JAMA Otolaryngology–Head & Neck Surgery | Original Investigation

Cochlear Implantation in Children With Single-Sided Deafness
A Systematic Review and Meta-analysis

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IMPORTANCE In 2019, the US Food and Drug Administration approved cochlear implantation for children with single-sided deafness (SSD). The absence of robust clinical data specific to pediatric patients to guide shared decision-making and to identify potential advantages is a challenge in family counseling.

OBJECTIVE To evaluate the audiological and patient-reported outcomes in children who underwent cochlear implantation for SSD and to assess the association between time of implantation, subjective outcomes, and cochlear implant device use rates.

DATA SOURCE MEDLINE, Embase, Scopus, Cochrane, and PubMed were searched for English-language articles that were published in a peer-reviewed journal from database inception to February 18, 2020.

STUDY SELECTION Inclusion criteria were designed to capture studies that evaluated pediatric patients (1) younger than 18 years, (2) with a diagnosis of SSD for which they underwent a cochlear implantation, and (3) with at least 1 outcome of interest measured numerically: speech perception, sound localization, device use, and patient-reported outcomes. Of the 526 articles reviewed, 12 (2.3%) met the selection criteria.

DATA EXTRACTION AND SYNTHESIS The Meta-analyses Of Observational Studies in Epidemiology (MOOSE) reporting guidelines were followed. Data were pooled using fixed-effect and random-effect models. The following information was obtained from each article: study characteristics, patient characteristics, hearing loss and intervention characteristics, and outcomes.

MAIN OUTCOMES AND MEASURES Outcomes were (1) postoperative changes in speech perception (in quiet was measured as a proportion of correct responses, and in noise was measured as decibel signal to noise ratio for speech reception threshold) and sound localization (measured in degree of localization error), (2) patient-reported audiological outcomes (measured by the speech, spatial, and qualities of hearing scale), and (3) device use rates among children who received cochlear implantation for SSD.

RESULTS Twelve observational studies that evaluated 119 children (mean [SD] age, 6.6 [4.0] years) with SSD who received a cochlear implant were included. Most children showed clinically meaningful improvement in speech perception in noise (39 of 49 children [79.6%]) and in quiet (34 of 42 children [81.0%]). Long duration of deafness (>4 years in congenital SSD and >7 years in perilingual SSD) was the most commonly proposed reason for lack of improvement. Sound localization as measured by degrees of error from true location (mean difference [MD], −24.78°; 95% CI, −34.16° to −15.40°; I^2 = 10%) improved statistically significantly after cochlear implantation. Patients with acquired SSD and shorter duration of deafness compared with those with congenital SSD reported greater improvements in speech (MD, 2.27; 95% CI, 1.89-2.65 vs 1.58; 95% CI, 1.00-2.16) and spatial (MD, 2.95; 95% CI, 2.66-3.24 vs 1.68; 95% CI, 0.96-2.39) hearing qualities. The duration of deafness among device nonusers was statistically significantly longer than the duration of deafness among regular device users (median difference, 6.84; 95% CI, 4.02-9.58).

CONCLUSIONS AND RELEVANCE This systematic review and meta-analysis found that cochlear implantation for children with SSD was associated with clinically meaningful improvements in audiological and patient-reported outcomes; shorter duration of deafness may lead to better outcomes. These findings can guide future research efforts, refine cochlear implantation candidacy criteria, and aid in family counseling and shared decision-making.

JAMA Otolaryngol Head Neck Surg. doi:10.1001/jamaoto.2020.3852
Published online November 5, 2020.

Supplemental content

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Sensorineural unilateral hearing loss (UHL) has an estimated incidence of 1 in 1000 live births in the United States.[1,2] The prevalence increases to approximately 3% to 6.3% among children aged 6 to 19 years once delayed-onset congenital UHL and acquired causes accumulate.[2-4]

Children with single-sided deafness (SSD), the most severe form of UHL, often struggle with speech perception in noise and sound localization because of lack of binaural auditory input. This outcome has been associated with the absence of binaural hearing effects, such as the binaural squelch effect,[5,6] the head shadow effect,[7,8] and the binaural redundancy effect.[9,10]

Single-sided deafness has been shown to have implications for children's speech-language development, cognition, and quality of life, placing them at an increased risk for psychosocial and behavioral difficulties and inferior functioning in educational settings compared with their peers with normal hearing.[2,11-13]

Until recently, standard clinical practice for auditory rehabilitation of children with SSD consisted of either observation alone, contralateral routing of signal hearing aids, or osseointegrated hearing devices, all of which rely on routing of signals to the normal hearing ear. Although cochlear implantation for SSD has increased over the past several years, it has been mostly limited to adults and to off-label use for children in the US.[14]

In a historic step, in July 2019, the US Food and Drug Administration granted a first-time approval of cochlear implantation for SSD in children 5 years or older.[15] The absence of robust clinical data to guide shared decision-making and to identify potential advantages represents a major challenge in the counseling of families of children with SSD. We performed this systematic review and meta-analysis to evaluate the audiological and patient-reported outcomes in children who underwent cochlear implantation for SSD and to assess the association between time of implantation, subjective outcomes, and cochlear implant use rates. We hypothesized that children with short duration of deafness prior to cochlear implantation would have improved audiological and patient-reported outcomes.

Key Points

Question Is cochlear implantation in children with single-sided deafness associated with improved audiological and patient-reported outcomes?

Findings In this systematic review and meta-analysis of 12 studies that evaluated 119 children with single-sided deafness, speech perception in noise and quiet as well as sound localization improved after cochlear implantation. Patient-reported audiological outcomes and cochlear implant use rates were higher among children with a shorter duration of deafness.

Meaning Findings from this study can be used to inform future research efforts, refine cochlear implantation candidacy criteria, and aid in family counseling and shared decision-making.

