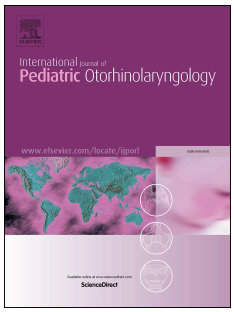
Accepted Manuscript



The Impact of Permanent Early-Onset Unilateral Hearing Impairment in Children – A Systematic Review

Kerttu Huttunen, Elsa Erixon, Ulrika Löfkvist, Elina Mäki-Torkko

PII: S0165-5876(19)30094-1

DOI: https://doi.org/10.1016/j.ijporl.2019.02.029

Reference: PEDOT 9396

To appear in: *International Journal of Pediatric Otorhinolaryngology*

Received Date: 20 October 2018

Revised Date: 13 February 2019

Accepted Date: 14 February 2019

Please cite this article as: K. Huttunen, E. Erixon, U. Löfkvist, E. Mäki-Torkko, The Impact of Permanent Early-Onset Unilateral Hearing Impairment in Children – A Systematic Review, *International Journal of Pediatric Otorhinolaryngology*, https://doi.org/10.1016/j.ijporl.2019.02.029.

The Impact of Permanent Early-Onset Unilateral Hearing Impairment in Children – A Systematic Review

Kerttu Huttunen, [a,b,c,d] *Elsa Erixon,* [e] *Ulrika Löfkvist* [f,g] *and Elina Mäki-Torkko* [h,i]

[a]Faculty of Humanities, Logopedics, and Child Language Research Center, University of Oulu, Finland;
[b]PEDEGO Research Unit, University of Oulu, Finland;
[c]MRC Oulu, Oulu, Finland;
[d]Oulu University Hospital, Department of Otorhinolaryngology, Head and Neck Surgery, Oulu, Finland;
[e]Uppsala University, Department of Surgical Sciences, Section of Otorhinolaryngology and Head and Neck Surgery, Uppsala, Sweden;
[f]University of Oslo, Department of Special Needs Education, Oslo, Norway;
[g]Karolinska Institute, Department of Clinical Science, Intervention and Technology, Stockholm, Sweden;
[h]Örebro University, School of Medical Sciences, Örebro, Sweden;
[i]Örebro University Hospital, Audiological Research Center, Örebro, Sweden

Short title: Impact of unilateral hearing impairment

Foot: Huttunen et al.

Address correspondence to:
Kerttu Huttunen, Faculty of Humanities, Logopedics, University of Oulu, P.O. Box 1000, FI-90014 Oulun yliopisto, Finland. Tel. +358 50 477 6610
Email: kerttu.huttunen@oulu.fi

Elsa Erixon, Akademiska sjukhuset, ing 78–79, SE-751 85 Uppsala, Sweden. Email: elsa.erixon@akademiska.se

Ulrika Löfkvist, University of Oslo, Faculty of Education, Department of Special Needs Education, P.O. Box 1140 Blindern, N-0318 Oslo, Norway. Email: ulrika.lofkvist@isp.uio.no

Elina Mäki-Torkko, Örebro University Hospital, Audiological Research Center, SE-701 85 Örebro, Sweden. Email: elina.maki-torkko@oru.se

ABSTRACT

Background: Decision-making on treatment and (re)habilitation needs to be based on clinical expertise and scientific evidence. Research evidence for the impact of permanent unilateral hearing impairment (UHI) on children's development has been mixed and, in some of the reports, based on fairly small, heterogeneous samples. Additionally, treatment provided has been highly variable, ranging from no action taken or watchful waiting up to single-sided cochlear implantation. Published information about the effects of treatment has also been heterogeneous. Moreover, earlier reviews and meta-analyses published on the impact of UHI on children's development have generally focused on select areas of development.

Objectives: This systematic review aimed to summarize the impact of children's congenital or early onset unilateral hearing impairment on listening and auditory skills, communication, speech and language development, cognitive development, educational achievements, psycho-social development, and quality of life.

Methods: Literature searches were performed to identify reports published from inception to February 16th, 2018 with the main electronic bibliographic databases in medicine, psychology, education, and speech and hearing sciences as the data sources. PubMed, CINALH, ERIC, LLBA, PsychINFO, and ISI Web of Science were searched for unilateral hearing impairment with its synonyms and consequences of congenital or early onset unilateral hearing impairment. Eligible were articles written in English, German, or Swedish on permanent unilateral hearing impairments that are congenital or with onset before three years of age. Hearing impairment had to be of at least a moderate degree with PTA ≥ 40 dB averaged over frequencies 0.5 to 2 or 0.5 to 4 kHz, hearing in the contralateral ear had to have $PTA_{0.5\text{-}2\ kHz}$ or $PTA_{0.5\text{-}4\ kHz}$ ≤ 20 dB, and consequences of unilateral hearing impairment needed to be reported in an unanimously defined population in at least one of the areas the review focused on.

Four researchers independently screened 1,618 abstracts and 566 full-text articles for evaluation of study eligibility. Eligible full-text articles were then reviewed to summarize the results and assess the quality of evidence. Additionally, data from 13 eligible case and multi-case studies, each having less than 10 participants, were extracted to summarize their results.

Quality assessment of evidence was made adapting the Grades of Recommendations, Assessment, Development, and Evaluation (GRADE) process, and reporting of the results adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards.

Results: Three articles with the quality of evidence graded as very-low to low, fulfilled the eligibility criteria set. Due to the heterogeneity of the articles, only a descriptive summary could be generated from the results. Unilateral hearing impairment was reported to have a negative impact on preverbal vocalization of infants and on sound localization and speech perception both in quiet and in noise.

Conclusions: No high-quality studies of consequences of early-onset UHI in children were found. Inconsistency in assessing and reporting outcomes, the relatively small number of participants, low directness of evidence, and the potential risk of confounding factors in the reviewed studies prevented any definite conclusions. Further well-designed prospective research using larger samples is warranted on this topic.

Keywords:

Single-sided hearing impairment; single-sided hearing loss; single-sided deafness; speech; language; auditory behavior

1. INTRODUCTION

Unilateral hearing impairment (UHI) in children has gained increasing scientific and clinical interest. Growing research base is particularly welcome as we may currently lack strong enough evidence-base to advise clinicians in the treatment and habilitation of children with UHI.

As a part of counseling, one is advised to reduce or eliminate background noise when communicating with the child and, when needed, to speak close to the child on the side of the child's nonimpaired ear. Good acoustics in the learning environment has also been perceived to be very important but, traditionally, in most UHI cases, no hearing technology has been prescribed [1]. Treatment options have included hearing aid fitting in the impaired ear or use of contralateral routing of signal (CROS) or a FM system, surgery (in some of the cases of atresia and other malformations, or consequences of infections), or implantation (Baha device, middle ear implant, cochlear implant). Cochlear implantation has recently garnered increased interest as an option in the treatment of children's UHI [2-3]. However, particularly for invasive treatment options, there first needs to be clear understanding of the effects of UHI in children.

1.1 Definition of UHI

In UHI, a person has one ear with any degree of impaired hearing, while the other ear has normal hearing ability. According to the definition of a European Expert Group [4], hearing impairment (HI) is in question if a person's $PTA_{0.5–4\ kHz}$ exceeds 20 dB. Single-sided deafness (SSD) is a term used when a person has normal hearing in one ear and, in the other ear has sensorineural HI which cannot be helped with acoustic amplification. In asymmetric HI, according to one definition, both ears are affected with the difference in pure tone audiometry between the ears in at least two frequencies across the frequencies from 0.5 to 4 kHz exceeding 10 dB [4].

1.2 Prevalence of Permanent Early-Onset UHI

Prevalence figures of permanent congenital or early-onset UHI have varied depending on the sample size and type, research methods, and the definition of HI used. Including even the mildest cases of congenital UHI, figures of 0.1–0.2% have been reported [5-8]. Some studies have reported a slight to considerable male prominence in prevalence ([5, 9-10], and there was no considerable left/right prominence, at least in the congenital cases that were reported [9, 11]. Most of children's UHIs represent the sensorineural type of a mild-to-moderate degree with about 20% being conductive cases [6,12].

1.3 Etiology of Early-Onset UHI

Permanent UHI can present itself early (being pre- or perilingual) or late (being postlingual), with some cases being progressive. Unilateral hearing impairment related to, for instance, structural anomalies, such as atresia, is congenital, but can also present later, as is often seen, for example, in large vestibular aqueduct syndrome. In both uni- and bilateral HI, the etiology and, especially the onset of hearing HI, usually remains unknown in a large proportion of children. Although Mehta et al. (2016) [13] used a combination of clinical, laboratory, and genetic diagnostics, it was possible to identify the definite molecular genetic etiology of children's UHI in only about every fourth case referred to a genetic hearing loss clinic. In a study conducted before the introduction of molecular genetic diagnostics, the etiology of UHI remained unknown in 51% (n = 43) of 84 children [10]. Yet, in two later studies on children with UHI, in 61% (n = 19) of 31 children [14] and 52% (n = 176) of 337 children [15], the etiology remained unknown.

