reported.

If no, please indicate why not.

*N/A*

Examples of regression models include but are not limited to: disease progression based on survival curves; risk profiles using regression analysis on a cohort; local cost estimates based on multi-level models; meta-regression; quality-of-life weights estimated using discrete choice analysis; mapping of disease-specific quality-of-life weights to utility values.

Examples of tests include but are not limited to: comparing model fit parameters ( $R^2$ , Akaike information criterion (AIC), Bayesian information criterion (BIC)); comparing alternative model specifications (covariates, distributional assumptions); comparing alternative distributions for survival curves (Weibull, lognormal, logit); testing the numerical stability of the outcomes (sufficient number of iterations); testing the convergence of the regression model; visually testing model fit and/or regression residuals.

## Part C: Validation of the computerized model (4 questions)

Part C discusses various techniques for validating the model as it is implemented in a software program. If there are any differences between the conceptual model (Part A) and the final computerized model, please indicate where these differences are reported and justified.

*N/A*

**C1/ External review:** Has the computerized model been examined by modelling experts?  
If yes, please provide information on the following aspects:  
- Who are these experts?  
- What is your justification for considering them experts?  
- Can these experts be qualified as independent?  
- Please indicate where the results of this review are reported, including a discussion of any unresolved issues.  
If no, please indicate why not.

*The computer model was examined by co-author experts in decision modelling: Evan R. Myers, Mohamed M. Diab, Osondu Ogbuoji, and Gillian D. Sanders Schmidler. These reviewers reviewed the model code to ensure it mapped to our conceptual model and to ensure we adequately documented model assumptions. They also reviewed the model for visible "bugs."*

Aspects to judge may include but are not limited to: absence of apparent bugs; logical code structure optimized for speed and accuracy; appropriate translation of the conceptual model.

**C2/ Extreme value testing:** Has the model been run for specific, extreme sets of parameter values in order to detect any coding errors?  
If yes, please indicate where these tests and their outcomes are reported.  
If no, please indicate why not.

*We performed extreme value testing and present those results in Appendix 6.*

Examples include but are not limited to: zero and extremely high (background) mortality; extremely beneficial, extremely detrimental, or no treatment effect; zero or extremely high treatment or healthcare costs.

**C3/ Testing of traces:** Have patients been tracked through the model to determine whether its logic is correct?  
If yes, please indicate where these tests and their outcomes are reported.  
If no, please indicate why not.

*We examined several patient traces to ensure the mode logic is correct and present sample patient traces in Appendix 7.*

In cohort models, this would involve listing the number of patients in each disease stage at one, several, or all time points (e.g., Markov traces). In individual patient simulation models, this would involve following several patients throughout their natural disease progression.

**C4/ Unit testing:** Have individual sub-modules of the computerized model been tested?  
If yes, please provide information on the following aspects:  
- Was a protocol that describes the tests, criteria, and acceptance norms defined beforehand?  
- Please indicate where these tests and their outcomes are reported.  
If no, please indicate why not.

N/A

Examples include but are not limited to: turning sub-modules of the program on and off; altering global parameters; testing messages (e.g., warning against illegal or illogical inputs), drop-down menus, named areas, switches, labelling, formulas and macros; removing redundant elements.

## Part D: Operational validation (4 questions)

Part D discusses techniques used to validate the model outcomes.

**D1/ Face validity testing (model outcomes):** Have experts been asked to judge the appropriateness of the model outcomes?

If yes, please provide information on the following aspects:

- Who are these experts?
- What is your justification for considering them experts?
- To what extent did they conclude that the model outcomes are reasonable?

If no, please indicate why not.

*We reviewed the model-projected outcomes with hearing health expert co-authors and Commissioners on the Lancet Commission for face validity. When model outcomes were not consistent with expert opinion, we reviewed input data affecting those outcomes and re-performed targeted literature reviews when necessary to better inform those input parameters. We also highlight input parameters and outcomes that are the most uncertain in the Discussion.*

Outcomes may include but are not limited to: (quality-adjusted) life years; deaths; hospitalizations; total costs.

**D2/ Cross validation testing (model outcomes):** Have the model outcomes been compared to the outcomes of other models that address similar problems?

If yes, please provide information on the following aspects:

- Are these comparisons based on published outcomes only, or did you have access to the alternative model?
- Can the differences in outcomes between your model and other models be explained?
- Please indicate where this comparison is reported, including a discussion of the comparability with your model.

If no, please indicate why not.

*Of the two hearing loss models that considered multiple interventions across the lifespan identified by our previous systematic review of model-based cost-effectiveness analyses of hearing healthcare, the results were reported in low- and middle-income countries and are not directly comparable to our current modelling efforts.*

Other models may include models that describe the same disease, the same intervention, and/or the same population.

**D3/ Validation against outcomes using alternative input data:** Have the model outcomes been compared to the outcomes obtained when using alternative input data?  
If yes, please indicate where these tests and their outcomes are reported.  
If no, please indicate why not.

*We indicate in the Methods, Results, and Discussion that outcomes in the model are dependent on several parameters, and our calibration efforts might adjust alternative parameters to achieve adequate fit. In the Discussion, we suggest that future efforts should target these parameters as potential sensitivity analyses to understand the impact of different parameters on achieving similar model-outcomes.*

Alternative input data can be obtained by using different literature sources or datasets, but can also be constructed by splitting the original data set in two parts, and using one part to calculate the model outcomes and the other part to validate against.

**D4/ Validation against empirical data:** Have the model outcomes been compared to empirical data?  
If yes, please provide information on the following aspects:  
- Are these comparisons based on summary statistics, or patient-level datasets?  
- Have you been able to explain any difference between the model outcomes and empirical data?  
- Please indicate where this comparison is reported.  
If no, please indicate why not.

**D4.A/** Comparison against the data sources on which the model is based (dependent validation).

*We performed dependent or internal validation as described in the Methods and Results. All comparisons were from published data, not at the patient-level. When differences arose between model outcomes and empirical data we performed calibration exercises as described in the Methods and Results.*

**D4.B/** Comparison against a data source that was not used to build the model (independent validation).

*We performed independent external validation to published estimates as described in the Methods and Results.*

## Part E: Other validation techniques (1 question)

**E1/ Other validation techniques:** Have any other validation techniques been performed?  
If yes, indicate where the application and outcomes are reported, or else provide a short summary here.

*We held a structured "walk-through" session with several co-authors and a Global Health Modelling course at Duke University where we reviewed the implementation of the conceptual model and ensured we adequately documented model assumptions.*

Examples of other validation techniques: structured "walk-throughs" (guiding others through the conceptual model or computerized program step-by-step); naive benchmarking ("back-of-the-envelope" calculations); heterogeneity tests; double programming (two model developers program components independently and/or the model is programmed in two different software packages to determine if the same results are obtained).

## Appendix K. Etiology Framework of Hearing Loss.

Table K.1: Etiology framework of hearing loss.

<b>PRENATAL</b>	<b>Etiologies included</b>
Infectious	Rubella Syphilis Toxoplasmosis HIV Infection Zika Lymphocytic choriomeningitis virus
Environmental	Iodine Deficiency Ototoxicity
Congenital causes including Genetic Causes, family history	Usher syndrome Alport syndrome Branchio oto renal syndrome Waardenburg syndrome Pendred syndrome Stickler syndrome Treacher Collins syndrome Chiari syndrome Jervell and Lange-Nielsen syndrome Aural atresia and microtia
<b>PERINATAL OR NEONATAL</b>	
Preterm birth, low birth weight	-
Birth Trauma, hypoxia	-
Severe jaundice	-
Infectious	Herpes simplex infection Cytomegalovirus infection
Environmental	Ototoxicity Exposure to excessive, prolonged incubator sound
<b>CHILDHOOD</b>	
Conductive HL	Cholesteatoma

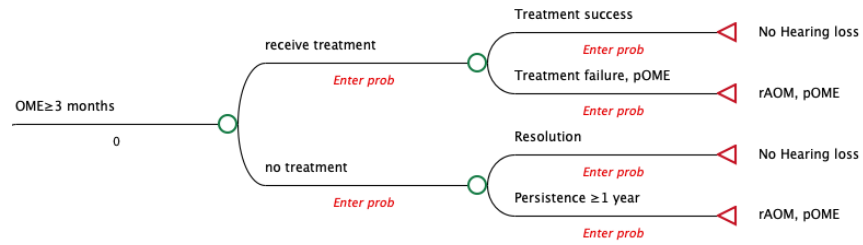
	<ul style="list-style-type: none"> <li>Impacted cerumen</li> <li>Otitis externa</li> <li>Foreign bodies</li> <li>Acute or chronic otitis media</li> </ul>
Infectious (without OM/OME)	<ul style="list-style-type: none"> <li>Measles, mumps</li> <li>Cerebral malaria</li> <li>Meningitis</li> <li>Borrelia burgdorferi</li> <li>Epstein-Barr virus</li> <li>Haemophilus influenzae</li> <li>Non-polio enteroviruses</li> <li>Streptococcus pneumoniae</li> <li>Varicella zoster virus</li> </ul>
Ototoxicity	-
<b>ADULTHOOD</b>	
Presbycusis	
Environmental	<ul style="list-style-type: none"> <li>Ototoxicity</li> <li>Smoking</li> <li>Work-related ototoxic chemicals</li> <li>Nutritional deficiencies</li> <li>Exposure to excessive and/or prolonged sound</li> </ul>
Infectious (without OM/OME)	<ul style="list-style-type: none"> <li>Encephalitis, meningitis</li> <li>Herpes simplex 1</li> <li>Herpes simplex 2</li> <li>HIV</li> <li>Lassa virus</li> <li>Ebola</li> <li>Ramsay Hunt syndrome/varicella zoster/shingles</li> <li>West Nile Virus</li> <li>Otosyphilis</li> <li>CMV</li> </ul>
Trauma	<ul style="list-style-type: none"> <li>Temporal bone trauma</li> <li>Penetrating trauma</li> </ul>

	Barotrauma Tympanic membrane perforation
Neoplasm	Acoustic neuroma/vestibular carcinoma Meningioma Osteoma Squamous cell carcinoma
Meniere's disease	-
Metabolic abnormalities	Diabetic vasculopathy Anemia or white blood cell dyscrasia Thyrotoxicosis
Conductive HL	Otosclerosis Exostosis Cholesteatoma Cerumen impaction Acute or chronic otitis media
Autoimmune disorders	Systemic Lupus Erythematosus Rheumatoid Arthritis Antiphospholipid syndrome Polyarteritis nodosa Wegener's granulomatosis Susac syndrome Sarcoidosis Cogan syndrome Behcet's syndrome Sjögren's syndrome Multiple Sclerosis Psoriasis
Cerebrovascular disease	-

## **Appendix L. Derivation of Sensorineural Hearing Loss Incidence.**

We derived the incidence of bilateral sensorineural hearing loss from NHANES prevalence estimates.<sup>4</sup> Using prevalence estimates of air conduction hearing loss estimates in the better ear from NHANES, we first estimated the age-specific proportion of total hearing loss that was predominately conductive using estimates on the proportion of total pediatric and adult hearing loss that is predominately conductive.<sup>182,184</sup> We then removed this proportion of hearing loss from total hearing loss to ascertain age-specific prevalence estimates of bilateral sensorineural hearing loss. To calculate male- and female-specific prevalence values at each decile, we incorporated age-specific risk ratios for hearing loss for males compared to females (range=1.21-3.21).<sup>183</sup> We applied similar calculations to 95% confidence intervals.

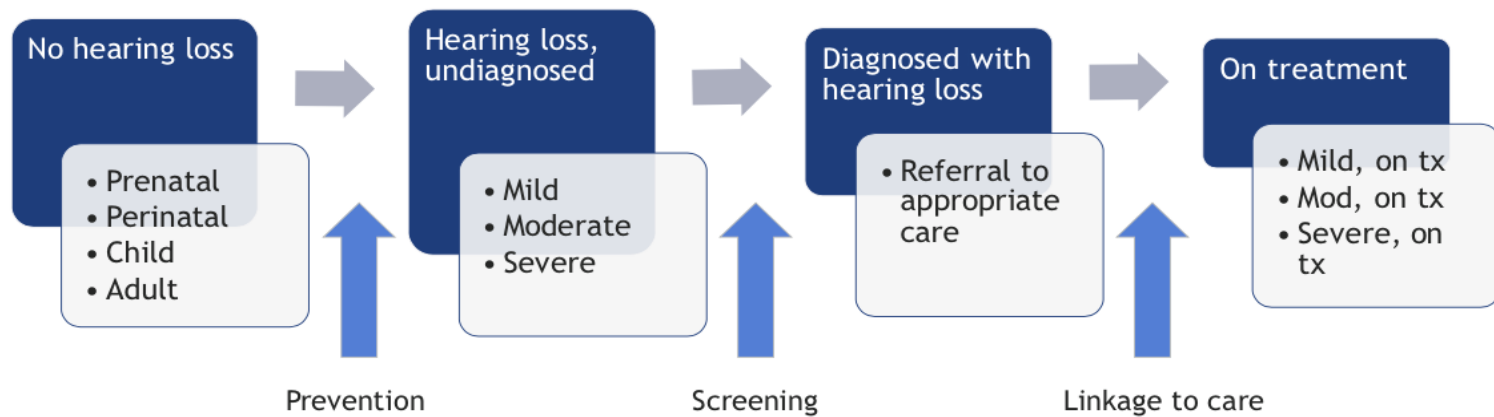
## Appendix M. Decision Nodes for Otitis Media with Effusion Treatment.



**Figure M.1: Decision nodes for otitis media with effusion treatment.**

**Legend:** This Figure shows the decision model framework for treatment/persistence of otitis media with effusion (OME) that lasts for greater than or equal to three months. Persons experiencing  $OME \geq 3$  months may receive treatment (including tympanostomy tubes) with subsequent success and resolution of OME or persistence of their OME (pOME). Persons that do not receive treatment may experience spontaneous resolution prior to 1 year, or persistence of their OME for  $\geq 1$  year.

## Appendix N. Hearing Healthcare Cascade of Care.



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**Figure N.1: Decision nodes for otitis media with effusion treatment.**

**Legend:** This figure represents the framework of the hearing healthcare cascade of care that was used to develop DeciBHAL-US. While only hearing aid uptake prompts a transition to another health states, the intermediary steps of diagnosis and linkage to care may be incorporated in input data or in considering simulation of interventions targeting specific steps in the cascade of care.