Methods

This systematic review and meta-analysis adhered to the Meta-analyses Of Observational Studies in Epidemiology (MOOSE) reporting guidelines (eTable 1 in the Supplement).[16] The need for institutional review board approval was waived because of the Common Rule and because the study analyzed data exclusively from published literature. This study was conducted from January 4, 2020, to April 4, 2020.

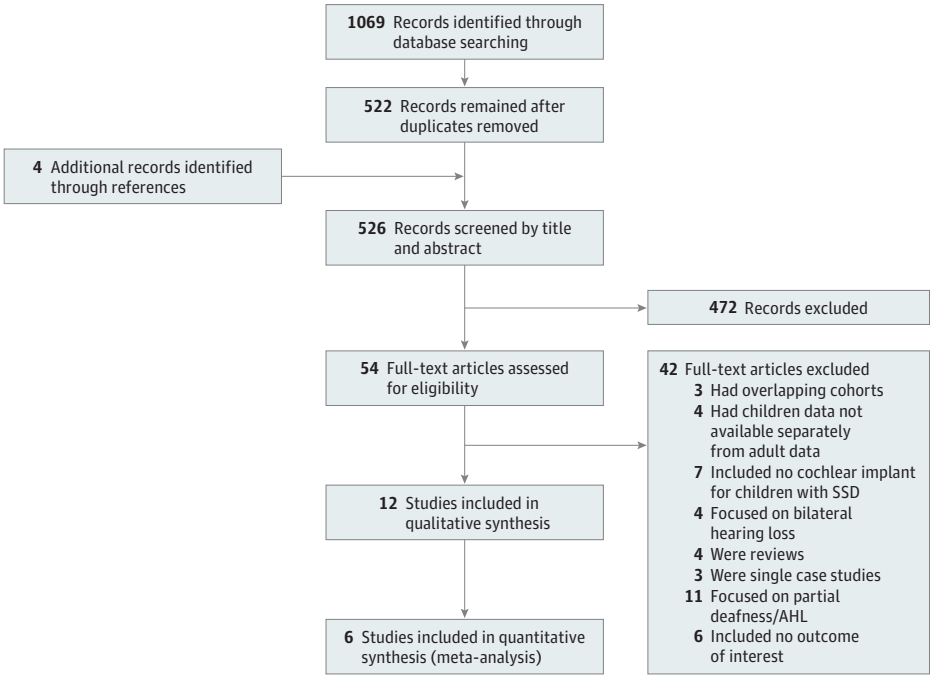
Study Selection and Search Strategy

Inclusion criteria were studies that involved patients (1) younger than 18 years, (2) with a diagnosis of SSD for which they underwent a cochlear implantation, and (3) with at least 1 outcome of interest measured numerically: speech perception, sound localization, device use, and patient-reported outcomes. Speech perception in quiet was measured as a proportion of correct responses, and speech perception in noise was measured as decibel (dB) signal to noise ratio for speech reception threshold; sound localization was measured in degree of localization error; device use was measured by hours per day of device use; and patient-reported outcomes were measured by the speech, spatial, and qualities of hearing scale (SSQ). The SSQ is a validated standardized questionnaire that has been shown to be sensitive in measuring bilateral and unilateral hearing abilities across 3 domains, thus yielding 3 subscale scores (score range: 1-10, with the highest score indicating the best result).[17,18] The SSQ has been validated for adults, children, and parent proxy for young children.[17-19]

The other 2 inclusion criteria were publication in a peer-reviewed journal and a study design that examined human participants. Only studies and patients who met the definition of SSD were deemed qualified for inclusion in this study. Single-sided deafness was defined as a 1-sided pure-tone average of 90 dB or higher or an auditory brain stem response of 80 or higher with normal hearing in the contralateral ear. Exclusion criteria included (1) studies that were not available in the English language, (2) studies in which pediatric data were not separable from adult data, (3) studies of cochlear implantation only for asymmetric hearing loss or partial deafness (residual hearing in low frequencies), and (4) single case reports.

A search of MEDLINE, Embase, Scopus, Cochrane, and PubMed databases was performed by a medical librarian for articles that were published from database inception to February 18, 2020. The terms SSD, cochlear implant, pediatric, and all of their synonyms were combined in the search strategy (the complete search strategy is outlined in the eMethods in the Supplement). After the initial search, duplicates were removed. Two of us (L.B., E.A.R.) independently screened the titles and abstracts of all potentially eligible articles and searched the bibliographies of each study to identify additional articles. Articles that appeared to meet eligibility criteria underwent a full-text screening. Selection criteria were applied, discrepancies in the article selection were resolved through discussion between the investigators, and a final list of studies was obtained. In case of overlapping cohorts, the most recent or comprehensive study was selected.

Figure 1. Flow Diagram for Search and Study Selection Process



AHL indicates asymmetric hearing loss; SSD, single-sided deafness.

Data Extraction and Quality Assessment

One of us (L.B.) extracted data from the included articles, and another (E.A.R.) independently validated the data using standardized data forms. The following information was obtained from each article: study characteristics (design, period, location, and follow-up time), patient characteristics (number, implantation age, and sex), hearing loss and intervention characteristics (hearing loss cause, duration of deafness, preimplant pure-tone average or auditory brain stem response, and device type), and outcomes (speech perception in noise and quiet, sound localization, and daily device use). No attempt was made to contact the authors of studies with missing information. For studies that reported data in graph form only, the values were estimated with digitizing software (Engauge Digitizer, version 12.1; Mark Mitchell[20]).

The Newcastle-Ottawa Scale (NOS; score range: 1-9, with the highest score indicating lowest risk of bias)[21] was completed independently by 2 of us (L.B., E.A.R.). Studies that received a score of less than 6 points were considered to have a high risk for bias, and the possibility of their exclusion was discussed by all authors (eTable 2 in the Supplement).