Malformations, most often without any existing syndrome (see, e.g., [6]), are a common cause of UHI. Based on a retrospective database review at a clinic specialized to genetic hearing loss, inner ear malformations were found in 73 of 150 children with sensorineural UHI [13]. In a recent study [6] of 108 cases of UHI, atresia, ossicular malformations, and inner ear malformations (enlarged vestibular aqueduct and Mondini malformation) were reported to constitute the most common cause (29%), while the second most common was genetically related (7%). Absent cochlear nerve and cochlear nerve anomalies are common causes of permanent congenital sensorineural UHI [13, 16-17]. Most of atresia cases are known to be unilateral. Korres et al. [18] found unilateral atresia of the external ear canal in up to 0.02% of newborns. Furthermore, congenital cytomegalovirus infection is a common cause of UHI (see, e.g., summary of Tharpe & Sladen 2008 [19]), and there is an increased risk of UHI in children born preterm, and newborns needing neonatal intensive care for other reasons (see, e.g., [12]).

1.4 Age at Identification

Before the era of systematic newborn hearing screening, detection of children's UHI was often an accidental finding (see, e.g., [20]) with ascertainment typically made at the age of five or six years [15,21-22] or at school-age [23], depending on the protocols used for hearing examinations. Universal newborn hearing screening (UNHS) has clearly lowered the detection age of children's HIs [15,24], with the age at ascertainment of HI in screened infants being similar between the uni- and bilateral cases ([9].

In the data of Fitzpatrick et al. (2017) [6], most of the UHI cases were congenital or with early-onset. Also, Ghogomu et al. [24], who combined UNHS with radiological imaging, suggested that, in most cases, children's UHI is congenital. However, there are several reasons why UHI is not necessarily identified early, even through UHNS. Passing of both ears is not required in all hospitals using neonatal hearing screening [25], mild impairments under 30 dB are not possible to

detect with otoacoustic emissions (OAE) [26], or screening protocols may aim to detect only moderate or more severe HIs. Detection of congenital UHI is also complicated by newborns' immature auditory system, which is reflected in the difficulty of interpreting the results of objective hearing examinations. HI can also present itself later in childhood or adolescence because of acquired causes and progressive sensorineural HIs.

1.5 Impact and habilitation of UHI

Compared to monaural listening, the advantages of binaural hearing are localization of sounds, better frequency selectivity, better discrimination ability both in quiet and especially in noise and reverberation, and better quality of sound (see, e.g., [27-28]). More specifically, studies on the physiology of hearing have shown that binaural hearing makes it possible or provides advantages for audibility, spatial hearing (and, as a part of it, sound localization), speech recognition in noise, head shadow effect, binaural squelch effect, and binaural summation [27,29-30]. Binaural hearing contributes to ease of listening and reduced need for attentional effort.

Unilateral hearing impairment is known to impair the ability to localize sounds and comprehend speech while listening in noise, particularly if the degree of HI is severe or profound (see, e.g., [31]. In adults with UHI, significant difficulty in hearing in noise, experiences of communication handicaps, exclusion, and difficulties with coping have been reported ([32]. However, evidence on children's speech and language outcomes has been more heterogeneous [33-35] and there is a need for a more comprehensive picture of the impact of UHI on a child's auditory and linguistic development, quality of life, and educational outcomes especially in the congenital and early acquired cases as the critical period for the anatomical and physiological maturation of the auditory brainstem takes place under the age of two years [36]. Schmithorst and colleagues [35], for example, suggest that in children monaural auditory input can have a global influence on the development of brain networks related to higher-order cognitive function by, for instance, missing multimodal interaction between secondary auditory and visual processing. This may have negative effects on spoken language processing.

Earlier, it was considered that UHI does not have such a negative impact on an individual's life that (re)habilitation should be provided. In the 1980s, Bess and colleagues (e.g., [37-38]) raised concerns about the impact of UHI on children's development. Their studies conducted in the 1980s and 1990s (e.g., [21,37-38]) have often been referred to when discussing the consequences of UHI. However, there are several issues to be considered when referring to these early studies. In these pioneer studies, the results of children with UHI and those with bilateral mild HI were combined. They were conducted before the implementation of UNHS. Thus, although the age at diagnosis was reported, it was not possible to verify the onset of UHI, which leaves a possibility for progressive cases in their data. Therefore, their studies may do not reflect the impact of early-onset UHI. Further, the process of recruiting children into those studies was not clearly reported, which causes a possible bias. Despite being much cited, the data of Bess and colleagues were

heterogeneous, and therefore difficult to interpret or use as the basis for selecting today's optimal treatment options for UHI.

Treatment should be based on the best available scientific evidence, clinical expertise, and patient preferences and goals [39]. Therefore, to be able to provide evidence-based practice, with quality care and (re)habilitation in audiology one needs to be aware of the possibilities and restrictions of the (re)habilitation options. Because CROS and bone-anchored hearing devices (Baha devices) are of limited benefit in most cases of sensorineural HI [40], cochlear implantation has recently garnered increased interest as one of the management options for both adults and children with UHI (see [40] for discussion, and [41] for review). However, invasive treatment always needs to be especially well-grounded.

1.6 Information from Reviews

Systematic reviews of current scientific evidence with a broad view of the consequences of UHI are needed because the need for treatment or (re)habilitation and information about the available effective methods are the basis for decisions taken in health care. Some recent systematic reviews are summarized in Table 1.

Table 1. Summary of three recent reviews or meta-analyses on children's UHI.

Authors, year, country, journal	Type of review	Main question/Aim	Inclusion criteria	Exclusion criteria	Databases searched	N of abstracts	N of articles included in the review	Results	Comment
Purcell et al. (2016) USA The Laryngoscope [42]	Systematic, including meta-analysis	Difference in IQ scores between children with UHL and children with normal hearing	Articles in English, journal peer-reviewed, observational study with a control group, children's age 2-18 years, permanent or longstanding UHI	Studies including children with cranio-facial anomalies	PubMed, CINAHL, Embase, PSYCINFO	N=261, n=26 full-text articles read	N=4	High quality studies suggest that there is a significant difference in full scale IQ and performance IQ between the groups.	Systematic review methodology used. Weaknesses of the review/meta-analysis performed discussed. Quality assessment based on the one used in another review [43]. No clear hearing criteria used in inclusion of the studies.
Appachi et al. (2017) USA Otolaryngol Head Neck Surg [44]	Systematic review	To characterize auditory outcomes of hearing rehabilitation options in UHI	Articles in English, concern humans, from inception until Jan 2016	Case reports	PubMed, Medline, Embase, CINAHL, Cochrane Library*	N=249, after title review n=144, n=39 full-text articles read	N=12	Overall moderate risk of bias in articles. Data evaluating functional and auditory outcomes following amplification in children with UHI are limited. In moderate to profound UHI most studies suggest improvement when using bone-conduction hearing aids. No conclusion could be	RoB assessed using the Newcastle Ottawa scale. Meta-analysis was not possible because of heterogeneity of the articles. Hearing measurements in UHI or normal ear not discussed.

								drawn regarding CROS hearing aids. In mild to moderate UHI: FM systems and conventional hearing aids seem to be of benefit.	
Anne et al. (2017) USA Otolaryngol Head Neck Surg ** [45]	Systematic review	To quantify the extent of the impact of UHL among children, with the use of objective measures of speech and language delay	Articles in English, concern humans, from inception until Jan 2016	Case reports	PubMed, Medline, Embase, CINAHL, Cochrane Library	N=429, n=139 abstracts read	N=13	Inferior speech and language performance (seven studies), no difference (four studies), and evaluation over time (two studies).	RoB assessed by the Newcastle Ottawa scale. Meta-analysis was not possible because of heterogeneity of the articles. Hearing measurements in UHI or normal ear not discussed, but the degree of UHL was described in a table.

* Three separate searches and the result of these was cross-referenced in order to find studies included in the review
** Same authors as in [44]
UHL = unilateral hearing loss

It is noteworthy that the scope of these three systematic reviews [42,44-45] was limited either to auditory outcomes of hearing rehabilitation or consequences of UHI to IQ or speech and language development of children. Further, in some reviews, articles were included in which not only UHI but also bilateral HI was covered. Measurement of participants' hearing in the reviewed articles was also not clearly described. This was the case especially regarding the ear considered to be nonimpaired and leaves the reader with uncertainty when it comes to the actual hearing ability of the target population of the articles. Namely, in many original articles it is common to combine the results on UHI of different degrees, mild bilateral HI, and UHI found only at high frequencies.

In addition to the systematic reviews or meta-analyses introduced in Table 1, other summaries on the effects of children's UHI or current state of management of UHI have also been recently published [46-53]. However, they represent more opinion papers or unstructured summaries because of severe shortcomings, including a very limited publishing time range of the original articles or a lack of description of any systematic methodology or review protocol used to search and review the articles. Moreover, in these summary articles a clear judgement on quality of the articles reviewed is only seldom available. Despite that, some (e.g. [52]) summary articles even include clinical recommendations for decision making. Therefore, to be able to advise clinicians on a sound basis, there is a need for wide-scale, carefully conducted systematic reviews on pediatric UHI with careful quality assessment of the articles included in the review.