## Appendix O. Internal Validation Extreme Value Testing.

Table O.1: Internal validation extreme value testing.

Extreme value imputed	Expected result	Model-projected result consistent
Probability of SNHL to 0	No hearing loss at any age	X
Probability of SNHL to 1	Hearing loss immediately, and for duration of the simulation	X
Probability of AOM to 0	No AOM cumulative incidence	X
Probability of AOM to 1	AOM cumulative incidence equivalent to person-time survived	X
Probability of recurrent AOM to 0; Probability of OME resolution prior to 1 year to 1	No recurrent AOM or persistent OME patients; No CSOM patients	X
SNHL PTA decline to 0 dB	All patients with HL have a PTA of 25 dB	X
SNHL PTA decline to 120 dB	All patients with HL have a PTA of 120 dB	X

Probability of CHL after CSOM to 0 and probability of non-CSOM-associated CHL to 0	No CHL	X
Probability of HA uptake to 0	No HA use for people with hearing loss	X
Probability of HA uptake to 1 and probability of HA discontinuation to 0	Immediate and persistent HA use for people with hearing loss	X
Probability of HA discontinuation to 0	No HA discontinuation	X
Probability of CI implantation to 0	No CI implantation	X
Probability of CI implantation to 1 and CI discontinuation to 0	Immediate and persistent CI implantation health state for persons with severe+ SNHL	X

## Appendix P. Internal Validation Exemplar Annotated Patient Trace Files.

### Patient 1

This patient acquired bilateral sensorineural hearing loss at age 65, received a hearing aid at age 70, and discontinued the hearing aid after 1 year of use:

*Patient 1 had a 2.33% probability of acquiring sensorineural hearing loss given their current age of 65 years, and sex (where 1=male), and they acquired SNHL. People with SNHL start with a PTA of 25 dB.*

```
probability / Acquire SNHL / thread 0 / _strategy 1 / _trial 1 / _stage 65
tSNHL_Inc[tr_age_current;Sex]
tr_age_current = 65
Sex = dSex_US
  dsex_us = 1
Sex = 1
tsnhl_inc[] = 0.023338007
tSNHL_Inc[tr_age_current;Sex] = 0.023338007
Probability (Node196) = 0.023338007
```

```
random walk to / Acquire SNHL / Rand(0,1) = 0.9833423744382668
```

```
tracker modification / Acquire SNHL / thread 0 / _strategy 1 / _trial 1 / _stage 65
1
1 = 1.0
T tr_snhl = 1
```

```
tracker modification / Acquire SNHL / thread 0 / _strategy 1 / _trial 1 / _stage 65
25
25 = 25.0
T tr_hldb = 25
```

*Each year after acquiring SNHL, Patient 1 experiences yearly decline in his PTA that was drawn from a defined distribution at model initiation (0.68 in this circumstance). In the year after Patient 1 acquired SNHL, they had a decline in PTA from 25 dB to 26 dB.*

```
tracker modification / SNHL only, no tx / thread 0 / _strategy 1 / _trial 1 / _stage 66
if(tr_SNHL>0 & tr_HLDb<120;tr_HLDb + tSNHLDeclineMult[tr_age_current]*dSNHLDbDecline;tr_HLDb)
tr_snhl = 1
tr_hldb = 25
tr_hldb = 25
tr_age_current = 65
tsnhldeclinemult[] = 1.6
dsnhldbdecline = 0.6823552455646356
if(tr_SNHL>0 & tr_HLDb<120;tr_HLDb + tSNHLDeclineMult[tr_age_current]*dSNHLDbDecline;tr_HLDb) =
26.09176839290342
(T) tr_hldb = 26.091768393
```

*At age 70 years, Patient 1 draws a probability to receive a hearing aid, based on his PTA in dB (30.46) and his age (70 years), this probability was 0.56%.*

```
probability / Receive HA / thread 0 / _strategy 1 / _trial 1 / _stage 70
t_HAUptake[tr_age_current; if(tr_HLDb>=40;2;1)]
tr_age_current = 70
tr_hldb = 30.45884196451709
t_hauptake[] = 0.005562969500000001
t_HAUptake[tr_age_current; if(tr_HLDb>=40;2;1)] = 0.005562969500000001
Probability (Node15) = 0.005562969500000001
```

*At age 71 years, Patient 1 discontinued hearing aid use. The probability for discontinuing hearing aids acquisition is based on time since acquisition, and in this circumstance was a 9.5% probability*

```
probability / D/c HA / thread 0 / _strategy 1 / _trial 1 / _stage 71
pHAdiscontinue
pHAdiscontinue = t_HA_discontinuation[tr_HAuse]
tr_hause = 2
t_ha_discontinuation[] = 0.094689436
pHAdiscontinue = 0.094689436
pHAdiscontinue = 0.094689436
Probability (Node29) = 0.094689436
```

## **Patient 2**

This patient acquired bilateral sensorineural hearing loss at age 65, received a hearing aid at age 70, and discontinued the hearing aid after 1 year of use.

*Age at 2 years, this patient acquired acute otitis media, based on their age the probability was 8.68%. The model tracks the cumulative incidence of AOM for each patient, and in this case, it increases to 1. After acute otitis media, this patient experienced the 17% probability of recurrent otitis media for age 3 years.*

```
probability / AOM / thread 0 / _strategy 1 / _trial 1 / _stage 2
tAOM_Inc[tr_age_current]
tr_age_current = 2
taom_inc[] = 0.0868
tAOM_Inc[tr_age_current] = 0.0868
Probability (Node192) = 0.0868
```

```
tracker modification / AOM / thread 0 / _strategy 1 / _trial 1 / _stage 2
tr_AOMcuminc + 1
tr_aomcuminc = 0
```

tr\_AOMcuminc + 1 = 1.0  
(T) tr\_aomcuminc = 1  
  
probability / rAOM / thread 0 / \_strategy 1 / \_trial 1 / \_stage 2  
prAOMgivenAOM  
prAOMgivenAOM = 0.17  
prAOMgivenAOM = 0.17  
Probability (Node281) = 0.17  
  
random walk to / rAOM / Rand(0,1) = 0.9422767958469402

*Patient 2 had resolution of their recurrent AOM at age 3, without any progression to CSOM or consequence to their hearing.*

probability / Resolution / thread 0 / \_strategy 1 / \_trial 1 / \_stage 3  
prAOMpOMEResolution  
prAOMpOMEResolution = 1/2  
prAOMpOMEResolution = 0.5  
prAOMpOMEResolution = 0.5  
Probability (Node90) = 0.5  
  
probability / Progression to CSOM / thread 0 / \_strategy 1 / \_trial 1 / \_stage 3  
Probability (Node380)  
  
probability / Progression to CSOM / thread 0 / \_strategy 1 / \_trial 1 / \_stage 3  
tCSOM\_Inc\_Given\_rAOMpOME[tr\_age\_current]  
tr\_age\_current = 3  
tcsom\_inc\_given\_raompome[] = 0.028909247  
tCSOM\_Inc\_Given\_rAOMpOME[tr\_age\_current] = 0.028909247  
Probability (Node380) = 0.028909247  
  
random walk to / Resolution / Rand(0,1) = 0.9119135928135164

*Patient 2 had no more cases of AOM or recurrent AOM until age 50 years, where they again had AOM and recurrent AOM.*

probability / AOM / thread 0 / \_strategy 1 / \_trial 1 / \_stage 51  
tAOM\_Inc[tr\_age\_current]  
tr\_age\_current = 51  
taom\_inc[] = 0.00988  
tAOM\_Inc[tr\_age\_current] = 0.00988  
Probability (Node192) = 0.00988  
  
random walk to / AOM / Rand(0,1) = 0.9942937355940914  
  
tracker modification / AOM / thread 0 / \_strategy 1 / \_trial 1 / \_stage 51  
tr\_AOMcuminc + 1  
tr\_aomcuminc = 1  
tr\_AOMcuminc + 1 = 2.0  
(T) tr\_aomcuminc = 2

random walk to / rAOM / Rand(0,1) = 0.8375318043021326

*Patient 2 experienced resolution of their recurrent AOM at age 52 years, without any progression to CSOM or consequence to their hearing.*

probability / Resolution / thread 0 / \_strategy 1 / \_trial 1 / \_stage 52  
prAOMpOMEResolution  
prAOMpOMEResolution = 1/2  
prAOMpOMEResolution = 0.5  
prAOMpOMEResolution = 0.5  
Probability (Node90) = 0.5

probability / Progression to CSOM / thread 0 / \_strategy 1 / \_trial 1 / \_stage 52  
Probability (Node380)

probability / Progression to CSOM / thread 0 / \_strategy 1 / \_trial 1 / \_stage 52  
tCSOM\_Inc\_Given\_rAOMpOME[tr\_age\_current]  
tr\_age\_current = 52  
tcsom\_inc\_given\_raompome[] = 0.425697777  
tCSOM\_Inc\_Given\_rAOMpOME[tr\_age\_current] = 0.425697777  
Probability (Node380) = 0.425697777

probability / Die / thread 0 / \_strategy 1 / \_trial 1 / \_stage 52  
Probability (Node120)

probability / Die / thread 0 / \_strategy 1 / \_trial 1 / \_stage 52  
tMort[tr\_age\_current;Sex]  
tr\_age\_current = 52  
Sex = dSex\_US  
dsex\_us = 2  
Sex = 2  
tmort[] = 0.003711457  
tMort[tr\_age\_current;Sex] = 0.003711457  
Probability (Node120) = 0.003711457

random walk to / Resolution / Rand(0,1) = 0.5166516300562424

*Patient 2 then acquired SNHL at age 81.*

probability / Acquire SNHL / thread 0 / \_strategy 1 / \_trial 1 / \_stage 81  
tSNHL\_Inc[tr\_age\_current;Sex]  
tr\_age\_current = 81  
Sex = dSex\_US  
dsex\_us = 2  
Sex = 2  
tsnhl\_inc[] = 0.091680307  
tSNHL\_Inc[tr\_age\_current;Sex] = 0.091680307  
Probability (Node196) = 0.091680307

random walk to / Acquire SNHL / Rand(0,1) = 0.9450825955590891

## **Appendix Q. Sensitivity Analysis on Select Model Input Parameters for the Model Development and Validation Efforts.**

We ran deterministic sensitivity analysis on three model parameters: 1) age-related sensorineural hearing loss progression, 2) the calibrated hearing aid uptake multiplier, and 3) hearing aid discontinuation rates. We based the low and high values for age-related sensorineural hearing loss progression and hearing aid discontinuation on published 95% confidence intervals.

### *Age-related sensorineural hearing loss progression*

We varied the mean decline in dB from a basecase value of 1.05 down to 0.95 and up to 1.15. When the value was varied to 0.95 dB/year, the CV-RMSE of the model-projected population average hearing level compared to the Baltimore Longitudinal Study on Aging improved to 7.8%. When the value was 1.15 dB/year, the CV-RMSE worsened to 14.0%.

### *Hearing aid uptake multiplier*

When we removed the calibrated delay to diagnosis factor (multiplier from 0.6 to 1.0), the CV-RMSE for the comparison of model-projected hearing aid prevalence worsened to 26.9%. See the below Table for the age-stratified results.

*Hearing aid discontinuation rates*

We varied the hearing aid discontinuation rates based on published 95% confidence intervals, ranging the mean discontinuation rate from 4.9% to 6.8%. Model-projected prevalence of hearing aid use at each decile remained in the NHANES 95% confidence intervals across the range of hearing aid discontinuation (see Table below).

**Table Q.1: Hearing aid use prevalence under varying uptake and discontinuation assumptions.**

Hearing Aid Use Prevalence, % of persons with hearing loss					
Age	Model Outcome, Uptake multiplier =0.6, %	Model Outcome, Uptake multiplier=1.0, %	Model Outcome, Discontinuation to 4.9%	Model Outcome, Discontinuation to 6.8%	NHANES, % (95% CI)
55	3.8	5.8	4.3	5.1	4.3 (0-8.8)
65	7.8	10.0	7.0	7.4	7.3 (3.6-10.9)
75	14.7	19.3	14.4	12.8	17.0 (12.4-21.6)
85	21.0	29.9	22.6	19.4	22.1 (18.5-25.8)

## Appendix R. The Model-Projected Age-Specific Proportion of Children Using Hearing Aids.

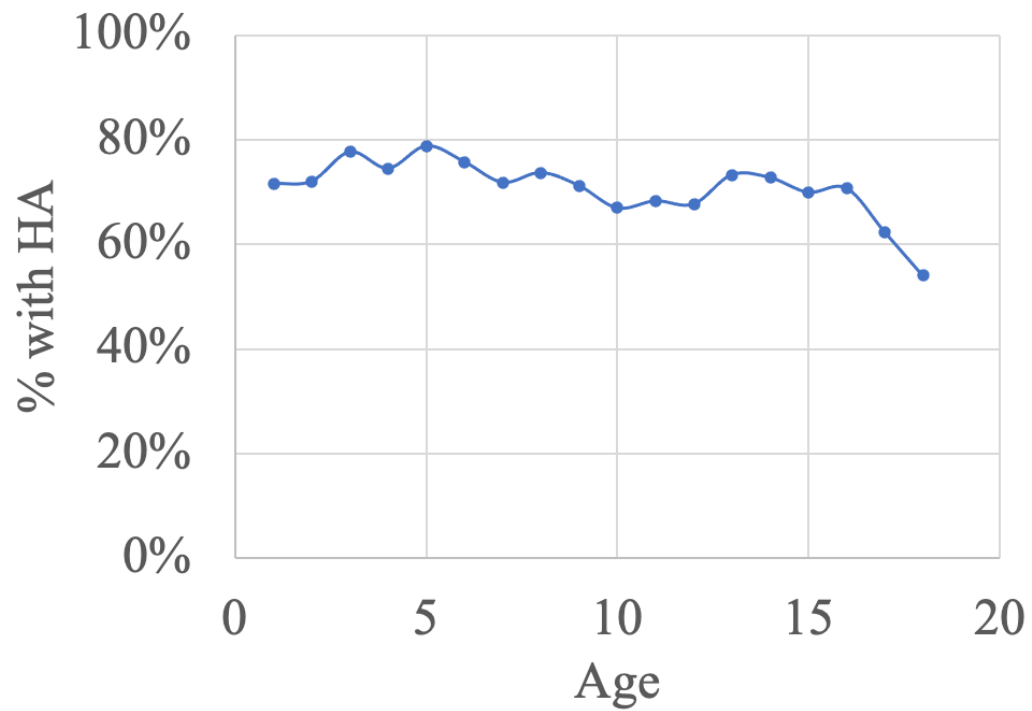


Figure R.1: The model-projected age-specific proportion of children using hearing aids.