Statistical Analysis

Review Manager, version 5.3 (Cochrane),[22] and Stata, version 15 (StataCorp LLC), were used to perform all of the analyses. Meta-analyses were conducted only when studies were comparable in terms of design and outcomes. If a meta-analysis was deemed inappropriate because of heterogeneous data or risk of bias, outcomes were evaluated at the individual study level through table and narrative review. Mean difference (MD) with 95% CIs was used for continuous data in studies that reported the same outcome measure and unit. In studies with median and range data only, we used an accepted method of estimating mean and SD.[23] Depending on heterogeneity, either the fixed-effects or the random-effects model was applied to obtain pooled effect size estimates, 95% CIs, and *P* values through the inverse variance method.[24] The I^2 and χ^2 statistics were used to evaluate the percentage variability of the results attributed to heterogeneity between studies.[25] If substantial heterogeneity was denoted (χ^2 $P \leq .10$ or $I^2 > 50\%$), we used the random-effects model; otherwise, the fixed-effects model was applied. Daily device use was stratified as regular (>7 hours/d), limited (1-7 hours/d), or none (<1 hour/d). Data for the duration of deafness and implantation age were pooled in meta-analyses. The pooled data distribution was determined via the Kolmogorov-Smirnov test of normality. We used the independent unpaired, 2-tailed *t* test to compare means when normal distribution was identified and the Mann-Whitney test to compare medians in cases of nonnormal distribution.

Results

The search strategy yielded 522 articles, of which 12 (2.3%) met the selection criteria for the systematic review (**Figure 1**). Six of these were included in the meta-analysis. Sound localization and patient-reported outcomes (through the SSQ) were amenable to a meta-analysis, whereas speech perception outcomes in noise and quiet were not based on high between-study heterogeneity. One study with 5 patients (1 of whom had UHL)[26] and a patient from an included study[27] were excluded because they did not meet the definition of SSD. All studies were case series with small sample sizes that ranged from 3 to

23 patients. The mean (SD) NOS score was 6.4 (0.9) (eTable 2 in the Supplement). For most studies, comparability points were deducted for lack of adjustments. Studies that scored 5 were still included because of the challenges with adjusting small cohorts and the valuable information obtained from each patient. Two pairs of studies[28-31] had 1 to 2 overlapping patients. However, all 4 studies were included because each evaluated a different outcome of interest (eTable 3 in the Supplement).

Table 1 summarizes the characteristics of analyzed studies[27-38] and patients. All 12 studies were observational cohort studies, collectively spanning more than a decade from 2004 to 2019. The studies were conducted in Europe (n = 8 [66.7%]), North America (3 [25.0%]), and Australia (1 [8.3%]). Overall, 119 children with a mean (SD) age of 6.6 (4.0) years were included, and most children (70 [58.8%]) had congenital SSD. The median (interquartile range [IQR]) duration of deafness was statistically significantly shorter in children with acquired SSD than in those with congenital SSD (1.3 [0.8-3.0] years vs 4.1 [1.7-6.9] years; median difference, 2.8; 95% CI, 1.08-4.52).

Audiological Outcomes

Speech Perception in Noise

Eight studies[27,28,30,32,34,36-38] (66.7%) evaluated 49 children in total assessed speech perception in noise (**Table 2**). All studies presented background noise at 60 to 70 dB, and although various configurations were used, all studies measured the sound and noise from 0° azimuth (S0N0) testing configuration, and we reported these results for consistency. Among the 5 studies (involving 35 of 49 children [71.4%] in whom speech perception in noise was assessed) whose outcome was the change in dB signal to noise ratio for speech reception threshold, the mean improvement with the implant ranged from 0 dB to 2.7 dB. Among the remaining 3 studies whose outcome was the percentage of correct answers on word and sentence tests, the mean improvement with the implant ranged from 2.0% to 51.7%. Thirty-nine of 49 children (79.6%) experienced improved speech perception in noise after cochlear implantation.

Overall, 5[30,32,34,37,38] of the 8 studies (with 30 of 49 children [61.2%]) that assessed speech perception in noise reported a clinically meaningful improvement with the implant among all patients. Two of these studies[32,37] (21 of 49 children [42.8%]) calculated and identified a statistically significant improvement. The remaining 3 studies[27,28,36] evaluated 19 children (38.8%). Arndt et al,[28] who consistently stratified the results by congenital or perilingual vs acquired (postlingual) SSD, did not report a clinically or statistically meaningful difference of sound perception in noise in the S0N0 testing condition among children (n = 9) with acquired SSD. They did report a clinically and statistically meaningful improvement in the speech deaf ear, noise normal hearing ear testing condition.[28] Arndt et al[28] attributed the lack of improvement in the 4 children with congenital or perilingual SSD to long duration of deafness (>4 years in congenital SSD; >7 years in perilingual SSD) and cytomegalovirus (CMV) deafness cause. Deep et al[27] evaluated 5 children and attributed the lack of improvement to a ceiling effect created by the excellent normal hearing ear. Távora-Vieira and Rajan[36] evaluated 1 child and attributed the lack of improvement to the long duration of deafness (>6.8 years), which included the critical period for binaural hearing development. Among these 3 studies, long duration of deafness was cited as the reason for the lack of improvement in 5 of the 10 (50%) children in whom no clinical or statistical improvement was noted.