The aim of this systematic review was to explore the reported impact of children's permanent UHI on children's: 1) auditory capabilities (hearing and listening), 2) communication and development of speech and language, 3) cognitive development, 4) school performance/educational achievements, and 5) psychosocial development (including quality of life).

2. MATERIALS AND METHODS

Data for this review were retrieved from published research, so no institutional review board approval was needed; however, the review project was registered in the PROSPERO (International prospective register of systematic reviews) [54] database). The method for conducting the review adheres to the Grades of Recommendations, Assessment, Development, and Evaluation (GRADE) process (e.g., [55-58]).

Reporting of the results adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards ([59]) and PRISMA for Abstracts ([60]). When necessary, the review and reporting processes were adapted because the above-mentioned systems for conducting and reporting systematic reviews were constructed for reviewing outcome studies, and our focus was on the impact of UHI.

2.1 Literature Search

In February 2017, an experienced librarian performed the first systematic literature searches on articles published up to the date of the search. The titles and abstracts were then screened, and eligible full-text articles were analyzed. Because making a systematic review is very time consuming and there are often delays in updating new articles into literature databases, a second, complementary search was later performed. It covered the period from January 2016 to February 16th, 2018. Again, the retrieved titles and abstracts were screened, and eligible full-text articles were analyzed. Together, the researchers and the librarian chose the search strategy, the target databases, and the search terms. Medical Subject Headings (MeSH) and predefined text terms were combined for the search strategy, which was implemented using the main electronic bibliographic databases in medicine, psychology, education and speech, language, and hearing sciences as data sources: PubMed, CINAHL, ERIC, LLBA, PsychINFO, and ISI Web of Science were included. Additionally, references of the eligible, reviewed, full-text articles and systematic reviews were manually searched to check that all relevant articles had been identified.

The search strategy used in the review comprised all types of research articles published in English, German, or Swedish in peer-reviewed scientific journals. The detailed search terms used and the syntax of the search strategy applied varied according to the features and structure of each database. The search strategy utilized for the PubMed database can be found in Supplementary Appendix A, as an example.

2.2 Eligibility Criteria for the Studies

UHIs of a moderate to profound degree ($PTA_{0.5–2\ kHz} \geq 40$ dB as the minimum frequency range, or $PTA_{0.5–4\ kHz} \geq 40$ dB) were included in the review. This restriction was set to prevent inclusion of studies on HIs that represent solely high frequencies, and because current OAE screening protocols may not identify infants with mild HIs [26,61]. In the child's contralateral ear, $PTA_{0.5–2\ kHz}$ as the minimum frequency range had to be ≤ 20 dB with the existence of contralateral ear's hearing assessment clearly mentioned. Additionally, a study was considered eligible if an infant's auditory brainstem response (ABR) threshold was worse than 30 dB in the impaired ear and 30 dB or better in the nonimpaired ear, or if OAE screening result in the nonimpaired ear was normal. The UHI had to be prelingual, meaning an onset before the age of three years, and it had to be permanent.

Both retrospective and prospective peer-reviewed studies were eligible to be included. Intervention studies were included if they contained preoperative or other kinds of pre-intervention data. For different study designs, even case reports and case series were included in the title and abstract screening phase, but, for the full-text articles to be reviewed, only studies containing 10 or more participants were accepted. Case and multi-case studies with fewer than 10 participants were searched only for qualitative analysis. Meta-analyses and systematic reviews were included to identify additional relevant references.

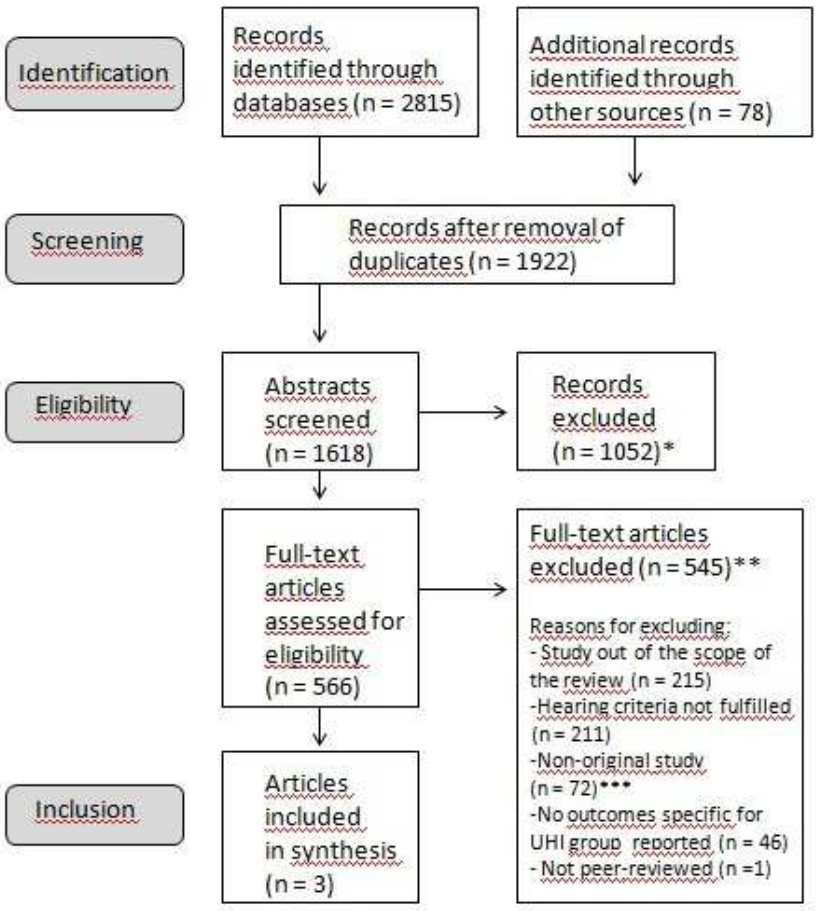
Of the inclusion criteria, consisting of participants, interventions, comparators, outcomes, and study design (PICOS), only participants, outcomes, and study design were used. The population in focus was children and adolescents but reports on adults who had had UHI since birth or early childhood (before three years of age) were also included in the literature searches. Articles on adults were accepted to obtain a view on the possible long-term impact of congenital UHI or early-onset UHI. Studies on animals and on simulated HIs, as well as those on tinnitus, were excluded from the material to be reviewed.

After the librarian had acquired all the abstracts, four reviewers (two physicians specialized in audiology and having experience in pediatric audiology, and two speech and language pathologists) independently, 1) selected the target articles based on titles and abstracts to be read in full-text form, 2) judged the appropriateness of the articles reviewed and quality of evidence, and 3) extracted the study characteristics and data from the articles meeting the inclusion criteria for synthesis on the impact of UHI.

2.3 Screening of the titles and abstracts

Upon screening the titles and the abstracts, a full-text article was admitted for review if at least one of the four authors suggested that it should be read. For narrative summary, case and multi-case studies with fewer than 10 participants were also searched in parallel with the articles eligible for GRADE analysis containing at least 10 participants. Discrepancies were resolved by discussion and ultimately mutual agreement.

A total of 2,815 records were identified through the searches from the six databases. After removing duplicates, the search resulted in 1,844 abstracts. Of these, 304 articles were studies on tinnitus or vestibular schwannoma which were removed because they were not within the scope of the review. An additional 78 titles were identified from references of the eligible, reviewed, full-text articles and, additionally, from systematic reviews; this resulted in 31 articles, of which none were eligible for the current review. The authors, therefore, reviewed a total of 1,618 abstracts, and 566 full-text articles were retrieved for eligibility (see Fig. 1).



*In addition to these, five articles were not found. **Additionally, descriptive summary was made on the data of 13 case and multi-case studies with less than 10 participants each. ***Non-original study = reviews, opinion papers and letters to the Editor.

Figure 1. Flow diagram of the study identification, eligibility of the articles and inclusion process.

When screening for eligibility, 215 (39%) of the articles were excluded because they were out of the scope of this review. Almost as many (n = 211) had to be excluded because hearing in the contralateral ear was not clearly reported, or it exceeded the normally hearing ear's criterion used in the present study. In many studies otherwise fitting the inclusion criteria of our review, information about children with UHI was not reported separately from other populations. There were often multiple reasons to exclude an article.

2.4 Judging the Quality of Evidence

The quality of evidence of the articles reviewed was judged, again independently, by the four researchers; results were coded using a table where the positive and negative features of a study were recorded. The quality judgment (certainty of evidence) was adapted from GRADE. In GRADE, the quality of evidence a research article provides is judged on a scale from from less than +1 (very low) to $\geq$ +4 (high). The GRADE score (see closer, e.g. [58]) is calculated by first awarding the

article four points and, if needed, then adding or deducting points if *type of evidence* (e.g., is it a question of a randomized controlled trial or e.g., observational study), *quality points* (such as sparse data, withdrawals, incomplete reporting of results), *consistency* (evidence of dose response, adjustment for confounders), *directness of evidence* (DoE; that is, risk of bias; use of co-interventions, generalizablity of results) and *effect size* based on relative risk and odds ratio are not reported, met at all or are not optimally met. Directness refers to the extent to which people and outcome measures are generalizable and similar to those of interest. Risk of bias (RoB) in, for example, selection bias, was assessed on the study level for the included articles based on PRISMA and GRADE, [59,62-63].