## Appendix S. Prevalence of Persistent Otitis Media with Effusion by Age.

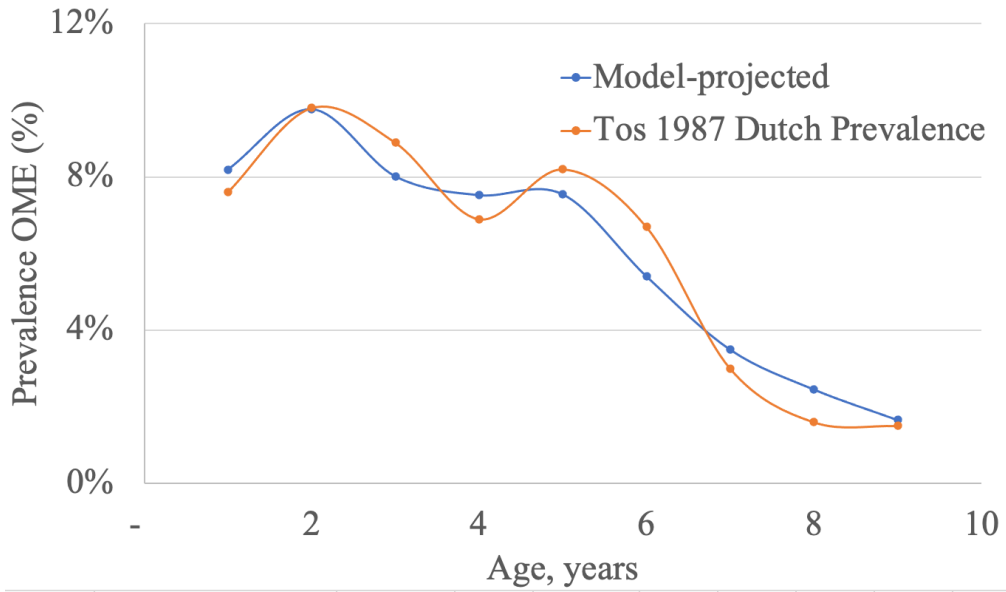


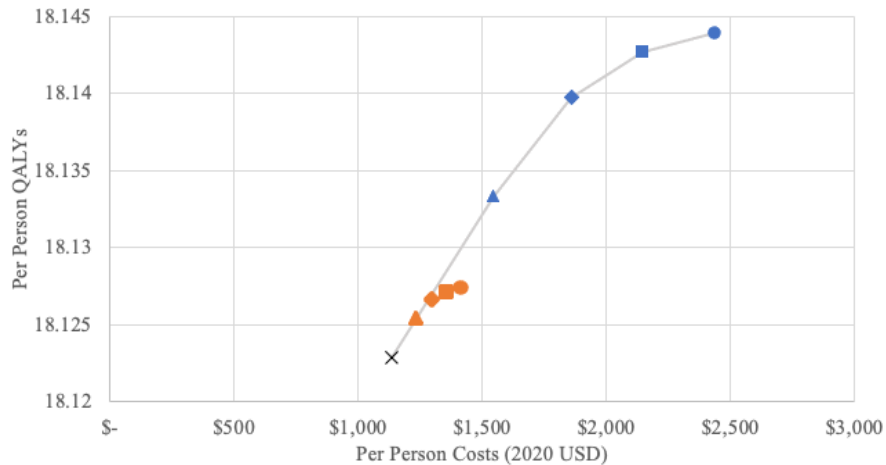
Figure S.1: The prevalence of persistent otitis media with effusion by age.

## **Appendix T. Expanded Budget Impact Analysis Methods.**

To estimate the 5-year budget impact of adult hearing screening implementation in the US, we first ran DeciBHAL-US in the current pace strategy from ages 40-100 years. Every 5 years, we collected the number of persons in each of 3 model health states: 1) sensorineural hearing loss, SNHL, without treatment; 2) SNHL with HA; and 3) SNHL with CI. We also collected the mean hearing loss severity in dB HL, and the standard deviation around that severity for each age and health state combination. These number of people in each health state and their severity predicted by DeciBHAL served as the inputs for the budget impact analysis.

To perform the budget impact analysis, we simulated 59 cohorts of persons aged 40-99 years over 5 years. We then scaled the model-projected undiscounted cost estimates by category to the United States population using age-specific US Census population estimates.<sup>284</sup> We report the average annual cost for the entire US population over that 5 year period.

## Appendix U. Efficiency Frontier for the Cost-Effectiveness Analysis.



**Figure U.1: Efficiency frontier for the cost-effectiveness analysis.**

**Legend:** This efficiency frontier shows the per-person quality-adjusted life-years (QALYs) on the y-axis and per-person costs on the x-axis for each simulated strategy. No hearing screening is indicated by an X, 5-yearly screening schedules are in orange, and yearly screening schedules are in blue. The age at hearing screening initiation is shown by the shape of the marker, with a 45-year-old age of initiation indicated with a circle, 55 with a square, 65 with a diamond, and 75 with a triangle. Non-dominated strategies fall on the efficiency frontier (grey line) and the slope of the frontier is equivalent to the incremental cost-effectiveness ratio (ICER) of the next most effective non-dominated strategy.

## **Appendix V. Expanded Budget Impact Analysis Results.**

The projected average annual costs for hearing aid purchasing (uptake) and maintenance (including batteries and device replacement) in the current detection strategy and under base-case costs were \$9.2B. This estimate is higher than a previously published hearing aid market value of \$6.5B in 2015.<sup>285</sup> This difference is likely due to our conservative cost assumptions of \$3,890 for hearing aid device purchases compared to \$3,515 in the published estimate, as well as our assumption of hearing aid replacement every four years. When we used similar device costs and assumed a more relaxed device replacement frequency of 6 years, our estimate for annual hearing aid uptake and maintenance costs were \$7.2B, which was in line with the published hearing aid market estimate. We maintained the more conservative estimates of hearing aid cost and replacement frequency in cost-effectiveness analysis, but varied the cost of the hearing aid device in sensitivity analysis.

## **Appendix W. Expanded Figure Legends.**

### **Figure 1: Literature Flow Diagram**

Figure 1 diagrams the flow of studies from search identification to eventual inclusion or exclusion. CEA: cost-effectiveness analysis, PRISMA: preferred reporting items for systematic review and meta-analyses.

### **Figures 2 and 3: Quality of Included Studies**

Figures 2 and 3 illustrate the quality score components assigned to individual studies (listed in each row). Score components are in each column, and the number of points (pts.) assigned for that component is noted in first row. Blue shading indicates that full score was given to the indicated component, while white shading indicates a score of zero for that component. Total quality score, aggregated across the weighted components, are listed in the right-most column.

### **Figure 4: Sensorineural hearing loss health state diagram**

This figure shows a schematic of the microsimulation model, where each circle represents a distinct health state. The arrows between health states, or returning to the health state, represent transition probabilities informed by the literature as described in the Methods. This Figure only shows the health states for untreated and treated sensorineural hearing loss, stratified by severity. Simulated persons experience yearly

probabilities of acquiring sensorineural hearing loss, worsening of existing hearing loss, and uptake or discontinuation of hearing loss treatment. An absorbing health state, death, is not shown.

CI: cochlear implant, HA: hearing aid, SNHL: sensorineural hearing loss, tx: treatment.

### **Figure 5: Conductive hearing loss health state diagram**

This health state transition diagram shows a schematic of the microsimulation model, where each circle represents a distinct health state and arrows represent transition probabilities. This figure illustrates the health states related to otitis media and conductive hearing loss in the simulation model. Simulated persons experience yearly probabilities of at least one episode of acute otitis media (AOM) and otitis media with effusion (OME)  $\geq 3$  months in the *No HL* state. A proportion of these patients might transition to the recurrent acute otitis media and persistent otitis media with effusion health state (*rAOM*, *pOME*). Patients with recurrent acute otitis media or persistent otitis media with effusion have a yearly probability of acquiring chronic suppurative otitis media (CSOM). After CSOM resolution (average of 3 years), simulated persons may resolve with no permanent conductive hearing loss, or transition to permanent conductive hearing loss. Non-otitis-media-related causes of conductive hearing loss are modeled in aggregate. All patients with conductive hearing loss have the potential to acquire sensorineural hearing loss each year. We assume that, once acquired, conductive

and sensorineural hearing loss persist for the remaining lifetime. For simplicity, treated states and an absorbing health state, death, are not shown.

AOM: acute otitis media, CHL: conductive hearing loss, CSOM: chronic suppurative otitis media, pOME: persistent otitis media with effusion, HL: hearing loss, rAOM: recurrent acute otitis media, SNHL: sensorineural hearing loss.

**Figure 6: Model projected bilateral sensorineural hearing loss severity compared to the Baltimore Longitudinal Study on Aging**

This figure shows model projected mean hearing loss (PTA in dB HL) across all simulated persons (with and without hearing loss) compared to those reported by the Baltimore Longitudinal Study on Aging. Age progresses on the x-axis from ages 30-90 years, with results shown at each decile. The blue points are model-represented means, and the orange points are the published estimates from the Baltimore Longitudinal Study on Aging. dB HL: decibel hearing level, PTA: pure tone average.

**Figure 7: One-way sensitivity analysis on the cost-effectiveness of yearly screening beginning at age 55 years.**

Figure 7 is a tornado diagram illustrating the effects of variation of single parameters (row) across their plausible range on the incremental cost-effectiveness ratio (ICER) of yearly screening beginning at age 55. The y-axis crosses the x-axis at the

basecase ICER of \$96,900/QALY. Each sensitivity analysis is presented with a basecase value; range explored, and the resulting ICERs from that range are plotted. The long-dashed line represents the US willingness-to-pay threshold of \$100,000/QALY, and the short-dashed line indicates an ICER of \$50,000/QALY.

**Figure 8: Three-way sensitivity analysis on the cost-effectiveness of adult hearing screening schedules in the United States.**

Figure 8 shows the impact of varying hearing screening effectiveness, hearing aid device cost, and hearing aid utility benefit on the incremental cost-effectiveness ratios (ICERs) of screening schedules. Screening effectiveness was varied from 1.05-2.25 on the x-axis, and hearing aid device cost was varied from \$800-6,580 on the y-axis. Panel A shows the base-case hearing aid utility benefit of +0.11 and panel B shows the results assuming a hearing aid utility benefit of +0.01-0.07 (varying with severity, similar to that assumed by the WHO and the Global Burden of Disease). Each combination of parameters yields an ICER that is color coded, with red indicating that all screening schedules had ICERs >\$100,000/QALY, orange indicating that only yearly screening at age 75 was below \$100,000/QALY, yellow that yearly screening at age 65 was below \$100,000/QALY, green that yearly screening at age 55 was between \$50-100,000/QALY, and blue that yearly screening at age 55 was less than \$50,000/QALY. The X marks the base-case input combination of screening effectiveness and hearing aid device cost.

### **Figure 9: Budget Impact Analysis**

Figure 9 depicts the model-projected average annual outlays over the first five years of the Current Detection and yearly screening beginning at age 55 years (55q1). The height of the bars represents the total annual cost of CD and the 55q1 screening schedule, with 2020 USD on the y axis. The components of the total cost are chronic suppurative otitis media (CSOM) treatment (blue), hearing aid (HA) uptake (grey), hearing aid maintenance (yellow), cochlear implant (CI) costs, and screening costs (orange).

### **Figure 10. Cost-effectiveness acceptability curve**

Figure 10 depicts the probability that each simulated screening schedule is the optimal strategy (i.e., the non-dominated strategy with the highest effectiveness and incremental cost-effectiveness ratio under the willingness to pay) on the y-axis, across willingness to pay values ranging from \$0-200,000/QALY on the x-axis. Current detection is noted as the blue line, yearly screening beginning at age 45 years in red, yearly screening beginning at age 55 years in green, yearly screening beginning at age 65

years in purple, yearly screening beginning at age 75 years in teal, and 5-yearly screening beginning at age 75 years in orange.

## References

1. Wilson BS, Tucci DL, Merson MH, O'Donoghue GM. Global hearing health care: new findings and perspectives. *The Lancet*. 2017;390(10111):2503-2515.
2. Global costs of unaddressed hearing loss and cost-effectiveness of interventions. World Health Organization, Geneva. 2017 Accessed 1 September 2020 at <https://apps.who.int/iris/bitstream/handle/10665/254659/9789241512046-eng.pdf;jsessionid=20CF4A0BAD3AEBA619EC067C4A8E5A25?sequence=1>.
3. Vos T, Allen C, Arora M, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet*. 2016;388(10053):1545-1602.
4. Goman AM, Lin FR. Prevalence of hearing loss by severity in the United States. *American Journal of Public Health*. 2016;106(10):1820-1822.
5. Chien W, Lin FR. Prevalence of hearing aid use among older adults in the United States. *Archives of Internal Medicine*. 2012;172(3):292-293.
6. Mulrow CD, Aguilar C, Endicott JE, et al. Quality-of-life changes and hearing impairment: a randomized trial. *Annals of internal medicine*. 1990;113(3):188-194.
7. Ferguson MA, Kitterick PT, Chong LY, Edmondson-Jones M, Barker F, Hoare DJ. Hearing aids for mild to moderate hearing loss in adults. *Cochrane Database of Systematic Reviews*. 2017;(9)
8. Davis A, Smith P, Ferguson M, Stephens D, Gianopoulos I. Acceptability, benefit and costs of early screening for hearing disability: a study of potential screening tests and models. *Health Technol Assess*. Oct 2007;11(42):1-294. doi:10.3310/hta11420
9. Simpson AN, Matthews LJ, Cassarly C, Dubno JR. Time from hearing aid candidacy to hearing aid adoption: a longitudinal cohort study. *Ear Hear*. May/Jun 2019;40(3):468-476. doi:10.1097/aud.0000000000000641
10. Yueh B, Collins MP, Souza PE, et al. Long-term effectiveness of screening for hearing loss: the screening for auditory impairment--which hearing assessment test

(SAI-WHAT) randomized trial. *J Am Geriatr Soc*. Mar 2010;58(3):427-34. doi:10.1111/j.1532-5415.2010.02738.x

11. US Preventative Services Task Force. Draft Evidence Review. Hearing Loss in Older Adults: Screening. 2020. Accessed 10 October 2020 at <https://www.uspreventiveservicestaskforce.org/uspstf/document/draft-evidence-review/hearing-loss-in-older-adults-screening-2021>.
12. Wilson BS, Tucci DL, O'Donoghue GM, Merson MH, Frankish H. A Lancet Commission to address the global burden of hearing loss. *The Lancet*. 2019;393(10186):2106-2108.
13. National Academies of Sciences, Engineering, and Medicine. Hearing health care for adults: priorities for improving access and affordability. Washington, DC: The National Academies Press; 2016.
14. World Health Organization. International Ear Care Day: make listening safe. Geneva, 2015. Accessed 1 September 2020 at [https://www.who.int/pbd/deafness/news/INTERNATIONAL\\_EAR\\_CARE\\_DAY\\_3\\_March\\_2015.pdf?ua=1](https://www.who.int/pbd/deafness/news/INTERNATIONAL_EAR_CARE_DAY_3_March_2015.pdf?ua=1).
15. Cheng AK, Rubin HR, Powe NR, Mellon NK, Francis HW, Niparko JK. Cost-utility analysis of the cochlear implant in children. *JAMA*. 2000;284(7):850-856.
16. Borre ED, Diab MM, Ayer A, Zhang G, Emmett SD, Tucci DL, Wilson BS, Ogbuoji O, Sanders GD. Evidence gaps in cost-effectiveness analyses of hearing healthcare: a systematic review. Society for Medical Decision Making Annual Meeting, Virtual Conference. October 2020.
17. WHO. WHO global estimates on prevalence of hearing loss. Geneva: World Health Organization. 2012. [http://www.who.int/pbd/deafness/WHO\\_GE\\_HL.pdf?ua=1](http://www.who.int/pbd/deafness/WHO_GE_HL.pdf?ua=1).
18. Lin FR, Albert M. Hearing loss and dementia—who is listening? *Aging & mental health*. 2014;18(6):671-673.
19. Nieman CL, Marrone N, Mamo SK, et al. The Baltimore HEARS Pilot Study: an affordable, accessible, community-delivered hearing care intervention. *The Gerontologist*. 2017;57(6):1173-1186.