Speech Perception in Quiet

Six studies[27,29,31,34,36,38] of 42 children, assessed speech perception in quiet in the implant ear–only (masking of normal hearing ear) (Table 2). The outcome in all studies was the proportion of correct answers. Six unique age-appropriate sentence tests and monosyllabic or multisyllabic word tests were used: Arizona Biomedical Institute Sentence Test,[38] consonant-vowel nucleus-consonant word test,[27,36,38] Freiburger Speech Test,[34] Lexical Neighborhood Test,[27,38] Mainzer speech perception test,[34] and the Northwestern University-Children's Perception of Speech.[36]

The mean scores achieved with the implant ranged from 0% to 100%. Overall, 34 children (81.0%) experienced improvement from the cochlear implantation, and their mean scores ranged from 56% to 100%. Three[27,31,38] of the 6 studies, evaluating 29 children (69.0%), reported an implant-associated change for all children. For example, Deep et al[27] noted that children who received an implant after a shorter duration of deafness (3 years) had greater improvement than children who underwent an implantation later. The remaining 3 studies[29,34,36] (evaluating 13 children [30.2%]) reported post-implantation advantages in 5 children. For the remaining 7 children (16.7%), the authors cited long duration of deafness (>4 years,[29,34] >7 years,[34] and >6.8 years[36]) as the probable reason for lack of observed improvement. None of the studies conducted a statistical analysis for speech perception in quiet outcome.

Sound Localization

Sound localization was assessed in 6 studies.[28,31,32,34,36,37] Researchers used between 3 to 13 loudspeakers, with various stimuli presented at 55 to 70 dB. Three of the studies[28,34,36] used the root-mean-square (RMS) localization error as the outcome unit to assess preoperative vs postoperative (1-2.2 years) binaural performance and were combined for a meta-analysis (**Figure 2**). Device use was associated with decreased RMS error and improved sound localization (MD, -24.78°; 95% CI, -34.16° to -15.40°). Heterogeneity was not substantial (I^2 = 10%; P = .36), and a fixed-effects model was used. Results of 3 studies[31,32,37] with data incompatible for meta-analysis are summarized in Table 2. Most children in these studies (n = 55 of 62 [88.7%]) showed improvement in sound localization 1 to 2 years after cochlear implantation, with mean reduction of 24.78° in localization error. All studies reported clinical improvement of sound localization at most angles.

Patient-Reported Outcomes

Four studies[28,29,31,37] used the SSQ as a patient-reported auditory questionnaire. The questionnaire items were scored

Table 1. Characteristics of Patients and Studies

Source	Location	Study period	No. of patients analyzed	Mean (SD) [range], y		Cause, No.	Preoperative PTA or ABR, mean (SD) [range], dB[a]		Device type, No.	Follow-up, mean (SD) [range], y[b]
				Age at implantation	Duration of deafness		Poor ear	Good ear		
Arndt et al,[28] 2015	Freiburg, Germany	2008-2014	14 (20 Total but 6 had no postoperative data)	10.9 (3.7) [4.3-18]	4.3 (4.0) [0.3-13.8]	Congenital: 2 CMV Acquired: 4 EVA, 2 unknown, 1 meningitis, 2 SHL, 2 premature birth, 1 labyrinthitis	NA	NA	6 Nucleus CI24 RE 2 Nucleus CI512 4 Nucleus CI422 2 MED-EL Concerto Flex	1
Beck et al,[29] 2017	Freiburg, Germany	NA	10	4.8 (3.5) [1.8-13.8]	4.8 (3.5) [1.8-13.8]	Congenital: 4 CMV, 3 unknown, 1 hypoxia (?), 1 ototoxic med, 1 ANSD	ABR threshold: >90	ABR: 21.1 (3.3) [20-30]	NA	1.4 (1.1) [0.3-2.8]
Deep et al,[27] 2020	New York, United States	2011-2019	13	4.5 (2.8) [1-9.3]	3.0 (2.2) [0.6-7]	Congenital: 4 unknown, 1 CAN, 1 Mondini (bilateral), 1 CMV, 1 hereditary Acquired: 4 unknown, 1 EVA (bilateral)	ABR: 108.1 (16.4) [90-125]	ABR: 15.1 (4.9) [10-25]	6 Nucleus CI512 5 Nucleus CI532 1 Nucleus CI24 RE 1 AB MSE	3.4 (1.6) [1.2-6]
Ehrmann-Mueller et al,[32] 2020	Wuerzburg, Germany	2011-2013	7	8.6 (4.3) [3.6-16.3]	7.7 (4.1) [3.8-16.3]	Congenital: 5 unknown, 1 CMV Acquired:1 trauma	ABR: 100	ABR: 10	7 MED-EL Concerto	6.3 [5.3-7.8]
Ramos Macías et al,[30] 2016	Gran Canaria, Spain	2004-2011	2 (11 Total but 9 had AHL)	4 (1) [3-5]	NA	Acquired: 2 unknown	NA	NA	2 Nucleus AG	1
Ramos Macías et al,[31] 2019	Gran Canaria, Spain	2013-2016	23	7.2 (2.9) [0.9-11.2]	1.3 (0.8) [0.5-4.1]	4 Congenital 19 Acquired	NA	NA	5 Nucleus CI512 6 Nucleus CI522 12 Nucleus CI532	1
Polonenko et al,[33] 2017	Toronto, Canada	NA	7	5.9 (5.9) [1.1-14.5]	2.5 (1.1) [1.1-3.6]	Congenital: 5 Acquired: 1 trauma, 1 unknown	NA	NA	NA	0.3 (0.4)
Rahne and Plontke,[34] 2016	Halle, Germany	2011-2014	4 (21 Total but 17 adults)	8.3 (1.3) [7-10]	6 (2.6) [1.5-8]	Congenital: 1 CN abnormality Acquired: 1 CN abnormality, 1 unknown, 1 trauma	ABR threshold: >90	ABR: 10 (2.8) [6-14]	3 Nucleus CI24 RE 1 Nucleus CI512	0.08, 0.25, 0.5, 1
Sangen et al,[35] 2019	Leuven, Belgium	NA	6	1.2 (0.5) [0.7-2.2]	1.2 (0.5) [0.7-2.2]	Congenital: 4 CMV, 1 CN abnormality, 1 trauma	ABR threshold: ≥80	ABR threshold: ≤35	NA	1.9 (1) [1-2.7]
Távora-Vieira and Rajan,[36] 2016	Australia	NA	3	4.2 (2.2) [1.4-6.8]	4.2 (2.2) [1.4-6.8]	Congenital: 3 unknown	ABR threshold: >90	ABR: 10 (5) [5-15]	3 MED-EL OPUS 2	1, 2, 3
Thomas et al,[37] 2017	Bochum, Germany	2012-2016	21	5.4 (3) [0.8-11.3]	5.4 (3) [0.8-11.3]	21 Congenital	NA	NA	4 Nucleus CI24 RE 5 Nucleus CI422 10 MED-EL Concerto 2 MED-EL Sonata	1.75 (1.25) [1.1-3.6]
Zeitler et al,[38] 2019	Arizona, United States	2011-2017	9	8.6 (3.8) [1.5-15.1]	4.1 (3.1) [0.8-9.5]	Congenital: 4 unknown Acquired: 3 sudden, 1 cholesteatoma, 1 progressive	ABR:101.3 (15.1) [72.5-120]	ABR threshold: ≤25	5 MED-EL Flex 28 1 MED-EL Standard 2 Nucleus CI522 1 Nucleus CI24 RE	1.1 (0.7) [0.25-2.3]