As in the screening phase, any discrepancies in the analyses were resolved by consensus. Each article passing the quality check was then reviewed by all four researchers for data extraction.

3. RESULTS

Three articles were identified, each including 10 or more children and fulfilling the inclusion criteria (Tables 2–4, see also Fig. 1). All were case series and contained observational data, proxy or self-assessment, or them all. In these studies, the number of participants for whom relevant outcome data could be extracted ranged from 19 to 57 of which 10 or more were children. These three studies dealt with the auditory consequences of UHI and preverbal development; no eligible articles were identified on cognitive development, educational achievements or psychosocial development (e.g., quality of life). Study and participant characteristics are presented in Tables 2 and 3. Due to the great variability of data, no quantitative summary was possible; only descriptive summary of the reported impacts of UHI could be made, as shown in Table 4.

TABLE 2. Characteristics of the studies reviewed

Author(s) (year)	**Method**				**Comment**
	Population	*Study design*		*Control group*	
Kishon-Rabin et al. (2015) [64]	Patient series	Prospective, matched controls	Cross-sectional	Yes	N = 331 controls with normal bilateral hearing
Kunst et al. (2007) [65]	Patient series	Prospective	Cross-sectional	No	Study design was prospective only regarding the effects of Baha
Priwin et al. (2007) [66]	Patient series	Prospective	Cross-sectional	No	

TABLE 3. Characteristics of participants with UHI in the studies reviewed

Author(s), (year), country		Participants			Characteristics of UHI				
	N	*Age (yrs)*	*Age at the time of the study (mean/ median)*	*Sex*	*Age at onset (yrs)*	*Ear*	*Etiology*	*Type of HI*	*Degree of HI*
Kishon-Rabin et al. (2015), Israel [64]	34	0.6–1	Median age 0.75–1 yrs	*	0	21 R 13 L	Varying	19 Sensorineural 13 Conductive 2 Mixed	Mild to profound**
Kunst et al. (2007), Netherlands [65]	19***	5–61 (n = 10 of the participants were 6–14 years old)	Mean age 8 yrs of the 10 children	*	0	14 R 5 L	Malformation	Conductive and mixed	Moderate-severe****
Priwin et al. (2007), Sweden [66]	57	3–80 (n = 8 of the participants were 3–10 years old, and n = 17 were 11–20 years old)	*****	43 M 14 F	0	34 R 23 L	Malformation	Conductive (but among the oldest subjects the inner ear function also was slightly to moderately impaired)	Bone conduction thresholds in the impaired ear: mean 15 dB (SD 12.8)

R = right ear, L = left ear, *Not reported, **Based on ABR, n = 2 classified as mild to moderate, ***One participant had to be excluded from the present review due to PTA exceeding 20 dB HL in the better ear, that is why N = 19 instead of 20, ****Max PTA ≥ 70 dB HL in five cases, *****Mean or median age not reported.

TABLE 4. Summary of findings in the three studies reviewed

Author(s) (year)	Research question(s) and outcome measure(s)	Statistical analysis	Main result
Kishon-Rabin et al. (2015) [64]	*The study explored the impact of UHI on early aural/oral communication skills of infants.* The Infant-Toddler Meaningful Auditory Integration Scale (IT-MAIS); 10 questions posed to the parents in an interview The Production of Infants Scale Evaluation (PRISE); parents were asked 11 questions in an interview	Fisher's exact test, McNemar's test, odds ratio, Cochran-Mantel-Haenszel statistics, Breslow-Day test, Pearson's rank correlation coefficient	In IT-MAIS, n = 7 (21%) of the children with UHI showed auditory performance below the normative range. In PRISE, n = 14 (41%) of the children with UHI showed preverbal vocalizations below the normative range. Presented as odds ratio, delayed auditory development was 3.86 times (95% CI, 1.42–10.48) and delayed preverbal vocalization 8.64 times (95% CI, 4.02–18.56) more common in infants with UHI compared to children with normal binaural hearing.
Kunst et al. (2007) [65]	*The study explored the audiologic outcome of Baha in patients with congenital unilateral conductive HI (aural atresia or ossicular chain anomaly).* Sound localization measurements in sound field Speech perception in quiet and in noise	Descriptives	Unaided word recognition score (n = 8 children): mean 51%. Sound localization (N = 9 children): in unaided condition, mean error 45 degrees, both at 500 Hz and at 3000 Hz.
Priwin et al. (2007) [66]	*The study explored hearing and self-assessed hearing problems in patients with congenital*	Clopper Pearson, linear regression	Speech recognition in quiet: mean 56% (SD = 22.7) in the malformed ear, with 73% of the participants

	unilateral conductive HI (ear malformation). Speech audiometry (words in quiet and in noise) Questionnaire H-70 on self-assessed hearing problems	analysis, Fisher's exact test, Kruskal-Wallis test	(children and adults) studied having poorer outcome than predicted. Speech recognition in noise: mean 32% (SD = 21.2) in the malformed ear, with 49% of the participants (children and adults) studied having poorer outcome than predicted. Of the respondents, - 64% complained of slightly and 13% of severely impaired hearing, - 47% reported slight to moderate and 37% severe problems in sound localization, - 16% reported problems when having a conversation in quiet with one person, - 77% reported slight to moderate and 14% severe difficulties when having a conversation with many persons, and - 63% reported slight to moderate and 19% severe problems when having a conversation in surrounding noise.

The GRADE scores assigned to the quality of evidence of the reviewed articles ranged from very low (–3, two studies) to low (+2, one study). Challenges and merits related to quality of evidence in each study are described in detail in Table 5. In two of the three studies assessed, results of both children and adults with UHI were reported. Reporting could also be conducted in a way that made data extraction very difficult or partially impossible if, for example, subjects were divided into age cohorts or reporting was based on the proportion of participants having certain results.

Possible RoB also caused concern. Recruiting controls from well-baby clinics, by newspaper advertisements, and on the Internet may have also caused a biased population explored in the Kishon-Rabin et al. study [64]. RoB was also strongly evident in the Priwin et al. study [66] in which they used the H-70 questionnaire, originally constructed for the elderly, as a proxy measure filled out by parents of, at least, the youngest participants. If applied in that way, it cannot be considered as a self-assessment of a hearing problem, but more of an indirect estimate given by caregivers.

Generalizability of the population was assessed by examining directness of evidence. In all studies the data were derived from only one or two hospitals or clinics. Additionally, generalizability was restricted to, for example, those who had received Baha as in Kunst et al. [65]; it is possible that parents of children with bigger problems choose Baha intervention. They also studied localization ability by plugging the nonimpaired ear, which does not reflect sound localization in more ecologically valid, everyday environments. In the study of Priwin et al. [66], the same speech recognition test, constructed more than fifty years ago, was used for both adults and children. For the youngest children, it may have been too difficult to perform in terms of their less developed vocabulary knowledge.

TABLE 5. Quality of evidence in the eligible articles analyzed using GRADE (high = ≥ +4, moderate = +3, low = +2, very low = less than +1)

Author(s) (year), overall GRADE score	**Problems with quality of evidence**	**Merits**
Kishon-Rabin et al. (2015) [64] **+2 (low)**	Observational evidence RoB (selection bias): parental socio-economic status not reported, normally hearing children were recruited from well-baby clinics and advertisements on the Internet and in local newspapers Indirectness of evidence and RoB: parental questionnaires used; parents vary in their ability to judge their child's development, and also recall bias is possible.	Prospective study Large control group Inclusion criteria clearly reported Congenital CMV infection and syndromes controlled for in the UHI group

	Only one data point per child, no follow-up Risk of imprecision and indirectness of evidence: - different number of relevant items in different age points: o some children were very young at the time when parents filled out the questionnaires; developmental milestones on e.g. canonical babbling could not yet be met due to infant's young age which caused missing data Hearing criteria of controls not reported	Hearing screening system described Odds ratios reported and were significant, confidence intervals reported Informative figures in reporting of results
Kunst et al. (2007) [65] **–3 (very low)**	Observational evidence Unclearly described group, missing data on speech recognition in children, additionally, one 13-year-old child included in the data of adults. Selection bias (intervention study) Indirectness of evidence: - speech recognition was assessed with different tests in children (maximal recognition score using words in noise) and adults (speech recognition threshold using sentences in noise) - word recognition test in noise constructed for adults was used to test children No description of possible confounding factors Imprecision: no effect size reported	Prospective study (but prospective only on Baha) Data on individual participants reported in tables Speech recognition assessed twice in adults, both in quiet and in noise
Priwin et al. (2007) [66] **–3 (very low)**	Observational evidence Mixed group, not very clearly reported Indirectness: very large age range of participants (aged 3–80 years) Reporting bias: data not reported in figures on children younger than 6 years of age, although pure tone audiometry was performed on all participants RoB: the youngest children were followed up only for a short time – not all effects of UHI could have come forth; difficult to compare with others Both children and adults tested with speech recognition test for adults; the test was constructed in 1954	Prospective study Pure tone audiometry results reported in figures in subgroups (age cohorts)

	Low directness of evidence: H-70 questionnaire was reported to have been filled out by all participants; some children were as young as 3 years old, but no information was available if parents filled out the questionnaire for all or for (only) the youngest children Low directness of evidence and high RoB: very vulnerable methodology in the viewpoint of young children regarding compromised internal validity as the questionnaire used concerned self-assessed hearing problems and had originally been devised for an elderly population	

Of the case and multi-case studies retrieved, each having less than 10 participants, altogether 13 (covering a total number of 48 heterogeneous patients) fit the criteria of the present review. They resulted in very heterogeneous contributions that could only be characterized. Quantitative research methods were used in all of them. Seven of the studies handled outcomes of different types of auditory implants (three concerned cochlear implantation), but the methods used to measure unaided preoperative hearing were not consistent across the studies ([67-73]. The rest of the studies dealt with various aspects of UHI, such as narrative skills and the neurofunctional organization of reading. There were too few patients studied with each method and per each outcome to allow any consistent qualitative summary based on these six reports [74-79].