20. Deal JA, Goman AM, Albert MS, et al. Hearing treatment for reducing cognitive decline: Design and methods of the Aging and Cognitive Health Evaluation in Elders randomized controlled trial. *Alzheimer's & Dementia: Translational Research & Clinical Interventions*. 2018;4:499-507.
21. Leroi I, Armitage CJ, Collin F, et al. A randomised controlled trial of hearing and vision support in dementia: protocol for a process evaluation in the SENSE-Cog trial. *Trials*. Feb 24 2020;21(1):223. doi:10.1186/s13063-020-4135-4
22. Contrera KJ, Sung YK, Betz J, Li L, Lin FR. Change in loneliness after intervention with cochlear implants or hearing aids. *The Laryngoscope*. 2017;127(8):1885-1889.
23. United States Preventative Services Task Force. Hearing Loss in Older Adults: Screening. 2020. Accessed 17 February 2022 at <https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/hearing-loss-in-older-adults-screening>.
24. Ciorba A, Bianchini C, Pelucchi S, Pastore A. The impact of hearing loss on the quality of life of elderly adults. *Clinical interventions in aging*. 2012;7:159.
25. Dalton DS, Cruickshanks KJ, Klein BE, Klein R, Wiley TL, Nondahl DM. The impact of hearing loss on quality of life in older adults. *The Gerontologist*. 2003;43(5):661-668.
26. Organization WH. *Global costs of unaddressed hearing loss and cost-effectiveness of interventions: a WHO report, 2017*. World Health Organization; 2017.
27. Keren R, Helfand M, Homer C, McPhillips H, Lieu TA. Projected cost-effectiveness of statewide universal newborn hearing screening. *Pediatrics*. 2002;110(5):855-864.
28. Cheng AK, Rubin HR, Powe NR, Mellon NK, Francis HW, Niparko JK. Cost-utility analysis of the cochlear implant in children. *Jama*. Aug 16 2000;284(7):850-6. doi:10.1001/jama.284.7.850.
29. Hutton B, Salanti G, Caldwell DM, et al. The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care

interventions: checklist and explanations. *Annals of internal medicine*. 2015;162(11):777-784.

30. Husereau D, Drummond M, Petrou S, et al. Consolidated health economic evaluation reporting standards (CHEERS)—explanation and elaboration: a report of the ISPOR Health Economic Evaluations Publication Guidelines Good Reporting Practices Task Force. *Value Health*. 2013;16(2):231-250.

31. Caro JJ, Briggs AH, Siebert U, Kuntz KM. Modeling good research practices—overview: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force—1. *Medical Decision Making*. 2012;32(5):667-677.

32. Walker DG, Wilson RF, Sharma R, et al. Best practices for conducting economic evaluations in health care: a systematic review of quality assessment tools. 2012;

33. Chiou C-F, Hay JW, Wallace JF, et al. Development and validation of a grading system for the quality of cost-effectiveness studies. *Medical care*. 2003:32-44.

34. The World Bank. International Financial Statistics and data files. Accessed 11.13.20 at <https://data.worldbank.org/indicator/FP.CPI.TOTL?end=2017&start=1960>.

35. Chao TK, Chen TH. Cost-effectiveness of hearing aids in the hearing-impaired elderly: a probabilistic approach. *Otol Neurotol*. Sep 2008;29(6):776-83. doi:10.1097/MAO.0b013e31817e5d1b.

36. Cheng LJ, Soon SS, Wu DB, Ju H, Ng K. Cost-effectiveness analysis of bilateral cochlear implants for children with severe-to-profound sensorineural hearing loss in both ears in Singapore. *PLoS One*. 2019;14(8):e0220439. doi:10.1371/journal.pone.0220439. eCollection 2019.

37. Chiou ST, Lung HL, Chen LS, et al. Economic evaluation of long-term impacts of universal newborn hearing screening. *Int J Audiol*. Jan 2017;56(1):46-52. doi:10.1080/14992027.2016.1219777. Epub 2016 Sep 6.

38. Fang TY, Cheng LJ, Wu DB, Wang PC. Cost-effective analysis of unilateral cochlear implantation under the Taiwan national healthcare insurance. *Int J Audiol*. Sep 9 2019:1-6. doi:10.1080/14992027.2019.1658907.

39. Hirano E, Fuji H, Onoe T, Kumar V, Shirato H, Kawabuchi K. Cost-effectiveness analysis of cochlear dose reduction by proton beam therapy for medulloblastoma in childhood. *J Radiat Res.* Mar 1 2014;55(2):320-7. doi:10.1093/jrr/rrt112. Epub 2013 Nov 1.
40. Kitano T, Onaka M, Ishihara M, Nishiyama A, Hashimoto N, Yoshida S. Static model simulation for routine mumps vaccination in Japan: With a result of mumps-related complications in a Japanese community hospital. Article. *Clinical and Experimental Vaccine Research.* 2017;6(2):120-127. doi:10.7774/cevr.2017.6.2.120
41. Wong BY, Hui Y, Au D, Wei W. Economic evaluation of cochlear implantation. *Adv Otorhinolaryngol.* 2000;57:377-81. doi:10.1159/000059216.
42. Beswick R, David M, Higashi H, et al. Integration of congenital cytomegalovirus screening within a newborn hearing screening programme. Article. *Journal of Paediatrics and Child Health.* 2019;55(11):1381-1388. doi:10.1111/jpc.14428
43. Butler JRG, McIntyre P, MacIntyre CR, Gilmour R, Howarth AL, Sander B. The cost-effectiveness of pneumococcal conjugate vaccination in Australia. *Vaccine.* 2004;22(9-10):1138-1149.
44. Carter R, Hailey D. Economic evaluation of the cochlear implant. *Int J Technol Assess Health Care.* Summer 1999;15(3):520-30.
45. Foteff C, Kennedy S, Milton AH, Deger M, Payk F, Sanderson G. Cost-Utility Analysis of Cochlear Implantation in Australian Adults. *Otol Neurotol.* Jun 2016;37(5):454-61. doi:10.1097/MAO.0000000000000999.
46. Foteff C, Kennedy S, Milton AH, Deger M, Payk F, Sanderson G. Economic Evaluation of Treatments for Pediatric Bilateral Severe to Profound Sensorineural Hearing Loss: An Australian Perspective. *Otol Neurotol.* Jun 2016;37(5):462-9. doi:10.1097/MAO.0000000000001000.
47. Kosaner Kliess M, Kluibenschaedl M, Zoehrer R, Schlick B, Scandurra F, Urban M. Cost-Utility of Partially Implantable Active Middle Ear Implants for Sensorineural Hearing Loss: A Decision Analysis. *Value Health.* Sep 2017;20(8):1092-1099. doi:10.1016/j.jval.2017.04.020. Epub 2017 May 31.

48. Lea AR, Hailey DM. The cochlear implant. A technology for the profoundly deaf. *Med Prog Technol.* 1995;21(1):47-52.
49. Merlin T, Hedayati H, Sullivan T, et al. Universal neonatal hearing screening. MSAC reference 17 Assessment report. *Canberra: MSAC.* 2007;
50. Newall AT, Reyes JF, McIntyre P, Menzies R, Beutels P, Wood JG. Retrospective economic evaluation of childhood 7-valent pneumococcal conjugate vaccination in Australia: Uncertain herd impact on pneumonia critical. Article. *Vaccine.* 2016;34(3):320-327. doi:10.1016/j.vaccine.2015.11.053
51. Nguyen KH, Smith AC, Armfield NR, Bensink M, Scuffham PA. Cost-Effectiveness Analysis of a Mobile Ear Screening and Surveillance Service versus an Outreach Screening, Surveillance and Surgical Service for Indigenous Children in Australia. *PLoS One.* 2015;10(9):e0138369. doi:10.1371/journal.pone.0138369. eCollection 2015.
52. Bilateral Cochlear Implantation: A Health Technology Assessment. *Ont Health Technol Assess Ser.* 2018;18(6):1-139.
53. Implantable Devices for Single-Sided Deafness and Conductive or Mixed Hearing Loss: A Health Technology Assessment. Article. *Ontario Health Technology Assessment Series.* 2020;20(1):1-165.
54. Bichey BG, Hoversland JM, Wynne MK, Miyamoto RT. Changes in quality of life and the cost-utility associated with cochlear implantation in patients with large vestibular aqueduct syndrome. *Otol Neurotol.* May 2002;23(3):323-7. doi:10.1097/00129492-200205000-00016.
55. Chen JM, Amoodi H, Mittmann N. Cost-utility analysis of bilateral cochlear implantation in adults: a health economic assessment from the perspective of a publicly funded program. *Laryngoscope.* Jun 2014;124(6):1452-8. doi:10.1002/lary.24537. Epub 2014 Jan 15.
56. Corabian PSD. <screening\_newborns\_for\_hearing.pdf>. 2007;

57. Criteria of candidacy for unilateral cochlear implantation in postlingually deafened adults II: cost-effectiveness analysis. *Ear Hear.* Aug 2004;25(4):336-60. doi:10.1097/01.aud.0000134550.80305.04.
58. Bamford J, Fortnum H, Bristow K, et al. Current practice, accuracy, effectiveness and cost-effectiveness of the school entry hearing screen. *Health Technol Assess.* Aug 2007;11(32):1-168, iii-iv. doi:10.3310/hta11320.
59. Boas G, Van Der Stel H, Peters H, Joore M, Anteunis L. Dynamic modeling in medical technology assessment: Fitting hearing aids in the Netherlands. Article. *International Journal of Technology Assessment in Health Care.* 2001;17(4):618-625.
60. Bond M, Mealing S, Anderson R, et al. The effectiveness and cost-effectiveness of cochlear implants for severe to profound deafness in children and adults: a systematic review and economic model. *Health Technol Assess.* Sep 2009;13(44):1-330. doi:10.3310/hta13440.
61. Bos JM, Rümke H, Welte R, Postma MJ. Epidemiologic impact and cost-effectiveness of universal infant vaccination with a 7-valent conjugated pneumococcal vaccine in the Netherlands. *Clinical therapeutics.* 2003;25(10):2614-2630.
62. Bos JM, Rumke HC, Welte R, Spanjaard L, van Alphen L, Postma MJ. Combination vaccine against invasive meningococcal B and pneumococcal infections: potential epidemiological and economic impact in the Netherlands. *Pharmacoeconomics.* 2006;24(2):141-53. doi:10.2165/00019053-200624020-00004.
63. Boshuizen HC, van der Lem GJ, Kauffman-de Boer MA, van Zanten GA, Oudesluys-Murphy AM, Verkerk PH. Costs of different strategies for neonatal hearing screening: a modelling approach. *Arch Dis Child Fetal Neonatal Ed.* Nov 2001;85(3):F177-81. doi:10.1136/fn.85.3.f177.
64. Brown J. Screening infants for hearing loss--an economic evaluation. *J Epidemiol Community Health.* Aug 1992;46(4):350-6. doi:10.1136/jech.46.4.350.
65. Bruce I, Harman N, Williamson P, et al. The management of Otitis Media with Effusion in children with cleft palate (mOMent): a feasibility study and economic evaluation. *Health Technol Assess.* Aug 2015;19(68):1-374. doi:10.3310/hta19680.

66. Burke MJ, Shenton RC, Taylor MJ. The economics of screening infants at risk of hearing impairment: an international analysis. *Int J Pediatr Otorhinolaryngol*. Feb 2012;76(2):212-8. doi:10.1016/j.ijporl.2011.11.004. Epub 2011 Nov 29.
67. Claes C, von der Schulenburg J-MG. Cost effectiveness of pneumococcal vaccination for infants and children with the conjugate vaccine PnC-7 in Germany. *Pharmacoeconomics*. 2003;21(8):587-600.
68. Clegg AJ, Loveman E, Gospodarevskaya E, et al. The safety and effectiveness of different methods of earwax removal: a systematic review and economic evaluation. *Health Technol Assess*. Jun 2010;14(28):1-192. doi:10.3310/hta14280.
69. Colquitt JL, Jones J, Harris P, et al. Bone-anchored hearing aids (BAHAs) for people who are bilaterally deaf: a systematic review and economic evaluation. *Health Technol Assess*. Jul 2011;15(26):1-200, iii-iv. doi:10.3310/hta15260.
70. Ess SM, Schaad UB, Gervaix A, Pinösch S, Szucs TD. Cost-effectiveness of a pneumococcal conjugate immunisation program for infants in Switzerland. *Vaccine*. 2003;21(23):3273-3281.
71. Fortnum H, Leighton P, Smith MD, et al. Assessment of the feasibility and clinical value of further research to evaluate the management options for children with Down syndrome and otitis media with effusion: a feasibility study. *Health Technol Assess*. Sep 2014;18(60):1-147, v-vi. doi:10.3310/hta18600.
72. Fortnum H, O'Neill C, Taylor R, et al. The role of magnetic resonance imaging in the identification of suspected acoustic neuroma: a systematic review of clinical and cost effectiveness and natural history. *Health Technol Assess*. Mar 2009;13(18):iii-iv, ix-xi, 1-154. doi:10.3310/hta13180.
73. Fortnum H, Ukoumunne OC, Hyde C, et al. A programme of studies including assessment of diagnostic accuracy of school hearing screening tests and a cost-effectiveness model of school entry hearing screening programmes. *Health Technol Assess*. May 2016;20(36):1-178. doi:10.3310/hta20360.
74. Grill E, Uus K, Hessel F, et al. Neonatal hearing screening: modelling cost and effectiveness of hospital- and community-based screening. *BMC Health Serv Res*. Feb 23 2006;6:14. doi:10.1186/1472-6963-6-14.