Abbreviations: ABR, auditory brain stem response; AHL, asymmetric hearing loss; ANSD, auditory neuropathy spectrum disorder; CMV, cytomegalovirus; CN, cochlear nerve; EVA, enlarged vestibular aqueduct; NA, not available; PTA, pure-tone average; SHL, sudden hearing loss.

[a] ABR is reported when PTA is not available.

[b] Individual postoperative assessment times are reported when mean follow-up time is not available.

Table 2. Audiological Outcomes

Source	Test conditions	No. of patients with available data[a]	Outcome by postoperative time		Meaning and notes[b]
			Without cochlear implant	With cochlear implant	
Speech perception in noise (SONO: speech and noise from front)					
Arndt et al,[28] 2015 (acquired)	Test: OlSa Outcome: dB SNR for 50% SRT	9	−4.2 (1.2) dB	12 mo −4.7 (1.3) dB	Improvement was statistically significant in the speech deaf ear/noise NH ear condition only.
Arndt et al,[28] 2015 (congenital/perilingual)	Test: OlSa Outcome: dB SNR for 50% SRT	4	−4.3 (0.6) dB	12 mo −4.8 (1.1) dB	No statistically significant improvement with device, which was attributed to long DD (>4 y) and CMV cause in congenital SSD (n = 2) and long DD (>7 y) in perilingual SSD.
Rahne and Plontke,[34] 2016	Test: OlSa Outcome: dB SNR for 50% SRT	4	−2.7 (1.5) dB	6 mo −5.4 (0.3) dB	Improvement with device in all children; subjective advantage also reported.
Thomas et al,[37] 2017	Test: OlSa Outcome: dB SNR for 50% SRT	14	Minimum 12 mo −4.1 (1.5) dB	Minimum 12 mo −5.1 (1.5) dB	Statistically significant improvement with implant; no statistically significant difference between implantation age of <6 y and >6 y. 9 Children (64%) had greater than 1.5 dB difference in noise-speech perception.
Deep et al,[27] 2020	Test: HINT, AZBio Outcome: % correct	5	31 (11) mo 93.4 (8.8) dB	31 (11) mo 95.4 (5.5) dB	No statistically significant improvement with implant, which was explained by excellent performance of acoustic ear alone, creating a ceiling effect in detecting a meaningful difference with binaural hearing.
Ehrman-Mueller et al,[32] 2020	Test: Wuerzburger Outcome: % correct	7	14 mo 12.5 (12.9) dB	14 mo 35.0 (23.7) dB	Statistically significant improvement with implant among all children, although widely variable. No clear association between outcomes and hearing loss cause, DD, or implantation age was observed.
Ramos Macías et al,[30] 2016	Test: Spanish sentence test Outcome: % correct	2	15.8 (2.8) dB	12 mo 67.5 (7.5) dB	Both children with acquired perilingual/postlingual HL improved postimplantation, which was attributed to DD <3 y.
Távora-Vieira and Rajan,[36] 2016	Test: BKB-SIN Outcome: dB SNR for 50% SRT	1	−5.5 dB	36 mo −5.5 dB	No difference with implant, which was attributed to long DD of 6.8 y.
Zeitler et al,[38] 2019	Test: HINT Outcome: ΔdB SNR for SRT	3	NA	12 mo dB SNR improvement, mean (range): 1.9 (1-3.5)	Improvement with implant in all children.
Speech perception in quiet (implant ear–only condition)					
Deep et al,[27] 2020	Test: WRS Outcome: % correct	6	9.3 (13.9%)	27 (12) mo 56.3 (30.4%)	Improvement with cochlear implant in all children. Children with shorter DD (1.1-3 y) had greater improvement (>40%) than children with longer DD (3-7 y).
Zeitler et al,[38] 2019	Test: WRS Outcome: % correct	6	17.8 (11.3%)	18 (5) mo 69.5 (18.2%)	Improvement with cochlear implant in all children. Because of small sample size, association of DD and deafness cause with % improvement could not be determined.
Beck et al,[29] 2017	Test: Mainzer I, Gottinger II, or Freiburger Outcome: % correct	7	NA	34.3 (36.6%)[c]	Patients receiving implantation at younger age (1.8-3.2 y; n = 3) had better outcomes than those at older age (4-13.8 y; n = 4). All had congenital SSD.