4. DISCUSSION

The aim was to review literature on the impact of early-onset moderate to profound UHI on children's auditory and cognitive abilities, communication, development of speech and language, educational achievements, and psychosocial development (including quality of life). As the review aimed to cover a wide range of impacts, it was done with an interdisciplinary research team.

Despite the many potential studies identified, only three articles fulfilled the inclusion criteria and were a target for quality assessment and data extraction. We did not find any randomized controlled studies on the impact of UHI on children's development that were closely related to the nature of the phenomena we studied. To fulfill the inclusion criteria, the reports had to include detailed enough description of the participants; age appropriate, clearly defined and reported hearing level, also in the contralateral, normally hearing ear; and information given about the onset of UHI.

According to the main findings reported in the three studies analyzed in detail, children with UHI were at risk for delayed auditory performance and preverbal vocalization ability as infants in their

everyday life. Their ability to localize sounds was clearly impaired, and unaided speech recognition in the impaired ear was poorer than normal in quiet and especially in noise. It is important to note that the clear majority of the participants had a conductive HI in the three studies of which the quality of evidence of the articles was reviewed. Self-assessed hearing problems surveyed in one study included slight to severe problems in sound localization, and slight to moderate difficulties in conversations with many persons at the same time and in conversations held especially when surrounded by noise [66].

4.1 Quality of Evidence in the Reports Reviewed

Of the full-text articles reviewed (N = 566), very few articles contained information that was exact and detailed enough for the review purposes. Although impacts of UHI were explored, 1) specification of population of interest was often not sufficient or the population was too restricted or too broad, 2) hearing level was defined variably, sometimes averaging over only two measured frequencies or the speech recognition threshold was used to patch missing information about pure tone average, 3) in many reports it was only vaguely mentioned that the nonimpaired ear indeed was normally hearing; often no information at all was given if the presumably normally hearing ear had been tested and whether it actually fulfilled normally hearing ear's criterion, 4) owing to difficulties in diagnostics, it was often not possible to know the participants' exact age of onset of UHI (age at ascertainment of UHI is not the age of onset), 5) although universal hearing screening combined with radiological imaging has shown that the majority of UHI cases are congenital [24], outcomes of closer etiological examinations were very seldom reported in the studies we reviewed, and 6) in many reports, it was impossible to get information about the direct impact of UHI (e.g., unilateral hearing impairments and mild bilateral were reported together as one group).

All the above mentioned methodological issues should be solved and required to be properly specified and reported, and overall, they also need to be considered during the review process before accepting the reports for publishing. When planning a new study, we advise to clearly define the eligibility criteria for the hearing loss of both ears and how it should be measured. It is also important to specify the onset of hearing loss and not mix pre- and perilingual hearing losses with each other in reporting.

Three articles, the evidence quality of which was analyzed with an adaptation of GRADE, were highly variable regarding the number (range 10–34), age (range a few months to late adulthood), impaired ear (although predominantly right), and the hearing level (range mild to moderate or profound) of the children studied. Furthermore, the more detailed research questions and methods used to collect the data varied from study to study. Pooling the data was not possible because of the heterogeneity of the three studies reviewed. For example, not only populations but also methods (tests, other measures) and outcomes differed from study to study. Especially, in (re)habilitation and education sectors, it is often difficult to find data collection methods that

correspond with, for instance, dose-response calculations that could be judged with GRADE (2004) or other quality control frameworks.

Quality assessment of the evidence provided by the three articles included in the review showed that, on a GRADE scale from –3 to at least +4, evidence in two articles was very low (–3), and in one article it was low (+2). Also, directness of the evidence was often fairly low in these articles, which severely restricts generalizability of the results. Two of the three articles focused on aural atresia or other ear malformations, so most, but not all, participants had a conductive HI. Compared to conductive hearing impairment, it is assumed that sensorineural HI could have a more severe negative impact on children. Because all the results were merged in the reporting, it was not possible to directly assess the impact of sensorineural or mixed HI on children's development. There is also a risk that patients participating in a study on Bahas [66] may have caused a bias as seeking remediation with implantable hearing devices may be an indication of having more severe problems than usual. All three reports analyzed were from the Western countries, so all information retrieved from these reports is probably not generalizable to other parts of the world.

Most of the results that Priwin et al. ([66]) presented were based on either adults' self-reports or proxy reports given by parents on behalf of their children. Adults' responses, direct or proxy, can differ from those of children. Additionally, while Priwin and colleagues found that their participants complained relatively often about the negative impact of UHI in everyday communication situations, Gay and colleagues (2015) [80] had just the opposite result. Adults (N = 20) of their study did not perceive their UHI as a major handicap. Differences in results may, naturally, derive from methodology, such as the query form (questionnaire, interview) and the different kinds of questions asked.

4.2 Clinical Implications

If there is only low evidence for or very heterogeneous view of the impact of UHI on children's development, representatives of health care need to carefully perceive the field and critically weigh the options available for care, including cochlear implantation, and habilitation.

Of the studies we reviewed, the results of Kishon-Rabin et al. [64] suggest that development of auditory and vocalization skills may be delayed already in children with UHI who are younger than 12 months of age. Close monitoring for speech and language difficulties would therefore be needed in UHI, as also suggested by Krishnan and Van Hyfte [46]. In counseling parents can be instructed to provide good spoken language models and pay attention to the typical developmental milestones in auditory and speech development to be attained. Parents may need particularly careful counseling because, in young children, variation in speech and language development is considerable even among normally hearing children. Additionally, early family-centered intervention in infancy, as well as later spoken language and auditory training, should be provided when necessary.

Based on the results of Kishon-Rabin et al. [64], amplification may be needed already in mild cases to secure an early good start. The Joint Committee on Infant Hearing (2007) [26] strongly recommends starting hearing intervention before six months of age, and Kishon-Rabin et al. [64] and Holstrum et al. [81] also stress the importance of other forms of early intervention in children with UHIs. In their pediatric amplification clinical practice guidelines, the American Academy of Audiology (2013) [82] recommends that children with unilateral hearing loss should be provided with a hearing aid on the impaired ear if aidable hearing exists. It would be particularly important to enhance fusing of auditory information on the brainstem level to secure processing speed. One of the goals of hearing aid fitting in children in UHI is also the need to obtain a more balanced subjective sense of hearing between the ears, although this goal cannot be adequately achieved with only minor hearing rests (see e.g., [83]). Early stimulation of the auditory system can be provided either with a behind-the-ear hearing aid or Baha device with a soft band providing stimulation through bone conduction. Additionally, Jensen and colleagues (2013) [1] argue that research should address the benefits of early amplification in children with UHI.

Cochlear implantation has recently garnered increased interest as an option in the treatment of children's UHI [69,84]. According to the systematic review conducted by Peters et al. (2016) [41], due to heterogeneous findings, no firm conclusions can currently be drawn on the effectiveness of cochlear implantation in children with UHI. Also, it has to be remembered that there is a high incidence of absent cochlear nerves [16] and cochlear and cochlear nerve anomalies among children with UHI. For example, Mehta et al. (2016) [13] identified every fifth of the 150 children with sensorineural UHI that they studied to have cochlear nerve abnormality. Friedman with his colleagues (2016) [85] considered the risk of the loss of hearing in the nonimpaired ear as an absolute indication for pediatric cochlear implantation in the impaired ear. In the studies of Uwiera et al. (2009) [22] 11% (n = 15 out of 142), in Haffey et al. (2013) [86] 11% (n = 10 out of 89), and in Fitzpatrick et al. (2017) [6] 17% (n = 16 out of 92) of the children with UHI studied had a condition which progressed to involve the contralateral ear. Conditions causing this kind of risk are genetic disorders, malformations, diseases and ototoxicity which lead to sudden or progressive HI caused by such things as congenital cytomegalovirus infection. Before assessing a child as a cochlear implant candidate, however, the general impact of UHI needs to be known, carefully weighed in each individual case, and discussed with parents.