75. Grutters JP, Joore MA, Van Der Horst F, Stokroos RJ, Anteunis LJ. Decision-analytic modeling to assist decision making in organizational innovation: the case of shared care in hearing aid provision. *Health Serv Res.* Oct 2008;43(5 Pt 1):1662-73. doi:10.1111/j.1475-6773.2008.00872.x. Epub 2008 Jun 3.
76. Hessel F, Grill E, Schnell-Inderst P, et al. Economic evaluation of newborn hearing screening: modelling costs and outcomes. *Ger Med Sci.* Dec 15 2003;1:Doc09.
77. Hutton J, Politi C, Seeger T. Cost-effectiveness of cochlear implantation of children. A preliminary model for the UK. *Adv Otorhinolaryngol.* 1995;50:201-6. doi:10.1159/000424460.
78. Joore MA, Van Der Stel H, Peters HJ, Boas GM, Anteunis LJ. The cost-effectiveness of hearing-aid fitting in the Netherlands. *Arch Otolaryngol Head Neck Surg.* Mar 2003;129(3):297-304. doi:10.1001/archotol.129.3.297.
79. Keren R, Helfand M, Homer C, McPhillips H, Lieu TA. Projected cost-effectiveness of statewide universal newborn hearing screening. *Pediatrics.* Nov 2002;110(5):855-64. doi:10.1542/peds.110.5.855.
80. Kruyt IJ, Bours MRW, Rovers MM, Hol MKS, Rongen J. Economic Evaluation of Percutaneous Titanium Implants for Bone Conduction Hearing: A Cost-benefit Analysis. *Otol Neurotol.* Jun 2020;41(5):580-588. doi:10.1097/mao.0000000000002616. doi:10.1097/MAO.0000000000002616.
81. Langer A, Brockow I, Nennstiel-Ratzel U, Menn P. The cost-effectiveness of tracking newborns with bilateral hearing impairment in Bavaria: a decision-analytic model. *BMC Health Serv Res.* Nov 22 2012;12:418. doi:10.1186/1472-6963-12-418.
82. Laske RD, Dreyfuss M, Stulman A, Veraguth D, Huber AM, Roosli C. Age Dependent Cost-Effectiveness of Cochlear Implantation in Adults. Is There an Age Related Cut-off? *Otol Neurotol.* Aug 2019;40(7):892-899. doi:10.1097/MAO.0000000000002275.
83. Linssen AM, Anteunis LJ, Joore MA. The Cost-Effectiveness of Different Hearing Screening Strategies for 50- to 70-Year-Old Adults: A Markov Model. *Value Health.* Jul 2015;18(5):560-9. doi:10.1016/j.jval.2015.03.1789. Epub 2015 May 14.

84. Lundkvist J, Ekman M, Ericsson SR, Jonsson B, Glimelius B. Cost-effectiveness of proton radiation in the treatment of childhood medulloblastoma. *Cancer*. Feb 15 2005;103(4):793-801. doi:10.1002/cncr.20844.
85. McIntosh EDG, Conway P, Willingham J, Lloyd A. The cost-burden of paediatric pneumococcal disease in the UK and the potential cost-effectiveness of prevention using 7-valent pneumococcal conjugate vaccine. *Vaccine*. 2003;21(19-20):2564-2572.
86. Melegaro A, Edmunds WJ. Cost-effectiveness analysis of pneumococcal conjugate vaccination in England and Wales. *Vaccine*. 2004;22(31-32):4203-4214.
87. Mohiuddin S, Payne K, Fenwick E, O'Brien K, Bruce I. A model-based cost-effectiveness analysis of a grommets-led care pathway for children with cleft palate affected by otitis media with effusion. *Eur J Health Econ*. Jul 2015;16(6):573-87. doi:10.1007/s10198-014-0610-8. Epub 2014 Jun 7.
88. Mohiuddin S, Schilder A, Bruce I. Economic evaluation of surgical insertion of ventilation tubes for the management of persistent bilateral otitis media with effusion in children. *BMC Health Serv Res*. Jun 13 2014;14:253. doi:10.1186/1472-6963-14-253.
89. Monksfield P, Jowett S, Reid A, Proops D. Cost-effectiveness analysis of the bone-anchored hearing device. *Otol Neurotol*. Oct 2011;32(8):1192-7. doi:10.1097/MAO.0b013e31822e5ae6.
90. Morris A. An Economic Model of Adult Hearing Screening. *Audiol Res*. May 10 2011;1(1):e16. doi:10.4081/audiore.2011.e16. eCollection 2011 May 10.
91. Morris AE, Lutman ME, Cook AJ, Turner D. An economic evaluation of screening 60- to 70-year-old adults for hearing loss. *J Public Health (Oxf)*. Mar 2013;35(1):139-46. doi:10.1093/pubmed/fds058. Epub 2012 Sep 30.
92. Navas E, Salleras L, Gisbert R, et al. Cost-benefit and cost-effectiveness of the incorporation of the pneumococcal 7-valent conjugated vaccine in the routine vaccination schedule of Catalonia (Spain). *Vaccine*. 2005;23(17-18):2342-2348.
93. Perez-Martin J, Artaso MA, Diez FJ. Cost-effectiveness of pediatric bilateral cochlear implantation in Spain. *Laryngoscope*. Dec 2017;127(12):2866-2872. doi:10.1002/lary.26765. Epub 2017 Aug 4.

94. Prusa AR, Kasper DC, Sawers L, Walter E, Hayde M, Stillwaggon E. Congenital toxoplasmosis in Austria: Prenatal screening for prevention is cost-saving. *PLoS Negl Trop Dis*. Jul 2017;11(7):e0005648. doi:10.1371/journal.pntd.0005648
- 10.1371/journal.pntd.0005648. eCollection 2017 Jul.
95. Salo H, Sintonen H, Pekka Nuorti J, et al. Economic evaluation of pneumococcal conjugate vaccination in Finland. *Scandinavian journal of infectious diseases*. 2005;37(11-12):821-832.
96. Summerfield AQ, Lovett RE, Bellenger H, Batten G. Estimates of the cost-effectiveness of pediatric bilateral cochlear implantation. *Ear Hear*. Oct 2010;31(5):611-24. doi:10.1097/AUD.0b013e3181de40cd.
97. Summerfield AQ, Marshall DH, Archbold S. Cost-effectiveness considerations in pediatric cochlear implantation. *Am J Otol*. Nov 1997;18(6 Suppl):S166-8.
98. Summerfield AQ, Marshall DH, Barton GR, Bloor KE. A cost-utility scenario analysis of bilateral cochlear implantation. *Arch Otolaryngol Head Neck Surg*. Nov 2002;128(11):1255-62. doi:10.1001/archotol.128.11.1255.
99. Summerfield AQ, Marshall DH, Davis AC. Cochlear implantation: demand, costs, and utility. *Ann Otol Rhinol Laryngol Suppl*. Sep 1995;166:245-8.
100. Theriou C, Fielden CA, Kitterick PT. The Cost-Effectiveness of Bimodal Stimulation Compared to Unilateral and Bilateral Cochlear Implant Use in Adults with Bilateral Severe to Profound Deafness. *Ear Hear*. Nov/Dec 2019;40(6):1425-1436. doi:10.1097/AUD.0000000000000727.
101. Vallejo-Torres L, Castilla I, Couce ML, et al. Cost-effectiveness analysis of a national newborn screening program for biotinidase deficiency. Article. *Pediatrics*. 2015;136(2):e424-e432. doi:10.1542/peds.2014-3399
102. Williams EJ, Gray J, Luck S, et al. First estimates of the potential cost and cost saving of protecting childhood hearing from damage caused by congenital CMV infection. *Arch Dis Child Fetal Neonatal Ed*. Nov 2015;100(6):F501-6. doi:10.1136/archdischild-2014-306756. Epub 2015 Jun 29.

103. Williamson I, Bengte S, Barton S, et al. A double-blind randomised placebo-controlled trial of topical intranasal corticosteroids in 4- to 11-year-old children with persistent bilateral otitis media with effusion in primary care. *Health Technol Assess.* Aug 2009;13(37):1-144. doi:10.3310/hta13370.
104. Wyatt JR, Niparko JK, Rothman ML, eLissovoy G. Cost effectiveness of the multichannel cochlear implant. *Am J Otol.* Jan 1995;16(1):52-62.
105. Wyatt JR, Niparko JK, Rothman M, deLissovoy G. Cost utility of the multichannel cochlear implants in 258 profoundly deaf individuals. *Laryngoscope.* 1996;106(7):816-21. doi:10.1097/00005537-199607000-00006
106. Veenstra DL, Harris J, Gibson RL, Rosenfeld M, Burke W, Watts C. Pharmacogenomic testing to prevent aminoglycoside-induced hearing loss in cystic fibrosis patients: potential impact on clinical, patient, and economic outcomes. *Genet Med.* Oct 2007;9(10):695-704. doi:10.1097/gim.0b013e318156dd07.
107. Turner RG. Comparison of four hearing screening protocols. *J Am Acad Audiol.* May 1992;3(3):200-7.
108. Simon MS, Weiss D, Geevarughese A, et al. Cost-Effectiveness of Meningococcal Vaccination among Men Who Have Sex with Men in New York City. Article. *Journal of Acquired Immune Deficiency Syndromes.* 2016;71(2):146-154. doi:10.1097/QAI.0000000000000822
109. Sharma A, Viets R, Parsons MS, Reis M, Chrisinger J, Wippold FJ. A two-tiered approach to MRI for hearing loss: incremental cost of a comprehensive MRI over high-resolution T2-weighted imaging. *AJR Am J Roentgenol.* Jan 2014;202(1):136-44. doi:10.2214/AJR.13.10610.
110. Semenov YR, Yeh ST, Seshamani M, et al. Age-dependent cost-utility of pediatric cochlear implantation. *Ear Hear.* Jul-Aug 2013;34(4):402-12. doi:10.1097/AUD.0b013e3182772c66.
111. Prager DA, Stone DA, Rose DN. Hearing loss screening in the neonatal intensive care unit: auditory brain stem response versus Crib-O-Gram; a cost-effectiveness analysis. *Ear Hear.* Aug 1987;8(4):213-6. doi:10.1097/00003446-198708000-00004.

112. Niparko JKWJR. Evaluating the cost-effectiveness of hearing rehabilitation. In: Cummings CW, Frederickson JM, Harker LA, Krause CJ, Schuller DE, eds. *Otolaryngology–Head and Neck Surgery Update*. 2nd ed. St Louis, Mo: Mosby– Year Book Inc; 1995:112-125.
113. Liu CF, Collins MP, Souza PE, Yueh B. Long-term cost-effectiveness of screening strategies for hearing loss. *J Rehabil Res Dev*. 2011;48(3):235-43. doi:10.1682/jrrd.2010.03.0041.
114. Lieu TA, Ray GT, Black SB, et al. Projected cost-effectiveness of pneumococcal conjugate vaccination of healthy infants and young children. Article. *Journal of the American Medical Association*. 2000;283(11):1460-1468. doi:10.1001/jama.283.11.1460
115. Leeds IL, Namasivayam V, Bamogo A, Sankhla P, Thayer WM. Cost Effectiveness of Meningococcal Serogroup B Vaccination in College-Aged Young Adults. Article. *American Journal of Preventive Medicine*. 2019;56(2):196-204. doi:10.1016/j.amepre.2018.09.020
116. Le P, Rothberg MB. Cost-effectiveness of herpes zoster vaccine for persons aged 50 years. Article. *Annals of Internal Medicine*. 2015;163(7):489-497. doi:10.7326/M150093
117. Kezirian EJ, White KR, Yueh B, Sullivan SD. Cost and cost-effectiveness of universal screening for hearing loss in newborns. *Otolaryngol Head Neck Surg*. Apr 2001;124(4):359-67. doi:10.1067/mhn.2001.113945.
118. Kemper AR, Downs SM. A cost-effectiveness analysis of newborn hearing screening strategies. *Arch Pediatr Adolesc Med*. May 2000;154(5):484-8. doi:10.1001/archpedi.154.5.484.
119. Hojjat H, Svider PF, Davoodian P, Hong RS, Folbe AJ, Eloy JA. To image or not to image? A cost-effectiveness analysis of MRI for patients with asymmetric sensorineural hearing loss. *Laryngoscope*. Apr 2017;127(4):939-944. doi:10.1002/lary.26231. Epub 2016 Sep 30.
120. Gillard DM, Harris JP. Cost-effectiveness of Stapedectomy vs Hearing Aids in the Treatment of Otosclerosis. *JAMA Otolaryngol Head Neck Surg*. Nov 7 2019;doi:10.1001/jamaoto.2019.3221.