(continued)

Table 2. Audiological Outcomes (continued)

Source	Test conditions	No. of patients with available data[a]	Outcome by postoperative time		Meaning and notes[b]
			Without cochlear implant	With cochlear implant	
Rahne and Plontke,[34] 2016	Test: multisyllabic/monosyllabic WRS Outcome: % correct	4	1-3 mo Multisyllabic: 20 (34.6%) Monosyllabic: 2.5 (4.3%)	6-12 mo Multisyllabic: 30 (41.2%) Monosyllabic: 16.3 (28.1%)	1 Child improved with cochlear implant over time (DD 1.5 y); 3 children did not improve over time (DD 7-8 y); 1 child had radiologically hypoplastic CN, and 1 had questionable patency of CN. They still received implantation because all children reported a positive response after electrical stimulation of the promontory.
Ramos Macías et al,[31] 2019	Test: disyllabic word score Outcome: % correct	17	NA	Minimum 12 mo Implant ear only: 61.2 (5.3%) Binaural: 98.1 (2.4%)	All children had scores ≥48% in implant ear–only condition, and ≥92% in binaural condition (no masking).
Távora-Vieira and Rajan,[36] 2016	Test: CNC, NU-CHIPS Outcome: % correct	2	NA	36 mo Patient 1: 100% Patient 2: 0%	Cochlear implant was advantageous only in the child with shorter (1.4 y) DD but not in the child with longer (6.8 y) DD-auditory stimulations perceived as vibration only.
Sound localization					
Ehrman-Mueller et al,[32] 2020	Setting: 3-9 loud speakers (00-900 intervals) according to child's age Stimulus: words at 55-70 dB Outcome: RMS error	4-6	24 mo 62.7 (28.8) dB	24 mo 44.7 (39.4) dB	Improvement with cochlear implant in all children, although it did not reach statistical significance. All parents reported observing improved localization abilities, especially in road traffic.
Ramos Macías et al,[31] 2019	Setting: 5 loudspeakers (45°-100° intervals) Stimulus: words (≤5 y), 1-2 kHz pure tone (≥6 y) at 65 dB Outcome: accuracy ratio ≥80% is a positive result	23	Negative result in all conditions in all children	12 mo 21 of 23 Children had positive result in all conditions; 2 of 23 children had positive result in all conditions except 450	Overall improvement with cochlear implant. 2 children with congenital SSD (DD 0.9 and 4.1 y) did not improve in the 45° condition.
Thomas et al,[37] 2017	Setting: 3 loudspeakers (900 intervals) Stimulus: OlSa pseudo-sentences at 65 dB Outcome: median % correct	14	0°: 60% −90°: 75% +90°: 95%	12 mo 80% 100% 100%	Statistically significant improvement with cochlear implant when stimuli presented at −90° (NH ear) and +90° (cochlear implant ear) but not from front (0°).

Abbreviations: AZBio, Arizona Biomedical Institute Sentence Test; BKB-SIN, Bamford-Kowal-Bench Speech in Noise test; CMV, cytomegalovirus; CN, cochlear nerve; dB, decibel; DD, duration of deafness; HINT, hearing in noise test; NH, normal hearing; NU-CHIPS, Northwestern University-Children's Perception of Speech; OlSa, Oldenberg Sentence Test; RMS, root mean square; SNR, signal to noise ratio; SRT, speech reception threshold; SSD, single-sided deafness; WRS, word recognition score.

[a] The number of patients may be smaller than total patients in each study as only those with available outcomes are reported.

[b] Statistical significance pertains to the significance reported in each source study.

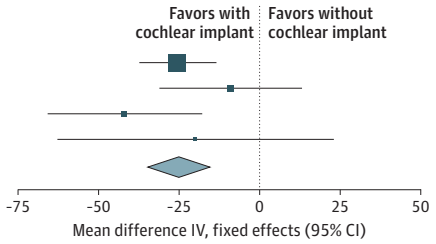
[c] Postoperative time was not available.

from 1 to 10, completed before and after (1-3 years) cochlear implantation, and combined in a meta-analysis (**Figure 3**). The outcomes were divided into congenital vs acquired SSD and are presented herein accordingly. Cochlear implantation was associated with statistically significant improvements in all 3 domains (speech hearing, spatial hearing, and hearing quality). Children with acquired SSD had statistically significantly greater improvements compared with children with congenital SSD in the speech (MD, 2.27; 95% CI, 1.89-2.65 vs 1.58; 95% CI, 1.00-2.16) (Figure 3A) and spatial (MD, 2.95; 95% CI, 2.66-3.24 vs 1.68; 95% CI, 0.96-2.39) (Figure 3B) hearing domains. The mean (SD) implantation age of children with congenital SSD was statistically significantly younger than the implantation age of children with acquired SSD (5.1 [3.2] years vs 9.5 [3.0] years; MD, 3.39; 95% CI, 1.41-7.39). The median (IQR) duration of deafness, however, was statistically significantly shorter in the acquired SSD group vs the congenital SSD group (1 [0.8-1.5] years vs 4.1 [1.7-6.8] years; median difference, 3.11; 95% CI, 1.29-3.91). Hearing quality scores (Figure 3C) had high heterogeneity (congenital I^2 = 81% vs acquired I^2 = 88%), even though the same SSQ questionnaire and same studies were used for the speech (Figure 3A) and spatial (Figure 3B) subscale categories. Given the low heterogeneity in the other 2 subscale categories, low risk of bias in all studies (NOS score ≥6), and no other justified reason to remove this part of the questionnaire, we retained this analysis.

Figure 2. Meta-analysis Forest Plots of Mean Differences for Sound Localization

Study or subgroup	With cochlear implant Mean	SD	Total	Without cochlear implant Mean	SD	Total	Mean difference IV, fixed effects (95% CI)
Arndt et al,[28] 2015 (acquired)	15	5.8	9	40.5	17.3	9	-25.50 (37.42 to -13.58)
Arndt et al,[28] 2015 (congenital/perilingual)	32.5	19.9	4	41.5	10.5	4	-9.00 (-31.05 to 13.05)
Rahner and Plontke,[34] 2016	29	22	4	71	10.7	4	-42.00 (-65.97 to -18.03)
Távora-Vieira and Rajan,[26] 2016	43	30	2	63	8	2	-20.00 (-63.03 to 23.03)
Total (95% CI)			**19**			**19**	**-24.78 (-34.16 to -15.40)**

Heterogeneity: $I^2 = 10\%$ (χ^2 $P = .26$)
Effect size: $z = 5.18$



Root-mean-square localization error is the outcome unit. Results of Arndt et al[28] are stratified according to the original article reporting. Boxes indicate relative sample size; diamonds, overall mean difference; IV, inverse variance model; and horizontal lines, 95% CIs.