4.3 Limitations of the Review

The strengths of the current systematic review are that we had a broad focus in searching for different impacts of UHI, and we used six major electronic bibliographic databases relevant to audiology and children's development. Moreover, an experienced librarian did the searches, and the review was conducted in an interdisciplinary group of four researchers, with all four reading all the materials in the screening and review phases. In addition, only five reports identified in the literature searches could not be retrieved in full-text form.

This review also has some limitations. To be able to find all the relevant studies including pre- and perilingual UHI, only reports on, at least, moderate UHI ($PTA_{0.5\text{-}2 \text{ or } 4 \text{ kHz}} \geq 40$ dB) were included, as mild hearing impairments are not necessarily detected during the pre- and perilingual period. We did not control for publication bias because only reports published in peer-reviewed journals in English, Swedish, and German were included in the present review. Therefore, the potential suggestive impact of UHI found in dissertations and conference proceedings was not tapped.

Consistency of impacts of UHI could not be compared across the reviewed studies because they mostly focused on different topics. Additionally, we did not exclude studies on adults with congenital UHI. This decreased the directness of evidence because, in two of the studies [65-66] reviewed, the results concerning adults were also reported, and the methodology used for data collection was not optimal for children (adults' word recognition test, reporting of localization ability of adults). However, studies on adults with prelingual moderate to profound UHI were included in the review because their situation was considered to reflect the long-term effects of UHI, such as aural atresia.

5. CONCLUSIONS

With the inclusion criteria used, no high-quality studies reporting on consequences of pre- or perilingual UHI were found. This review identified only three studies eligible for closer quality analysis. Because of the heterogeneity of studies and their methodological limitations, no definitive conclusions can be drawn on the impact of early-onset UHI on children's development based on the reports reviewed. Further high-quality case studies and large prospective clinical studies addressing the impact of all grades of UHI on children are warranted to obtain information for evidence-based clinical decision-making.

ACKNOWLEDGMENTS

We warmly thank librarian Margareta Landin for performing the literature searches.

Conflict of interest and source funding

The authors report no conflict of interest. This research was funded in part by University of Oulu, Örebro University, School of Medical Sciences and Örebro University Hospital, Audiological Research Center, Örebro, Sweden. Additionally, funding was received by a grant from the Stiftelsen Acta Otolaryngologica, Sweden (to E.E.), which is gratefully acknowledged.

REFERENCES

[1] D.R. Jensen, L.M. Grames, J.E.C. Lieu, Effects of aural atresia on speech development and learning. Retrospective analysis from a multidisciplinary craniofacial clinic, JAMA Otolaryngol. Head Neck Surg. 139 (2013) 797–802. DOI: 10.1001/jamaoto.2013.3859.
[2] S. Arndt, S. Prosse, R. Laszig, T. Wesarq, A. Aschendorff, F. Hassepass, Cochlear implantation in children with single-sided deafness: does aetiology and duration of deafness matter? Audiol. Neurootol. 20 (2015) 21–30. DOI: 10.1159/000380744.
[3] F. Hassepass, A. Aschendorff, T. Wesarg, S. Kröger, R. Leszig, R.L. Beck, C. Schild, S. Arndt, Unilateral deafness in children: audiologic and subjective assessment of hearing ability after cochlear implantation, Otol. Neurotol. 34 (2013) 53–60. doi: 10.1097/MAO.0b013e31827850f0.
[4] EU Work Group on Genetics of Hearing Impairment, in: A. Martini (Ed.), European Commission Directorate, Biomedical and Health Research Programme Hereditary Deafness, Epidemiology and Clinical Research (HEAR), Infoletter 2 (1996) 8–9.
[5] E. Berninger, B. Westling, Outcome of a universal newborn hearing-screening programme based on multiple transient-evoked otoacoustic emissions and clinical brainstem response audiometry, Acta Otolaryngol. 131 (2011) 728–739. doi: 10.3109/00016489.2011.554440.
[6] E.M. Fitzpatrick, R.S. Al-Essa, J. Whittingham, J. Fitzpatrick, Characteristics of children with unilateral hearing loss, Int. J. Audiol. 56 (2017) 819–828. doi: 10.1080/14992027.2017.1337938.
[7] Ghirri, P., Liumbruno, A., Lunardi, S., Forli, F., Boldrini, A., Baggiani, A., Berrettini, S., 2011. Universal neonatal audiological screening: Experience of the University Hospital of Pisa, Ital. J. Pediatr. 37, 16. doi: 10.1186/1824-7288-37-16.
[8] S. Iwasaki, Y. Hayashi, A. Seki, M. Naqura, Y. Hashimoto, G. Oshima, T. Hoshino, A model of two-stage newborn hearing screening with automated auditory brainstem response, Int. J. Ped. Otorhinolaryngol. 67 (2003) 1099–1104.
[9] L. Dalzell, M. Orlando, M. MacDonald, A. Berg, M. Bradley, A. Cacace, D. Campbell, J. DeCristofaro, J. Gravel, E. Greenberg, S. Gross, J. Pinheiro, J. Regan, L. Spivak, F. Stevens, B. Prieve. The New York State Universal Newborn Hearing Screening Demonstration Project: Ages of hearing loss identification, hearing aid fitting, and enrollment in early intervention, Ear Hear. 21 (2000) 118–130.
[10] E. Vartiainen, S. Karjalainen, Prevalence and etiology of unilateral sensorineural hearing, Int. J. Pediatr. Otorhinolaryngol. 43 (1998) 253–259.
[11] R. Reed, M. Hubbard, B.W. Kesser, Is there a right ear advantage in congenital aural atresia? Otol. Neurotol. 37 (2016) 1577–1582. DOI: 10.1097/MAO.0000000000001204.
[12] J.E. Widen, R.C. Folsom, B. Cone-Wesson, L. Carty, J.J. Dunnell, K. Koebsell, A. Levi, L. Manchl, B. Ohlrich, S. Trouba, M.P. Gorga, Y.S. Sininger, B.R. Vohr, S.J. Norton, Identification of neonatal hearing impairment: hearing status at 8 to 12 months corrected age using a visual reinforcement audiometry protocol, Ear Hear. 21 (2000) 471–487.
[13] D. Mehta, S.E. Noon, E. Schwartz, A. Wilkens, E.C. Bedoukian, I. Scarano, E.B. Crenshaw 3rd, I.D. Kranzig, Outcomes of evaluation and testing of 660 individuals with hearing loss in a pediatric genetics of hearing loss clinic, Am. J. Med. Genet., Part A 170A (2016) 2523–2530. doi: 10.1002/ajmg.a.37855.
[14] C. Kiese-Himmel, Unilateral sensorineural hearing impairment in childhood: Analysis of 31 consecutive cases, Int. J. Audiol. 41 (2002) 57–63.

[15] E.M. Fitzpatrick, J. Wittingham, A. Durieux-Smith, Mild bilateral and unilateral hearing loss in childhood: A 20-year view of hearing characteristics, and audiologic practices before and after newborn hearing screening, Ear Hear. 35 (2014) 10–18. doi: 10.1097/AUD.0b013e31829e1ed9.
[16] A.M. Laury, S. Casey, S. McKay, J.A. Germiller, Etiology of unilateral neural hearing loss in children, Int. J. Pediatr. Otorhinolaryngol. 73 (2009) 417–427. doi: 10.1016/j.ijporl.2008.11.012.
[17] A. Paul, S. Marlin, M. Parodi, I. Rouillon, J. Guerlain, V. Pingault, V. Couloigner, E.N. Garabedian, F. Denoyelle, N. Loundon, Unilateral sensorineural hearing loss: Medical context and etiology, Audiol. Neurotol. 22 (2017) 83–88. doi: 10.1159/000474928.
[18] S.G. Korres, D.G. Balatsouras, C.P. Lyra, G.S. Korres , I. Kantas, C.E. Papadakis, Hearing evaluation in newborns with congenital aural malformation, B-ENT 5 (2009) 79–82.
[19] A.M. Tharpe, D.P. Sladen, Causation of permanent unilateral and mild bilateral hearing loss in children, Trends Amplif. 12 (2008) 17–25. doi: 10.1177/1084713807313085.
[20] J. Hartvig Jensen, P.A. Johansen, S. Borre, Unilateral sensorineural hearing loss in children and auditory performance with respect to right/left ear differences, Br. J. Audiol. 23 (1989) 207–213.
[21] F.H. Bess, A.M. Tharpe, Case history data on unilaterally hearing-impaired children, Ear Hear. 7 (1986) 14–19.
[22] T.C. Uwiera, A. DeAlarcon, J. Meinzen-Derr, A.P. Cohen, B. Rasmussen, G. Shott, J. Greinwald, Hearing loss progression and contralateral involvement in children with unilateral sensorineural hearing loss, Ann. Otol. Rhinol. Laryngol. 118 (2009) 781−785.
[23] P. Brookhouser, D. Worthington, W. Kelly, Unilateral hearing loss in children, Laryngoscope, 101 (1991) 1264–1272.
[24] N. Ghogomu, A. Umansky, J. Lieu, Epidemiology of unilateral sensorineural hearing loss with universal newborn hearing screening, Laryngoscope. 214 (2014) 295–300. doi: 10.1002/lary.24059.
[25] F. Sloot, H.L. Hoeve, M.L. de Kroon, A. Goedegebure, H.J. Griffiths, H.J. Simonsz for the EUS€REEN study group, Inventory of current EU paediatric vision and hearing screening programmes, J. Med. Screen. 22 (2015) 55–64. doi: 10.1177/0969141315572403.
[26] Joint Committee on Infant Hearing, Year 2007 Position Statement: Principles and Guidelines for Early Hearing Detection and Intervention Programs, Pediatr. 120 (2007) 898–921. DOI: 10.1542/peds.2007-2333.
[27] M.A. Akeroyd, The psychoacoustics of binaural hearing, Int. J. Audiol. 45 (2006) S25–S33. DOI: 10.1080/14992020600782626.
[28] H.S. Colburn, B. Shinn-Cunningham, G. Kidd, N. Durlach, The perceptual consequences of binaural hearing, Int. J. Audiol. 45(Suppl. 1) (2006) 34–44. DOI: 10.1080/14992020600782642.
[29] C.C. Dunn, R.S. Tyler, S. Oakley, B.J. Gantz, W. Noble, Comparison of speech recognition and localization performance in bilateral and unilateral cochlear implant users matched on duration of deafness and age at implantation, Ear Hear. 29 (2008) 352–359. doi: 10.1097/AUD.0b013e318167b870.
[30] M.M. Van Wanrooij, A.J. Van Opstal, Contribution of head shadow and pinna cues to chronic monaural sound localization, J. Neurosci. 24 (2004) 4163–4171. DOI: https://doi.org/10.1523/JNEUROSCI.0048-04.2004.
[31] J.B. Firszt, R.M. Reeder, L.K. Holden, L.K. Unilateral hearing loss: Understanding speech recognition and localization variability-implications for cochlear implant candidacy, Ear Hear. (2017) 38, 159–173. doi: 10.1097/AUD.0000000000000380.
[32] O.B. Wie, A.H. Pripp, O. Tvete, Unilateral deafness in adults: Effects on communication and social interaction, Ann. Otol. Rhinol. Laryngol. 119 (2010) 772–781.