121. Garcia SL, Smith KJ, Palmer C. Cost-Effectiveness Analysis of a Military Hearing Conservation Program. *Mil Med.* Sep 1 2018;183(9-10):e547-e553. doi:10.1093/milmed/usx112.
122. Gantt S, Dionne F, Kozak FK, et al. Cost-effectiveness of Universal and Targeted Newborn Screening for Congenital Cytomegalovirus Infection. *JAMA Pediatr.* Dec 1 2016;170(12):1173-1180. doi:10.1001/jamapediatrics.2016.2016.
123. Francis HW, Chee N, Yeagle J, Cheng A, Niparko JK. Impact of cochlear implants on the functional health status of older adults. *Laryngoscope.* Aug 2002;112(8 Pt 1):1482-8. doi:10.1097/00005537-200208000-00028.
124. Dempsey AF, Pangborn HM, Prosser LA. Cost-effectiveness of routine vaccination of adolescent females against cytomegalovirus. *Vaccine.* Jun 8 2012;30(27):4060-6. doi:10.1016/j.vaccine.2012.04.011. Epub 2012 Apr 21.
125. Daniels RL, Shelton C, Harnsberger HR. Ultra high resolution nonenhanced fast spin echo magnetic resonance imaging: cost-effective screening for acoustic neuroma in patients with sudden sensorineural hearing loss. *Otolaryngol Head Neck Surg.* Oct 1998;119(4):364-9. doi:10.1016/S0194-5998(98)70080-4.
126. Crowson MG, Rocke DJ, Hoang JK, Weissman JL, Kaylie DM. Cost-effectiveness analysis of a non-contrast screening MRI protocol for vestibular schwannoma in patients with asymmetric sensorineural hearing loss. *Neuroradiology.* Aug 2017;59(8):727-736. doi:10.1007/s00234-017-1859-2. Epub 2017 Jun 16.
127. Bichey BG, Miyamoto RT. Outcomes in bilateral cochlear implantation. *Otolaryngol Head Neck Surg.* May 2008;138(5):655-61. doi:10.1016/j.otohns.2007.12.020.
128. Berman S, Roark R, Luckey D. Theoretical cost effectiveness of management options for children with persisting middle ear effusions. *Pediatrics.* Mar 1994;93(3):353-63.
129. Abrams H, Chisolm TH, McArdle R. A cost-utility analysis of adult group audiologic rehabilitation: are the benefits worth the cost? *J Rehabil Res Dev.* Sep-Oct 2002;39(5):549-58.

130. Schnippel K, Firnhaber C, Page-Shipp L, Sinanovic E. Impact of adverse drug reactions on the incremental cost-effectiveness of bedaquiline for drug-resistant tuberculosis. *Int J Tuberc Lung Dis*. Aug 1 2018;22(8):918-925. doi:10.5588/ijtld.17.0869.
131. Pugh SJ, Fletcher MA, Charos A, Imekraz L, Wasserman M, Farkouh R. Cost-Effectiveness of the Pneumococcal Conjugate Vaccine (10- or 13-Valent) Versus No Vaccination for a National Immunization Program in Tunisia or Algeria. Article. *Infectious Diseases and Therapy*. 2019;8(1):63-74. doi:10.1007/s40121-018-0226-x
132. Kuznik A, Iliyasu G, Lamorde M, et al. Cost-effectiveness of expanding childhood routine immunization against *Neisseria meningitidis* serogroups C, W and Y with a quadrivalent conjugate vaccine in the African meningitis belt. Article. *PLoS ONE*. 2017;12(11)doi:10.1371/journal.pone.0188595
133. Emmett SD, Tucci DL, Smith M, et al. GDP Matters: Cost Effectiveness of Cochlear Implantation and Deaf Education in Sub-Saharan Africa. *Otol Neurotol*. Sep 2015;36(8):1357-65. doi:10.1097/MAO.0000000000000823.
134. Baltussen R, Smith A. Cost effectiveness of strategies to combat vision and hearing loss in sub-Saharan Africa and South East Asia: mathematical modelling study. *Bmj*. Mar 2 2012;344:e615. doi:10.1136/bmj.e615.
135. Baltussen R, Smith A. Cost-effectiveness of selected interventions for hearing impairment in Africa and Asia: A mathematical modelling approach. Article. *International Journal of Audiology*. 2009;48(3):144-158. doi:10.1080/14992020802538081
136. Tobe RG, Mori R, Huang L, Xu L, Han D, Shibuya K. Cost-effectiveness analysis of a national neonatal hearing screening program in China: conditions for the scale-up. *PLoS One*. 2013;8(1):e51990. doi:10.1371/journal.pone.0051990. Epub 2013 Jan 16.
137. Rob B, Vinod JA, Monica P, et al. Costs and health effects of screening and delivery of hearing aids in Tamil Nadu, India: an observational study. *BMC Public Health*. May 12 2009;9:135. doi:10.1186/1471-2458-9-135
- 10.1186/1471-2458-9-135.

138. Rivera AS, Lam HY, Chiong CM, Reyes-Quintos MRT, Ricalde RR. The cost-effectiveness and budget impact of a community-based universal newborn hearing screening program in the Philippines. *Acta Medica Philippina*. 2017;51(1)
139. Qiu J, Yu C, Ariyaratne TV, et al. Cost-Effectiveness of Pediatric Cochlear Implantation in Rural China. *Otol Neurotol*. Jul 2017;38(6):e75-e84. doi:10.1097/MAO.0000000000001389.
140. Ning G, Yin Z, Li Y, Wang H, Yang W. Cost-effectiveness of the Haemophilus influenzae type b vaccine for infants in mainland China. *Hum Vaccin Immunother*. Jan 2 2018;14(1):36-44. doi:10.1080/21645515.2017.1385687. Epub 2017 Nov 27.
141. Huang LH, Zhang L, Tobe RY, et al. Cost-effectiveness analysis of neonatal hearing screening program in China: should universal screening be prioritized? *BMC Health Serv Res*. Apr 17 2012;12:97. doi:10.1186/1472-6963-12-97.
142. Emmett SD, Sudoko CK, Tucci DL, et al. Expanding Access: Cost-effectiveness of Cochlear Implantation and Deaf Education in Asia. *Otolaryngol Head Neck Surg*. Oct 2019;161(4):672-682. doi:10.1177/0194599819849917. Epub 2019 Jun 18.
143. Dorji K, Phuntsho S, Pempa K, et al. Towards the introduction of pneumococcal conjugate vaccines in Bhutan: A cost-utility analysis to determine the optimal policy option. Article. *Vaccine*. 2018;36(13):1757-1765. doi:10.1016/j.vaccine.2018.02.048
144. Saunders JE, Barrs DM, Gong W, Wilson BS, Mojica K, Tucci DL. Cost Effectiveness of Childhood Cochlear Implantation and Deaf Education in Nicaragua: A Disability Adjusted Life Year Model. *Otol Neurotol*. Sep 2015;36(8):1349-56. doi:10.1097/MAO.0000000000000809.
145. Izquierdo G, Torres JP, Santolaya ME, Valenzuela MT, Vega J, Chomali M. Cost-effectiveness analysis of a multicomponent meningococcal serogroup B vaccine in hypothetical epidemic situation in a middle-income country. Article. *Human Vaccines and Immunotherapeutics*. 2015;11(4):875-883. doi:10.1080/21645515.2015.1010885
146. Emmett SD, Tucci DL, Bento RF, et al. Moving Beyond GDP: Cost Effectiveness of Cochlear Implantation and Deaf Education in Latin America. *Otol Neurotol*. Sep 2016;37(8):1040-8. doi:10.1097/MAO.0000000000001148.

147. Moradi-Lakeh M, Shakerian S, Esteghamati A. Immunization against Haemophilus Influenzae type B in Iran; cost-utility and cost-benefit analyses. Article. *International Journal of Preventive Medicine*. 2012;3(5):332-340.
148. Heidari S, Manesh AO, Rajabi F, Moradi-Joo M. Cost-effectiveness analysis of automated auditory brainstem response and otoacoustic emission in universal neonatal hearing screening. Article. *Iranian Journal of Pediatrics*. 2017;27(2)doi:10.5812/ijp.5229
149. Wong LY, Espinoza F, Alvarez KM, Molter D, Saunders JE. Otoacoustic Emissions in Rural Nicaragua: Cost Analysis and Implications for Newborn Hearing Screening. *Otolaryngol Head Neck Surg*. May 2017;156(5):877-885. doi:10.1177/0194599817696306. Epub 2017 Feb 1.
150. Montes F, Penaranda A, Correa S, et al. Cochlear Implants Versus Hearing Aids in a Middle-Income Country: Costs, Productivity, and Quality of Life. *Otol Neurotol*. Jun 2017;38(5):e26-e33. doi:10.1097/MAO.0000000000001393.
151. Sanders GD, Neumann PJ, Basu A, et al. Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses: second panel on cost-effectiveness in health and medicine. *JAMA*. 2016;316(10):1093-1103.
152. Beutels P, Thiry N, Van Damme P. Convincing or confusing?. Economic evaluations of childhood pneumococcal conjugate vaccination-a review (2002-2006). Review. *Vaccine*. 2007;25(8):1355-1367. doi:10.1016/j.vaccine.2006.10.034
153. Bond M, Elston J, Mealing S, et al. Systematic reviews of the effectiveness and cost-effectiveness of multi-channel unilateral cochlear implants for adults. *Clin Otolaryngol*. Apr 2010;35(2):87-96. doi:10.1111/j.1749-4486.2010.02098.x.
154. Bond M, Elston J, Mealing S, et al. Effectiveness of multi-channel unilateral cochlear implants for profoundly deaf children: A systematic review. Article. *Clinical Otolaryngology*. 2009;34(3):199-211. doi:10.1111/j.1749-4486.2009.01916.x
155. Bruchhage KL, Leichtle A, Schonweiler R, et al. Systematic review to evaluate the safety, efficacy and economical outcomes of the Vibrant Soundbridge for the treatment of sensorineural hearing loss. *Eur Arch Otorhinolaryngol*. Apr 2017;274(4):1797-1806. doi:10.1007/s00405-016-4361-2. Epub 2016 Oct 31.

156. Cheng AK, Niparko JK. Cost-utility of the cochlear implant in adults: a meta-analysis. *Arch Otolaryngol Head Neck Surg*. Nov 1999;125(11):1214-8. doi:10.1001/archotol.125.11.1214.
157. Colgan S, Gold L, Wirth K, et al. The cost-effectiveness of universal newborn screening for bilateral permanent congenital hearing impairment: systematic review. *Acad Pediatr*. May-Jun 2012;12(3):171-80. doi:10.1016/j.acap.2012.02.002.
158. Crathorne L, Bond M, Cooper C, et al. A systematic review of the effectiveness and cost-effectiveness of bilateral multichannel cochlear implants in adults with severe-to-profound hearing loss. *Clin Otolaryngol*. Oct 2012;37(5):342-54. doi:10.1111/coa.12011.
159. Crowson MG, Tucci DL. Mini Review of the Cost-Effectiveness of Unilateral Osseointegrated Implants in Adults: Possibly Cost-Effective for the Correct Indication. *Audiol Neurootol*. 2016;21(2):69-71. doi:10.1159/000443629. Epub 2016 Feb 20.
160. Davis A, Bamford J, Wilson I, Ramkalawan T, Forshaw M, Wright S. A critical review of the role of neonatal hearing screening in the detection of congenital hearing impairment. *Health Technol Assess*. 1997;1(10):i-iv, 1-176.
161. Lammers MJ, Grolman W, Smulders YE, Rovers MM. The cost-utility of bilateral cochlear implantation: a systematic review. *Laryngoscope*. Dec 2011;121(12):2604-9. doi:10.1002/lary.22387.
162. Magro I, Emmett SD, Saunders J. Cost-effectiveness of CI in developing countries. *Curr Opin Otolaryngol Head Neck Surg*. Jun 2018;26(3):190-195. doi:10.1097/MOO.0000000000000451.
163. O'Donovan J, Verkerk M, Winters N, Chadha S, Bhutta MF. The role of community health workers in addressing the global burden of ear disease and hearing loss: a systematic scoping review of the literature. *BMJ Glob Health*. 2019;4(2):e001141. doi:10.1136/bmjgh-2018-001141. eCollection 2019.
164. Sharma R, Gu Y, Ching TYC, Marnane V, Parkinson B. Economic Evaluations of Childhood Hearing Loss Screening Programmes: A Systematic Review and Critique. *Appl Health Econ Health Policy*. Jun 2019;17(3):331-357. doi:10.1007/s40258-018-00456-1.

165. Taylor RS, Paisley S, Davis A. Systematic review of the clinical and cost effectiveness of digital hearing aids. *Br J Audiol*. Oct 2001;35(5):271-88. doi:10.1080/00305364.2001.11745246.
166. Turchetti G, Bellelli S, Palla I, Berrettini S. Systematic review of the scientific literature on the economic evaluation of cochlear implants in adult patients. *Acta Otorhinolaryngol Ital*. Oct 2011;31(5):319-27.
167. Turchetti G, Bellelli S, Palla I, Forli F. Systematic review of the scientific literature on the economic evaluation of cochlear implants in paediatric patients. *Acta Otorhinolaryngol Ital*. Oct 2011;31(5):311-8.
168. Vegter S, Boersma C, Rozenbaum M, Wilffert B, Navis G, Postma MJ. Pharmacoeconomic evaluations of pharmacogenetic and genomic screening programmes: A systematic review on content and adherence to guidelines. Review. *PharmacoEconomics*. 2008;26(7):569-587. doi:10.2165/00019053-200826070-00005
169. Huddle MG, Goman AM, Kernizan FC, et al. The economic impact of adult hearing loss: a systematic review. *JAMA Otolaryngology–Head & Neck Surgery*. 2017;143(10):1040-1048.
170. Livingston G, Sommerlad A, Orgeta V, et al. Dementia prevention, intervention, and care. *The Lancet*. 2017;390(10113):2673-2734.
171. Livingston G, Huntley J, Sommerlad A, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *Lancet*. Aug 8 2020;396(10248):413-446. doi:10.1016/s0140-6736(20)30367-6
172. Ching TYC, Dillon H, Leigh G, Cupples L. Learning from the Longitudinal Outcomes of Children with Hearing Impairment (LOCHI) study: summary of 5-year findings and implications. *Int J Audiol*. May 2018;57(sup2):S105-s111. doi:10.1080/14992027.2017.1385865
173. Simpson AN, Simpson KN, Dubno JR. Higher health care costs in middle-aged US adults with hearing loss. *JAMA Otolaryngology–Head & Neck Surgery*. 2016;142(6):607-609.