Device Use and Duration of Deafness

Eleven studies[27-29,31,32,35-40] reported on both the duration of deafness and the frequency of device use after a median (IQR) follow-up of 1.6 (1-2.1) years. To capture device use, 3 of the studies[27,33,35] reported device data logging (n = 36). Of 101 children, most (75 [74.3%]) used the device regularly. The remaining 21 children (20.8%) reported limited device use, and 5 (4.9%) became nonusers. Nonuse was explained by the lack of advantage (n = 3),[28,37,38] unpleasant electrical stimulation (n = 1),[36] and lack of adequate family support (n = 1).[27] The median (IQR) duration of deafness among nonusers was statistically significantly longer than the duration of deafness of limited users (9.0 [5.8-11.7] years vs 3.3 [1.2-5.4] years; median difference, 5.75; 95% CI, 2.45-9.05) and regular users (9.0 [5.8-11.7] years vs 2.2 [1.1-5.3] years; median difference, 6.84; 95% CI, 4.02-9.58) (eFigure in the Supplement). The mean (SD) implantation age of nonusers was statistically significantly older than the implantation age of limited users (9.3 [3.3] years vs 4.1 [3.4] years; MD, 5.21; 95% CI, 1.70-8.70) and regular users (9.3 [3.3] years vs 6.0 [3.4] years; MD, 3.26; 95% CI, 0.18-6.42).

Discussion

Cochlear implantation for children with SSD has been performed worldwide for several years. However, comprehensive clinical data that evaluate the outcomes are scant. Only 1 systematic review of 5 studies[41] and 1 nonsystematic review[42] are available in the literature and both were published before the 2019 Food and Drug Administration approval for this indication in the US.[15]

Results of the present systematic review show that most children (79.6%) experienced improved speech perception in noise after cochlear implantation, which was clinically meaningful according to the study authors.[27,28,30,32,34,36-38] Two studies,[28-32,34,36,37] however, emphasized the lack of improvement among children with congenital SSD who received an implant after age 4 years. In addition, these studies reported a high prevalence of CMV-related SSD, which was possibly a factor in inferior outcomes.[28,37,43-45] The heterogeneity of demographic and clinical factors within small cohorts may have also had implications for the outcomes, as suggested by Deep et al.[27]

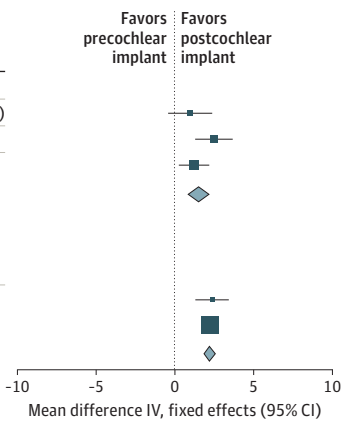
In this review, 4 studies[26,27,31,38] reported implant-associated changes for most children, such as higher scores in speech perception in quiet, whereas 3 studies[29,34,36] indicated that only children with shorter duration of deafness (<4-7 years) acquired a clinically significant speech recognition improvement after implantation. Shorter duration of deafness in the ear without an implant was recognized as advantageous in a previous multicenter clinical trial by Peters et al,[46] which found that, among children who underwent sequential bilateral cochlear implants, the duration of less than 4 years in between implants was associated with faster and greater degree of improvements in speech perception in quiet. Studies of sequential bilateral cochlear implants in children reported mean preoperative speech perception in quiet outcome of 0% to 17% with monaural hearing aid-only condition, increasing to mean speech perception in quiet outcome of 40% to 100% after 3 months to 1 year of a second implant.[46,47] The studies in this review reported that the cochlear implantation–only condition mean preoperative speech perception in quiet scores were between 0% to 36%,[27,38] increasing to mean postoperative speech perception in quiet scores of 30% to 100%.[26,27,29,31,36,38] The comparability in the cochlear implantation–only speech perception in quiet outcome between children with SSD and conventional cochlear implantation candidates suggests that the presence of normal hearing in the contralateral ear (either after the implant normalizing hearing thresholds in 1 ear or in the setting of SSD) did not impair the performance of the device. This finding is contrary to those in some adult studies, which suggest that cochlear implantation for people with SSD is associated with inferior performance in the cochlear implant–only condition.[48,49]

Most children (55 of 62 children [88.7%] in whom sound localization was assessed) also showed improvement in sound localization 1 to 2 years after cochlear implantation. Although not all studies reached individual statistical significance, largely owing to their small sample size, the present meta-analysis detected a clinically and statistically significant improvement. We identified a statistically significant decrease of 24.78° in RMS localization error, with postimplantation means that ranged from 15° to 43° RMS, which was comparable to the RMS in children with bilateral implants.[50] Evaluating 127 children with bilateral implants, Killan et al[50] identified shorter interimplant inter-

Figure 3. Meta-analysis Forest Plots of Mean Differences in Scores on Speech, Spatial, and Qualities (SSQ) of Hearing Stratified by Congenital vs Acquired Single-Sided Deafness