[33] T.M. Klee, E. Davis-Dansky, A comparison of unilaterally hearing-impaired children and normal-hearing children on a battery of standardized language tests, Ear Hear. 7 (1986) 27–37.
[34] J.E.C. Lieu, Unilateral hearing loss in children: Speech-language and school performance, B-ENT. 21(Suppl 21) (2013) 107–115.
[35] V.J. Schmithorst, E. Plante, S. Holland, Unilateral deafness in children affects development of multi-modal modulation and default mode networks, Front. Hum. Neurosci. 8 (2014) 164. doi: 10.3389/fnhum.2014.00164.
[36] D. Tibussek, H. Meister, M. Walger, A. Foerst, H. von Wendel, Hearing loss in early infancy affects maturation of the auditory pathway, Dev. Med. Child Neurol. 44 (2002) 123–129.
[37] F.H. Bess, A.M. Tharpe, A.M. Gibler, Auditory performance of children with unilateral sensorineural hearing loss, Ear Hear. 7 (1986) 20–26.
[38] F.H. Bess, A.M. Tharpe, Performance and management of children with unilateral sensorineural hearing loss, Scand. Audiol. Suppl. 30 (1988) 75–79.
[39] L. Wong, L. Hickson, Evidence-based practice in audiology, Plural Publishing, San Diego.
[40] P.J. Boyd, Potential benefits from cochlear implantation of children with unilateral hearing loss, Cochlear Impl. Int. 16 (2015) 121–136. doi: 10.1179/1754762814Y.0000000100.
[41] J.P. Peters, G.G. Ramakers, A.L. Smith, W. Grolman, Cochlear implantation in children with unilateral hearing loss: A systematic review, Laryngoscope. 126 (2016) 713–721. doi: 10.1002/lary.25568.
[42] P. Purcell, J. Shinn, G. Davis, K. Sie, Children with unilateral hearing loss may have lower intelligence quotient scores: A meta-analysis, Laryngoscope. 126 (2016) 746–754. doi: 10.1002/lary.25524.
[43] E. L. Mozurkewich, B. Luke, M. Avni, F. M. Wolf, Working conditions and adverse pregnancy outcome: A meta-analysis. Obstet. Gynecol. 95 (2000) 623635.
[44] S. Appachi, J.L. Specht, N. Raol, J.E.C. Lieu, K. Dedhia, S. Anne, Auditory outcomes with hearing rehabilitation in children with unilateral hearing loss: A systematic review, Otolaryngol. Head Neck Surg. 157 (2017) 565–571. doi: 10.1177/0194599817726757.
[45] S. Anne, J.E.C. Lieu, M.S. Cohen, Speech and language consequences of unilateral hearing loss: A systematic review, Otolaryngol. Head Neck Surg. 157 (2017) 572−579. doi: 10.1177/0194599817726326.
[46] L.A. Krishnan, S. Van Hyfte, S. Management of unilateral hearing loss, Int. J. Pediatr. Otorhinolaryngol. 88 (2016) 63–73. doi: 10.1016/j.ijporl.2016.06.048.
[47] J.R. Dornhoffer, J.L. Dornhoffer, Pediatric unilateral sensorineural hearing loss, Curr. Opin. Otolaryngol. Head Neck Surg. 24 (2016) 522–528. DOI: 10.1097/MOO.0000000000000311.
[48] K. Kuppler, M. Lewis, A.K. Evans, A review of unilateral hearing loss and academic performance: Is it time to reassess traditional dogmata? Int. J. Pediatr. Otorhinolaryngol. 77 (2013) 617−622. doi: 10.1016/j.ijporl.2013.01.014.
[49] J. Lieu, Permanent unilateral hearing loss (UHL) and child development, Curr. Otorhinolaryngol. Rep. 6 (2018) 74–81. doi: 10.1007/s40136-018-0185-5.
[50] A.-K. Rohlfs, J. Friedhoff, A. Bohnert, A. Breitfuss, M. Hess, F. Müller, A. Strauch, M. Röhrs, T. Wiesner, Unilateral hearing loss in children: A retrospective study and a review of the current literature, Eur. J. Pediatr. 176 (2017) 475–486. doi: 10.1007/s00431-016-2827-2.
[51] A. van Wieringen, A. Boudewyns, A. Sangen, J. Wouters, C. Desloovere, Unilateral congenital hearing loss in children: Challenges and potentials. Hear. Res. 372 (2019) 29–41. https://doi.org/10.1016/j.heares.2018.01.010.

[52] A.M. Winiger, J.M. Alexander, A.O. Diefendorf, Minimal hearing loss: From a failure-based approach to evidence-based practice, Am. J. Audiol. 25 (2016) 232–245. doi: 10.1044/2016_AJA-15-0060.
[53] C.V.A. van Hövell tot Westerflier, J.A.A. van Heteren, C.C. Breugem, A.L. Smit, I. Stegeman, Impact of unilateral congenital aural atresia on academic performance: A systematic review, Int. J. Ped. Otorhinolaryngol. 114 (2018)175–179. doi: 10.1016/j.ijporl.2018.09.002.
[54] PROSPERO. International prospective register of systematic reviews. https://www.crd.york.ac.uk/prospero/ (accessed 15 October 2018)
[55] H. Balshem, M. Helfand, H.J. Schünemann, A.D. Oxman, R. Kunz, J. Brozak, G.E. Vist, Y. Falck-Ytter, J. Meerpohl, S. Norris, G.H. Guyatt, GRADE guidelines: 3. Rating the quality of evidence, J. Clin. Epidemiol. 64 (2011) 401–406. doi: 10.1016/j.jclinepi.2010.07.015.
[56] G. Guyatt, A.D. Oxman, E.A. Akl, R. Kunzl, G. Vist, J. Brozek, S. Norris, Y. Flack-Ytter, P. Glasziou, H. deBeer, R. Jaeschke, D. Rind, J. Meerpohl, P. Dahm, H.J. Schünemann, GRADE guidelines: 1. Introduction: GRADE evidence profiles and summary of findings tables, J. Clin. Epidemiol. 64 (2011) 383–394. doi: 10.1016/j.jclinepi.2010.04.026.
[57] GRADE Working Group, Grading quality of evidence and strength of recommendations. BMJ. 328 (2004) 1490–1494.
[58] GRADE Working Group (2012).What is GRADE? http://clinicalevidence.bmj.com/x/set/static/ebm/learn/665072.html (accessed 15 October 2018)
[59] D. Moher, A. Liberati, J. Tetzlaff, D.G. Altman and The PRISMA Group, Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 6 (2009) e1000097. doi: 10.1371/journal.pmed.1000097.
[60] Beller, E.M., Glasziou, P.P., Altman, D.G., Hopewell, S., Bastian, H., Chalmers, I., Gøtzsche, P.C., Lasserson, T., Tovey, D. PRISMA for Abstracts: Reporting Systematic Reviews in Journal and Conference Abstracts, PLoS Med., 10 (2013) e1001419. doi: 10.1371/journal.pmed.1001419.
[61] B. Vohr, D. Topol, N. Girard, L. StPierre, V. Watson, R. Tucker, Language outcomes and service provision of preschool children with congenital hearing loss, Early Hum. Dev. 88 (2012) 493–498. doi: 10.1016/j.earlhumdev.2011.12.007.
[62] Higgins, J. P. T. (2011). The Cochrane Collaboration's tool for assessing risk of bias in randomized controlled trials. BMJ, 343, d5928.
[63] Higgins, P. T., & Green, S. (Eds). Cochrane (2011). Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 [updated March 2011], http://handbook.cochrane.org/ (accessed 15 October 2018)
[64] L. Kishon-Rabin, J. Kuint, M. Hildesheimer, D. Ari-Even Roth, Delay in auditory behaviour and preverbal vocalization in infants with unilateral hearing loss, Dev. Med. Child Neurol. 57 (2015) 1129–1136. doi: 10.1111/dmcn.12812.
[65] S.J.W. Kunst, J.M. Leijendeckers, E.A.M. Mylanus, M.K. Hol, A.F. Snik, C.W. Cremers, Bone-anchored hearing aid system application for unilateral congenital conductive hearing impairment: Audiometric results, Otol. Neurotol. 29 (2007) 2–9. doi: 10.1097/mao.0b013e31815ee29a.
[66] C. Priwin, R. Jönsson, L. Magnusson, M. Hultcrantz, G. Granstrom, Audiological evaluation and self-assessed hearing problems in subjects with single-sided congenital external ear malformations and associated conductive hearing loss, Int. J. Audiol. 46 (2007) 162–171. DOI: 10.1080/14992020601077984.
[67] A.F. Snik, E.A. Mylanus, C.W. Cremers, The bone-anchored hearing aid in patients with a unilateral air-bone gap, Otol. Neurotol. 23 (2002) 61–66.