174. Simpson AN, Simpson KN, Dubno JR. Healthcare costs for insured older US adults with hearing loss. *Journal of the American Geriatrics Society*. 2018;66(8):1546-1552.
175. World Health Organization. World report on hearing. Geneva 2021. Accessed 17 February 2022 at <https://www.who.int/publications/i/item/world-report-on-hearing>.
176. National Institute on Deafness and Other Communication Disorders (NIDCD). 2017-2021 NIDCD Strategic Plan. Accessed 17 February 2022 at <https://www.nidcd.nih.gov/sites/default/files/Documents/NIDCD-StrategicPlan2017-508.pdf>.
177. National Academies of Sciences, Engineering, and Medicine 2016. Hearing Health Care for Adults: Priorities for Improving Access and Affordability. Washington, DC: The National Academies Press. <https://doi.org/10.17226/23446>.
178. Neumann PJ, Sanders GD, Russell LB, Siegel JE, Ganiats TG. *Cost-effectiveness in health and medicine*. Oxford University Press; 2016.
179. Borre ED, Diab MM, Ayer A, et al. Evidence gaps in economic analyses of hearing healthcare: a systematic review. *EClinicalMedicine*. 2021;35:100872.
180. Vemer P, Ramos IC, Van Voorn G, Al M, Feenstra T. AdViSHE: a validation-assessment tool of health-economic models for decision makers and model users. *Pharmacoeconomics*. 2016;34(4):349-361.
181. Arias E, Xu JQ. United States life tables, 2018. National Vital Statistics Reports; vol 69, no 12. Hyattsville, MD: National Center for Health Statistics. 2020.
182. Homans NC, Metselaar RM, Dingemans JG, et al. Prevalence of age-related hearing loss, including sex differences, in older adults in a large cohort study. *The Laryngoscope*. 2017;127(3):725-730.
183. Cruickshanks KJ, Wiley TL, Tweed TS, et al. Prevalence of hearing loss in older adults in Beaver Dam, Wisconsin: the epidemiology of hearing loss study. *American journal of epidemiology*. 1998;148(9):879-886.

184. Van Naarden K, Decouflé P, Caldwell K. Prevalence and characteristics of children with serious hearing impairment in metropolitan Atlanta, 1991–1993. *Pediatrics*. 1999;103(3):570-575.
185. Rodenburg-Vlot MB, Ruytjens L, Oostenbrink R, Goedegebure A, van der Schroeff MP. Systematic Review: Incidence and Course of Hearing Loss Caused by Bacterial Meningitis: In Search of an Optimal Timed Audiological Follow-up. *Otol Neurotol*. Jan 2016;37(1):1-8. doi:10.1097/mao.0000000000000922
186. Bertolini P, Lassalle M, Mercier G, et al. Platinum compound-related ototoxicity in children: long-term follow-up reveals continuous worsening of hearing loss. *Journal of pediatric hematology/oncology*. 2004;26(10):649-655.
187. Lee F-S, Matthews LJ, Dubno JR, Mills JH. Longitudinal study of pure-tone thresholds in older persons. *Ear and Hearing*. 2005;26(1):1-11.
188. Monasta L, Ronfani L, Marchetti F, et al. Burden of disease caused by otitis media: systematic review and global estimates. *PLoS one*. 2012;7(4):e36226.
189. Rosenfeld RM, Kay D. Natural history of untreated otitis media. *The Laryngoscope*. 2003;113(10):1645-1657.
190. Rosenfeld RM, Shin JJ, Schwartz SR, et al. Clinical practice guideline: otitis media with effusion (update). *Otolaryngology–Head and Neck Surgery*. 2016;154(1\_suppl):S1-S41.
191. Tos M. Epidemiology and natural history of secretory otitis. *Am J Otol*. Oct 1984;5(6):459-62.
192. Avnstorp MB, Homøe P, Bjerregaard P, Jensen RG. Chronic suppurative otitis media, middle ear pathology and corresponding hearing loss in a cohort of Greenlandic children. *International journal of pediatric otorhinolaryngology*. 2016;83:148-153.
193. Aarhus L, Tambs K, Kvestad E, Engdahl B. Childhood otitis media: a cohort study with 30-year follow-up of hearing (the HUNT study). *Ear and hearing*. 2015;36(3):302.

194. Zhang L, Links AR, Boss EF, White A, Walsh J. Identification of potential barriers to timely access to pediatric hearing aids. *JAMA Otolaryngology–Head & Neck Surgery*. 2020;146(1):13-19.
195. Walker EA, McCreery RW, Spratford M, et al. Trends and predictors of longitudinal hearing aid use for children who are hard of hearing. *Ear and Hearing*. 2015;36(0 1):38S.
196. Lipschitz N, Kohlberg GD, Scott M, Smith MM, Greinwald Jr JH. Socioeconomic Disparities in Pediatric Single-Sided Deafness. *Otolaryngology–Head and Neck Surgery*. 2020;163(4):829-834.
197. Takahashi G, Martinez CD, Beamer S, et al. Subjective measures of hearing aid benefit and satisfaction in the NIDCD/VA follow-up study. *Journal of the American Academy of Audiology*. 2007;18(4):323-349.
198. Kochkin S, Beck DL, Christensen LA, et al. MarkeTrak VIII: The impact of the hearing healthcare professional on hearing aid user success. *Hearing Review*. 2010;17(4):12-34.
199. American Cochlear Implant Alliance. Cochlear Implants. Accessed 17 February 2022 at <https://www.acialliance.org/page/CochlearImplant>.
200. Howie VM, Ploussard JH, Sloyer J. The otitis-prone condition. *American Journal of Diseases of Children*. 1975;129(6):676-678.
201. Bluestone CD, Klein JO. *Otitis media in infants and children*. PMPH-USA; 2007.
202. National Collaborating Centre for Women’s and Children’s Health Surgical management of otitis media with effusion in children. National Institute for Health and Clinical Excellence 2008. Accessed 13 July 2021 at <https://www.nice.org.uk/guidance/cg60/documents/cg60-surgical-management-of-ome-full-guideline2>.
203. ZIELHUIS GA, RACH GH, VAN DEN BROEK P. The occurrence of otitis media with effusion in Dutch pre-school children. *Clinical Otolaryngology & Allied Sciences*. 1990;15(2):147-153.

204. Kogan MD, Overpeck MD, Hoffman HJ, Casselbrant ML. Factors associated with tympanostomy tube insertion among preschool-aged children in the United States. *American Journal of Public Health*. 2000;90(2):245.
205. Browning GG, Rovers MM, Williamson I, Lous J, Burton MJ. Grommets (ventilation tubes) for hearing loss associated with otitis media with effusion in children. *Cochrane Database Syst Rev*. Oct 6 2010;(10):Cd001801. doi:10.1002/14651858.CD001801.pub3
206. Acuin, J. Chronic suppurative otitis media: burden of illness and management options. Geneva: World Health Organization, 2004.
207. Quaranta N, Besozzi G, Fallacara RA, Quaranta A. Air and bone conduction change after stapedotomy and partial stapedectomy for otosclerosis. *Otolaryngology-Head and Neck Surgery*. 2005;133(1):116-120.
208. Semenov YR, Yeh ST, Seshamani M, et al. Age-dependent cost-utility of pediatric cochlear implantation. *Ear and hearing*. Jul-Aug 2013;34(4):402-412. doi:10.1097/AUD.0b013e3182772c66
209. Contrera KJ, Choi JS, Blake CR, Betz JF, Niparko JK, Lin FR. Rates of long-term cochlear implant use in children. *Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology*. 2014;35(3):426-430. doi:10.1097/MAO.0000000000000243
210. Raine CH, Summerfield Q, Strachan DR, Martin JM, Totten C. The cost and analysis of nonuse of cochlear implants. *Otology & Neurotology*. 2008;29(2):221-224.
211. Fitzpatrick EM, Durieux-Smith A, Whittingham J. Clinical practice for children with mild bilateral and unilateral hearing loss. *Ear and hearing*. 2010;31(3):392-400.
212. Marttila TI, Karikoski JO. Hearing aid use in Finnish children—impact of hearing loss variables and detection delay. *International journal of pediatric otorhinolaryngology*. 2006;70(3):475-480.
213. Sorkin DL. Cochlear implantation in the world's largest medical device market: utilization and awareness of cochlear implants in the United States. *Cochlear Implants International*. 2013;14(sup1):S12-S4.

214. Reddy KP, Bulteel AJ, Levy DE, et al. Novel microsimulation model of tobacco use behaviours and outcomes: calibration and validation in a US population. *BMJ Open*. 2020;10(5):e032579.
215. Vanni T, Karnon J, Madan J, et al. Calibrating models in economic evaluation. *Pharmacoeconomics*. 2011;29(1):35-49.
216. Morrell CH, Gordon-Salant S, Pearson JD, Brant LJ, Fozard JL. Age-and gender-specific reference ranges for hearing level and longitudinal changes in hearing level. *The Journal of the Acoustical Society of America*. 1996;100(4):1949-1967.
217. Claxton KP, Sculpher MJ. Using value of information analysis to prioritise health research. *Pharmacoeconomics*. 2006;24(11):1055-1068.
218. Global effects of hearing loss on human productivity. PROSPERO: International prospective register of systematic reviews. 2021. CRD42021225790. Accessed 19 July 2021 at [https://www.crd.york.ac.uk/prospERO/display\\_record.php?RecordID=225790](https://www.crd.york.ac.uk/prospERO/display_record.php?RecordID=225790).
219. Hearing Loss Untreated and Treated Health State Utilities. PROSPERO: International prospective register of systematic reviews. 2021. CRD42021253314. Accessed 19 July 2021 at [https://www.crd.york.ac.uk/prospERO/display\\_record.php?RecordID=253314](https://www.crd.york.ac.uk/prospERO/display_record.php?RecordID=253314).
220. Da Costa SS, Rosito LPS, Dornelles C. Sensorineural hearing loss in patients with chronic otitis media. *European Archives of Oto-Rhino-Laryngology*. 2009;266(2):221-224.
221. Mosnier I, Bebear J-P, Marx M, et al. Improvement of cognitive function after cochlear implantation in elderly patients. *JAMA Otolaryngology–Head & Neck Surgery*. 2015;141(5):442-450.
222. Amieva H, Ouvrard C, Giulioli C, Meillon C, Rullier L, Dartigues JF. Self-reported hearing loss, hearing aids, and cognitive decline in elderly adults: A 25-year study. *Journal of the American Geriatrics Society*. 2015;63(10):2099-2104.
223. Barnett M, Hixon B, Okwiri N, et al. Factors involved in access and utilization of adult hearing healthcare: a systematic review. *The Laryngoscope*. 2017;127(5):1187-1194.

224. Brodie A, Smith B, Ray J. The impact of rehabilitation on quality of life after hearing loss: a systematic review. *European Archives of Oto-Rhino-Laryngology*. 2018;275(10):2435-2440.
225. Yang EL, Macy TM, Wang KH, Durr ML. Economic and demographic characteristics of cerumen extraction claims to medicare. *JAMA Otolaryngology–Head & Neck Surgery*. 2016;142(2):157-161.
226. Otitis Media in Early Childhood: An NIDCD Virtual Workshop. National Institute on Deafness and Other Communication Disorders 2020. Accessed 19 July 2021 at <https://www.nidcd.nih.gov/workshops/2020/summary>.
227. Chan S, Hixon B, Adkins M, Shinn JB, Bush ML. Rurality and determinants of hearing healthcare in adult hearing aid recipients. *The Laryngoscope*. 2017;127(10):2362-2367.
228. Nieman CL, Marrone N, Szanton SL, Thorpe Jr RJ, Lin FR. Racial/ethnic and socioeconomic disparities in hearing health care among older Americans. *Journal of aging and health*. 2016;28(1):68-94.
229. Serchen J, Doherty R, Atiq O, Hilden D. Racism and health in the United States: a policy statement from the American College of Physicians. *Annals of Internal Medicine*. 2020;173(7):556-557.
230. Haile LM, Kamenov K, Briant PS, et al. Hearing loss prevalence and years lived with disability, 1990–2019: findings from the Global Burden of Disease Study 2019. *The Lancet*. 2021;397(10278):996-1009.
231. Lin FR, Thorpe R, Gordon-Salant S, Ferrucci L. Hearing loss prevalence and risk factors among older adults in the United States. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences*. 2011;66(5):582-590.
232. Bainbridge KE, Wallhagen MI. Hearing loss in an aging American population: extent, impact, and management. *Annual review of public health*. 2014;35:139-152.
233. Gopinath B, McMahon CM, Burlutsky G, Mitchell P. Hearing and vision impairment and the 5-year incidence of falls in older adults. *Age and ageing*. 2016;45(3):409-414.

234. Kamil RJ, Betz J, Powers BB, et al. Association of hearing impairment with incident frailty and falls in older adults. *Journal of aging and health*. 2016;28(4):644-660.
235. Lin FR, Ferrucci L. Hearing loss and falls among older adults in the United States. *Archives of internal medicine*. 2012;172(4):369-371.
236. Deal JA, Reed NS, Kravetz AD, et al. Incident Hearing Loss and Comorbidity: A Longitudinal Administrative Claims Study. *JAMA Otolaryngol Head Neck Surg*. Jan 1 2019;145(1):36-43. doi:10.1001/jamaoto.2018.2876
237. Lin FR, Metter EJ, O'Brien RJ, Resnick SM, Zonderman AB, Ferrucci L. Hearing loss and incident dementia. *Arch Neurol*. Feb 2011;68(2):214-20. doi:10.1001/archneurol.2010.362
238. Shukla A, Nieman CL, Price C, Harper M, Lin FR, Reed NS. Impact of hearing loss on patient-provider communication among hospitalized patients: a systematic review. *Am J Med Qual*. May/June 2019;34(3):284-292. doi:10.1177/1062860618798926
239. Folmer RL, Saunders GH, Vachhani JJ, et al. Hearing health care utilization following automated hearing screening. *Journal of the American Academy of Audiology*. 2021;
240. Zazove P, Plegue MA, McKee MM, et al. Effective hearing loss screening in primary care: the early auditory referral-primary care study. *The Annals of Family Medicine*. 2020;18(6):520-527.
241. American Speech-Language-Hearing Association. Preferred practice patterns for the profession of audiology. Rockville, MD: ASHA National Office; 2006. Accessed 17 February 2022 at <https://www.asha.org/policy/pp2006-00274/>.
242. Yueh B, Shekelle P. Quality indicators for the care of hearing loss in vulnerable elders. *J Am Geriatr Soc*. 2007;55(Suppl 2):S335-9.
243. Krist AH, Davidson KW, Mangione CM, et al. Screening for hearing loss in older adults: US Preventive Services Task Force recommendation statement. *JAMA*. 2021;325(12):1196-1201.

244. Feltner C, Wallace IF, Kistler CE, Coker-Schwimmer M, Jonas DE. Screening for hearing loss in older adults: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. 2021;325(12):1202-1215.
245. Borre ED, Myers ER, Dubno JR, et al. Development and validation of DeciBHAL-US: A novel microsimulation model of hearing loss across the lifespan in the United States. *EClinicalMedicine*. 2022;44:101268.
246. Neumann PJ, Cohen JT, Weinstein MC. Updating cost-effectiveness—the curious resilience of the \$50,000-per-QALY threshold. *N Engl J Med*. 2014;371(9):796-797.
247. Vanness DJ, Lomas J, Ahn H. A health opportunity cost threshold for cost-effectiveness analysis in the United States. *Annals of internal medicine*. 2021;174(1):25-32.
248. Husereau D, Drummond M, Petrou S, et al. Consolidated health economic evaluation reporting standards (CHEERS)—explanation and elaboration: a report of the ISPOR health economic evaluation publication guidelines good reporting practices task force. *Value in health*. 2013;16(2):231-250.
249. Centers for Medicare & Medicaid Services. Cochlear Implantation. Accessed 17 February 2022 at <https://www.cms.gov/Medicare/Coverage/Coverage-with-Evidence-Development/Cochlear-Implantation->.
250. Borre ED, Kaalund K, Frisco N, Zhang G, Ayer A, Kelly-Hedrick M, Reed SD, Emmett SD, Francis HW, Tucci DL, Wilson BW, Kosinski A, Ogbuoji O, Sanders Schmidler GD. The impact of hearing loss and its treatment on health-related quality of life utility: a systematic review and meta-analysis. Under Review.
251. Grutters JP, Joore MA, van der Horst F, Verschuure H, Dreschler WA, Anteunis LJ. Choosing between measures: comparison of EQ-5D, HUI2 and HUI3 in persons with hearing complaints. *Quality of Life Research*. 2007;16(8):1439-1449.
252. Kaur P, Chong SL, Kannapiran P, et al. Cost-utility analysis of hearing aid device for older adults in the community: a delayed start study. *BMC health services research*. 2020;20(1):1-11.
253. Liu C-F, Collins MP, Souza PE, Yueh B. Long-term cost-effectiveness of screening strategies for hearing loss. *Journal of Rehabilitation Research & Development*. 2011;48(3)

254. Hojjat H, Svider PF, Davoodian P, et al. To image or not to image? A cost-effectiveness analysis of MRI for patients with asymmetric sensorineural hearing loss. *The Laryngoscope*. 2017;127(4):939-944.
255. Gillard DM, Harris JP. Cost-effectiveness of stapedectomy vs hearing aids in the treatment of otosclerosis. *JAMA Otolaryngology–Head & Neck Surgery*. 2020;146(1):42-48.
256. Chao T-K, Chen TH-H. Cost-effectiveness of hearing aids in the hearing-impaired elderly: a probabilistic approach. *Otology & Neurotology*. 2008;29(6):776-783.
257. Zobay O, Dillard LK, Naylor G, Saunders GH. A measure of long-term hearing-aid use persistence based on battery re-ordering data. *Ear and hearing*. 2021;
258. Wyatt JR, Niparko JK, Rothman M, DeLissovoy G. Cost utility of the multichannel cochlear implant in 258 profoundly deaf individuals. *The Laryngoscope*. 1996;106(7):816-821.
259. Salomon JA, Haagsma JA, Davis A, et al. Disability weights for the Global Burden of Disease 2013 study. *The Lancet Global Health*. 2015;3(11):e712-e723.
260. Schousboe JT, Sprague BL, Abraham L, et al. Cost-effectiveness of screening mammography beyond age 75 years: a cost-effectiveness analysis. *Annals of internal medicine*. 2022;175(1):11-19.
261. Morris A, Lutman M, Cook A, Turner D. An economic evaluation of screening 60-to 70-year-old adults for hearing loss. *Journal of Public Health*. 2013;35(1):139-146.
262. Linszen AM, Anteunis LJ, Joore MA. The cost-effectiveness of different hearing screening strategies for 50-to 70-year-old adults: a Markov model. *Value in Health*. 2015;18(5):560-569.
263. Bettger JP, Dolor RJ, Witsell DL, et al. Comparative implementation-effectiveness of three strategies to perform hearing screening among older adults in primary care clinics: study design and protocol. *BMC Geriatrics*. 2020;20:1-10.
264. Khan KM, Bielko SL, Barnes PA, Evans SS, Main AL. Feasibility of a low-cost hearing screening in rural Indiana. *BMC public health*. 2017;17(1):1-9.

265. Saunders G, Frederick M, Silverman S, Arnold M, Chisolm T. Community-based hearing screening: pros, cons, and lessons learned. *Innovation in Aging*. 2018;2(Suppl 1):360.
266. Saunders GH, Frederick MT, Silverman SC, et al. Hearing screening in the community. *Journal of the American Academy of Audiology*. 2019;30(02):145-152.
267. Mahomed-Asmail F, Swanepoel DW, Eikelboom RH, Myburgh HC, Hall J. Clinical validity of hearScreen™ smartphone hearing screening for school children. *Ear and hearing*. 2016;37(1):e11-e17.
268. United States Senate. Over-the-Counter Hearing Aid Act of 2017. Accessed 17 February 2022 at <https://www.congress.gov/bill/115th-congress/senate-bill/670>.
269. Kirchner DB, Evenson E, Dobie RA, et al. Occupational noise-induced hearing loss: ACOEM task force on occupational hearing loss. *Journal of occupational and environmental medicine*. 2012;54(1):106-108.
270. Lakdawalla DN, Doshi JA, Garrison Jr LP, Phelps CE, Basu A, Danzon PM. Defining elements of value in health care—a health economics approach: an ISPOR Special Task Force report [3]. *Value in Health*. 2018;21(2):131-139.
271. Emmett SD, Francis HW. The socioeconomic impact of hearing loss in US adults. *Otology & Neurotology*. 2015;36(3):545-50.
272. Yueh B, Piccirillo JF. Screening for Hearing Loss in Older Adults: Insufficient Evidence Does Not Mean Insufficient Benefit. *JAMA*. 2021;325(12):1162-1163.
273. O'Hagan A, McCabe C, Akehurst R, et al. Incorporation of uncertainty in health economic modelling studies. *Pharmacoeconomics*. 2005;23(6):529-536.
274. Rothery C, Strong M, Koffijberg HE, et al. Value of information analytical methods: report 2 of the ISPOR Value of information analysis emerging good practices task force. *Value in Health*. 2020;23(3):277-286.
275. Briggs AH, Weinstein MC, Fenwick EA, et al. Model parameter estimation and uncertainty: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force-6. *Value in Health*. 2012;15(6):835-842.

276. Briggs A, Sculpher M, Claxton K. *Decision modelling for health economic evaluation*. Oxford University Press; 2006.
277. Cruickshanks KJ, Tweed TS, Wiley TL, et al. The 5-year incidence and progression of hearing loss: the epidemiology of hearing loss study. *Archives of Otolaryngology–Head & Neck Surgery*. 2003;129(10):1041-1046.
278. National Institutes of Health. NIH RePORTER. Accessed 23 February 2022 at <https://reporter.nih.gov/search/Izy1bocxy0uRzLeRaBUzaA/projects>.
279. National Institute on Deafness and Other Communication Disorders. FY 2021 Congressional Justification. Accessed 23 February 2022 at <https://www.nidcd.nih.gov/sites/default/files/Documents/FY-2021-NIDCD-CJ.pdf>.
280. Ades A, Lu G, Claxton K. Expected value of sample information calculations in medical decision modeling. *Medical decision making*. 2004;24(2):207-227.
281. Heath A. Calculating Expected Value of Sample Information Adjusting for Imperfect Implementation. *Medical Decision Making*. 2022:0272989X211073098.
282. Heath A, Kunst N, Jackson C, et al. Calculating the expected value of sample information in practice: considerations from 3 case studies. *Medical Decision Making*. 2020;40(3):314-326.
283. Cookson R, Mirelman AJ, Griffin S, et al. Using cost-effectiveness analysis to address health equity concerns. *Value in Health*. 2017;20(2):206-212.
284. US Census Bureau. Projected 5-Year Age Groups and Sex Composition: Main Projections Series for the United States, 2017-2060. U.S. Census Bureau, Population Division: Washington, DC. Accessed 25 January 2022 at from: <https://www.census.gov/data/tables/2017/demo/popproj/2017-summary-tables.html>.
285. Nassiri AM, Ricketts TA, Carlson ML. Current Estimate of Hearing Aid Utilization in the United States. *Otology & Neurotology Open*. 2021;1(1):e001.
286. Vicent MA, Borre ED, Swoap SJ. Central activation of the A1 adenosine receptor in fed mice recapitulates only some of the attributes of daily torpor. *Journal of Comparative Physiology B*. 2017;187(5):835-845.

287. Walensky RP, Borre ED, Bekker L-G, et al. Do less harm: evaluating HIV programmatic alternatives in response to cutbacks in foreign aid. *Annals of internal medicine*. 2017;167(9):618-629.
288. Walensky RP, Borre ED, Bekker L-G, et al. The anticipated clinical and economic effects of 90–90–90 in South Africa. *Annals of internal medicine*. 2016;165(5):325-333.
289. Freedberg KA, Kumarasamy N, Borre ED, et al. Clinical Benefits and Cost-Effectiveness of Laboratory Monitoring Strategies to Guide Antiretroviral Treatment Switching in India. *AIDS research and human retroviruses*. 2018;34(6):486-497.
290. Ouattara EN, MacLean RL, Danel C, et al. Cost-effectiveness and budget impact of immediate antiretroviral therapy initiation for treatment of HIV infection in Côte d’Ivoire: A model-based analysis. *PloS one*. 2019;14(6):e0219068.
291. Borre ED, Hyle EP, Paltiel AD, et al. The clinical and economic impact of attaining national HIV/AIDS strategy treatment targets in the United States. *The Journal of infectious diseases*. 2017;216(7):798-807.
292. Losina E, Hyle EP, Borre ED, et al. Projecting 10-year, 20-year, and Lifetime Risks of Cardiovascular Disease in Persons Living With Human Immunodeficiency Virus in the United States. *Clin Infect Dis*. Oct 15 2017;65(8):1266-1271. doi:10.1093/cid/cix547
293. Borre ED, Goode A, Raitz G, et al. Predicting thromboembolic and bleeding event risk in patients with non-valvular atrial fibrillation: a systematic review. *Thrombosis and haemostasis*. 2018;118(12):2171-2187.
294. Lowenstern A, Al-Khatib SM, Sharan L, et al. Interventions for preventing thromboembolic events in patients with atrial fibrillation: a systematic review. *Annals of internal medicine*. 2018;169(11):774-787.

## Biography

Ethan Borre graduated from Williams College, magna cum laude, with honors in Biology and Music in 2015. His honors thesis in biology, investigating the role of A1 adenosine receptors in torpor, resulted in a co-first author publication in the *Journal of Comparative Physiology B*.<sup>286</sup>

After graduation, he joined the Medical Practice Evaluation Center of Massachusetts General Hospital where he assessed the effectiveness and cost-effectiveness of alternative HIV prevention, diagnosis, and treatment policies using a policy simulation model. During this time, he authored several manuscripts advancing global HIV health policy under the mentorship of Drs. Rochelle Walensky and Ken Freedberg. Two studies published in *Annals of Internal Medicine* considered the significant benefits of HIV scale-up, and the potential harms of HIV funding budgetary cuts, in South Africa and Côte d'Ivoire.<sup>287,288</sup> The study of the potential benefits of HIV scale-up was presented at the United Nations and featured in the National Institutes of Health Director's Blog and *New England Journal of Medicine* JWatch. Two additional global health analyses investigated the most cost-effective HIV laboratory monitoring strategy in India and the cost-effectiveness of immediate antiretroviral therapy initiation in Côte d'Ivoire.<sup>289,290</sup>

Domestically, Ethan led an analysis projecting the clinical and economic effects of achieving United States HIV treatment goals, and in particular for vulnerable

populations. This analysis was published in the *Journal of Infectious Diseases* and found that increased investments in HIV treatment for Black men who have sex with men were especially cost-effective.<sup>291</sup> This work was cited in the Department of Health and Human Services National HIV/AIDS Strategy 2017 strategic update, selected as an editor's choice article in the *Journal of Infectious Diseases*, and featured in the *New England Journal of Medicine* JWatch. Lastly, Ethan co-authored an analysis investigating the lifetime risks of cardiovascular disease among persons living with HIV in the United States published in *Clinical Infectious Diseases*, finding significantly increased risk of cardiovascular disease in this population given increases in survival due to antiretroviral therapy.<sup>292</sup> Ethan left this experience determined to impact global health policy as a physician investigator using decision science methods.

After his tenure at MGH, Ethan matriculated into the MD/PhD program at Duke University in the Summer of 2017. He soon began working with Dr. Gillian Sanders Schmidler and the Evidence Synthesis Group on an Agency for Healthcare Research and Quality systematic review investigating the predictive validity of risk prediction calculations for stroke and bleeding risk for persons with atrial fibrillation, and the comparative effectiveness of atrial fibrillation treatments. These efforts led to a first-authored publication in *Thrombosis and Haemostasis* and a co-authored publication in *Annals of Internal Medicine*.<sup>293,294</sup> This work helped impact clinical practice and health policy by identifying the most valid risk prediction tools, and was featured in *European*

*Heart Journal* Year in Cardiology Review, and was cited by the 2020 European Society of Cardiology Guidelines for atrial fibrillation.

Upon initiation of his PhD program, Ethan soon identified the care of older adults as an area of research interest. Ethan's scholarship led to his selection as a Margolis Scholar in Health Policy at Duke University. He applied for and was awarded a Ruth L. Kirschstein F30 dissertation research award from the National Institute on Deafness and Other Communication Disorders to support research around adult hearing screening in the United States. This research forms the basis for the current Dissertation. He led a systematic review of model-based cost-effectiveness analyses in hearing healthcare and developed and validated a decision model of hearing loss prevention, natural history, diagnosis, and treatment in the United States, both published in *eClinicalMedicine*.<sup>179,245</sup> In 2020, Ethan was a finalist for the Lusted prize for best student Abstract and in 2021 won the Milt Weinstein Award for Outstanding Presentation in Applied Health Economic by the Society for Medical Decision Making. Ethan's long-term career goal is become an independent academic physician scientist, using decision science to enhance the provision and value of chronic disease care to aging populations. He plans to apply for a residency in internal medicine after completion of his MD and PhD degrees.