[68] C. Priwin, R. Jönsson, L. Magnusson, M. Hultcrantz, G. Granstrom, BAHA in children and adolescents with unilateral or bilateral conductive hearing loss: A study of outcomes, Int. J. Pediatr. Otorhinolaryngol. 71 (2007) 135–145. DOI: 10.1016/j.ijporl.2006.09.014.
[69] S. Arndt, S. Prosse, R. Laszig, T. Wesarg, A. Aschendorff, F. Hassepass, Cochlear-implantation in children with single-sided deafness: Does aetiology and duration of deafness matter? Audiol. Neurotol. 20(Suppl 1) (2015) 21–30. DOI: 10.1159/000380744.
[70] F. Hassepass, S. Bulla, A. Aschendorff, The bonebridge as a transcutaneous bone conduction hearing system: Preliminary surgical and audiological results in children and adolescents, Eur. Arch. Otorhinolaryngol. 272 (2015) 2235–2241. doi: 10.1007/s00405-014-3137-9.
[71] D. Tavora-Vieira, G.P. Rajan, Cochlear implantation in children with congenital unilateral deafness: Mid-term follow-up outcomes, Eur. Ann. Otorhinolaryngol. Head Neck Disord. 133(Suppl 1) (2016) S12–S14. DOI: 10.1016/j.anorl.2016.04.016.
[72] O.M. Canete, S.C. Purdy, M. Neeff,C.R.S. Brown, P.R. Thorne, Cortical auditory evoked potential (CAEP) and behavioural measures of auditory function in a child with a single-sided deafness. Cochlear Impl. Int. 18 (2017) 335–346. doi: 10.1080/14670100.2017.1373499.
[73] E. Vyskocil, R. Liepins, A. Kaider, M, Blineder, S. Hamzavi, Sound localization in patients with congenital unilateral conductive hearing loss with a transcutaneous bone conduction implant. Otol. Neurotol. 38 (2017) 318–324. doi: 10.1097/MAO.0000000000001328.
[74] W.H. Slattery III, J.C. Middlebrooks, Monaural sound localization: Acute versus chronic unilateral impairment, Hear. Res. 75 (1994) 38–46.
[75] J.P. Vasama, J.P. Mäkelä, Auditory cortical responses in humans with profound unilateral sensorineural hearing loss from early childhood, Hear Res. 104 (1997) 183–190.
[76] G.A. Young, D.G. James, K. Brown, F. Giles, L. Hemmings, J. Hollis, S. Keagan, M. Newton, The narrative skills of primary school children with a unilateral hearing impairment, Clin. Ling. Phon. 11 (1997) 115–138. doi: 10.1080/02699209708985186.
[77] D.E. Shub, S.P. Carr, Y. Kong, H.S. Colburn, Discrimination and identification of azimuth using spectral shape, J. Acoust. Soc. Am. 124 (2008) 3132–3141. doi: 10.1121/1.2981634.
[78] R. Adorni, M. Manfredi, A.M. Proverbio, Congenital unilateral deafness affects cerebral organization of reading, Brain Sci. 2 (2013) 908–922. doi: 10.3390/brainsci3020908.
[79] L. Van der Haegen, F. Acke, G. Vingerhoets, I. Dhooge, E. De Leenheer, Q. Cai, M. Brysbaert, Laterality and unilateral deafness: Patients with congenital right ear deafness do not develop atypical language dominance, Neuropsychol. 93 (2016) 482–492. doi: 10.1016/j.neuropsychologia.2015.10.032.
[80] A. Gay, N. Guinand, M. Miffon, J.P. Guyot, Perception of discomfort caused by a unilateral hearing loss in people suffering from a total bilateral vestibular loss, ORL J. Otorhinolaryngol. Relat. Spec. 77 (2015)248–253. DOI: 10.1159/000433552.
[81] W.J. Holstrum, M. Gaffney, J.S. Gravel, R.F. Oyler, D.S. Ross, Early intervention for children with unilateral and mild bilateral degrees of hearing loss, Trends Amplif. 12 (2008) 35–41. doi: 10.1177/1084713807312172.
[82] American Academy of Audiology, 2013, American Academy of Audiology Clinical Practice Guidelines. Pediatric Amplification. https://audiology-web.s3.amazonaws.com/migrated/PediatricAmplificationGuidelines.pdf_539975b3e7e9f1.74471798.pdf, 2013 (accessed 16 October 2018)
[83] S. McKay, Audiological management of children with single-sided deafness, Semin. Hear. 31 (2010) 290–312. DOI: 10.1055/s-0030-1268031.

[84] F. Hassepass, A. Aschendorff, T. Wesarg, S. Kröger, R. Leszig, R.L. Beck, C. Schild, S. Arndt, Unilateral deafness in children: audiologic and subjective assessment of hearing ability after cochlear implantation, Otol. Neurotol. 34 (2013) 53–60. doi: 10.1097/MAO.0b013e31827850f0.
[85] D.R. Friedmann, O.H. Ahmed, S.O. McMenomey, W.H. Shapiro, S.B. Waltzman, J.T. Roland Jr, Single-sided deafness cochlear implantation: Candidacy, evaluation, and outcomes in children and adults, Otol. Neurotol. 37 (2016) e154–e160.
[86] T. Haffey, N. Fowler, S. Anne, Evaluation of unilateral sensorineural hearing loss in the pediatric patient, Int. J. Pediatr. Otorhinolaryngol. 77 (2013) 955–958. doi: 10.1016/j.ijporl.2013.03.015.

Supplementary Appendix

Example of the search strategies used in the systematic review

PubMed Central (United States National Library of Medicine and National Institutes of Health)

Searched on 17.2.2016 and 16.2.2017

Search **(((hearing loss, unilateral[MeSH Terms]) OR (((((unilateral[Title/Abstract]) OR single-sided[Title/Abstract]) OR asymmetric[Title/Abstract])) AND (((hearing loss[Title/Abstract]) OR hearing impairment[Title/Abstract]) OR deafness[Title/Abstract])))) AND ((((((((((((((speech[MeSH Terms]) OR Speech perception[MeSH Terms]) OR language development[MeSH Terms]) OR language development disorders[MeSH Terms]) OR language tests[MeSH Terms]) OR verbal behavior[MeSH Terms]) OR cognition[MeSH Terms]) OR learning disorders[MeSH Terms]) OR educational measurement[MeSH Terms]) OR educational status[MeSH Terms]) OR auditory perception[MeSH Terms]) OR quality of life[MeSH Terms])) OR ((((((((((((((communicat*[[Title/Abstract]) OR "sound localisation"[Title/Abstract]) OR "sound localization"[Title/Abstract]) OR "auditory localisation"[Title/Abstract]) OR "auditory localization"[Title/Abstract]) OR speech[Title/Abstract]) OR language[Title/Abstract]) OR verbal[Title/Abstract]) OR cognitive[Title/Abstract]) OR cognition[Title/Abstract]) OR learning[Title/Abstract]) OR "quality of life"[Title/Abstract]) OR psychosocial[Title/Abstract]) OR psycho-social[Title/Abstract]) OR educational[Title/Abstract])) OR ((((((academic performance[Title/Abstract]) OR academic progress[Title/Abstract]) OR academic difficult*[Title/Abstract]) OR academic achievment*[Title/Abstract]) OR academic outcome*[Title/Abstract]) OR academic success[Title/Abstract]))**