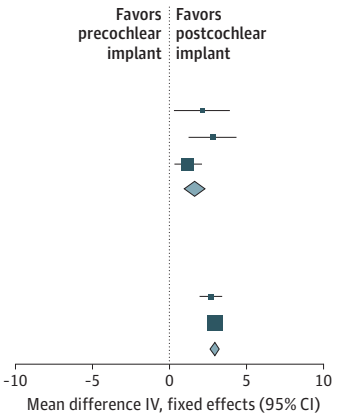
A Patient-reported speech hearing

Study	Postcochlear implant Mean	SD	Total	Precochlear implant Mean	SD	Total	Mean difference IV, fixed effects (95% CI)
Speech hearing (congenital)							
Beck et al,[29] 2017: SSQ speech—parent (congenital)	7.1	1.5	9	6.1	1.5	9	1.00 (-0.39 to 2.39)
Ramos-Macías et al,[31] 2019: SSQ speech—parent (congenital)	8.25	0.9	4	5.75	0.6	4	2.50 (1.44 to 3.56)
Thomas et al,[37] 2017: SSQ speech—parent (congenital)	8.25	1.1	19	7	1.4	9	1.25 (0.45 to 2.05)
Subtotal (95% CI)			**32**			**32**	**1.58 (1.00 to 2.16)**
Heterogeneity: $I^2 = 44\%$ Effect size: $z = 4.23$ ($P < .001$)							
Speech hearing (acquired)							
Arndt et al,[28] 2015: SSQ speech—child (acquired)	7.3	0.9	7	4.9	1.1	7	2.40 (1.35 to 3.45)
Ramos-Macías et al,[31] 2019: SSQ speech—parent (acquired)	8.25	0.75	19	6	0.5	19	2.25 (1.84 to 2.66)
Subtotal (95% CI)			**26**			**26**	**2.27 (1.89 to 2.65)**
Heterogeneity: $I^2 = 0\%$ Effect size: $z = 11.76$ ($P < .001$)							



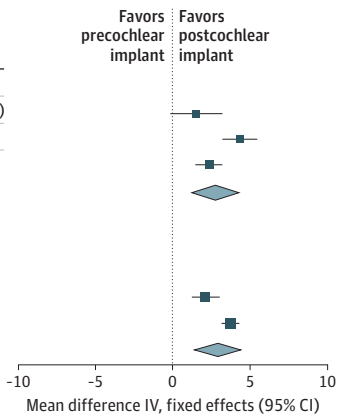
B Patient-reported spatial hearing

Study	Postcochlear implant Mean	SD	Total	Precochlear implant Mean	SD	Total	Mean difference IV, fixed effects (95% CI)
Spatial hearing (congenital)							
Beck et al,[29] 2017: SSQ spatial—parent (congenital)	5.7	2.2	9	3.6	1.7	9	2.10 (0.28 to 3.92)
Ramos-Macías et al,[31] 2019: SSQ spatial—parent (congenital)	7.8	1.5	4	5	0.5	4	2.80 (1.25 to 4.35)
Thomas et al,[37] 2017: SSQ spatial—parent (congenital)	8.2	1.3	19	7	1.5	19	1.20 (0.31 to 2.09)
Subtotal (95% CI)			**32**			**32**	**1.68 (0.96 to 2.39)**
Heterogeneity: $I^2 = 40\%$ Effect size: $z = 4.62$ ($P < .001$)							
Spatial hearing (acquired)							
Arndt et al,[28] 2015: SSQ spatial—child (acquired)	6.1	0.7	7	3.4	0.7	7	2.70 (1.97 to 3.43)
Ramos-Macías et al,[31] 2019: SSQ spatial—parent (acquired)	9	0.5	19	6	0.5	19	3.00 (2.68 to 3.32)
Subtotal (95% CI)			**26**			**26**	**2.95 (2.66 to 3.24)**
Heterogeneity: $I^2 = 0\%$ Effect size: $z = 19.84$ ($P < .001$)							



C Patient-reported hearing quality

Study	Postcochlear implant Mean	SD	Total	Precochlear implant Mean	SD	Total	Mean difference IV, fixed effects (95% CI)
Hearing quality (congenital)							
Beck et al,[29] 2017: SSQ hearing—parent (congenital)	7.8	1.6	9	6.3	2	9	1.50 (-0.17 to 3.17)
Ramos-Macías et al,[31] 2019: SSQ hearing—parent (congenital)	8.5	0.8	4	4.2	0.6	4	4.30 (3.19 to 5.41)
Thomas et al,[37] 2017: SSQ hearing—parent (congenital)	8.6	1.3	19	6.3	1.4	19	2.30 (1.44 to 3.16)
Subtotal (95% CI)			**32**			**32**	**2.77 (1.20 to 4.33)**
Heterogeneity: $I^2 = 81\%$ Effect size: $z = 3.47$ ($P < .001$)							
Hearing quality (acquired)							
Arndt et al,[28] 2015: SSQ hearing—child (acquired)	8	1	7	5.9	0.7	7	2.10 (1.20 to 3.00)
Ramos-Macías et al,[31] 2019: hearing—parent (acquired)	9	1	19	5.3	0.8	19	3.70 (3.12 to 4.28)
Subtotal (95% CI)			**26**			**26**	**2.94 (1.37 to 4.51)**
Heterogeneity: $I^2 = 88\%$ Effect size: $z = 3.68$ ($P < .001$)							



Boxes indicate relative sample size; diamonds, overall mean difference; IV, inverse variance model; and horizontal lines, 95% CIs.

val, later deafness onset, prolonged experience with 2 devices, and a MED-EL device as statistically significantly associated with superior localization abilities. Although the small sample size in the present study precluded us from performing a similar linear regression analysis as that in the Killan et al[50] study, it is possible that 1 or more of the factors they found had implications for the wide range of localization abilities.

Four studies evaluated patient-reported outcomes with the SSQ questionnaire. Caregivers filled out the questionnaire in 3 studies,[29,31,37] and children filled it out in 1 study.[28]

Results of this study suggest that children with congenital SSD had inferior results on patient-reported auditory performance questionnaires compared with children with acquired SSD. In addition, among those who completed the SSQ questionnaire, patients with acquired SSD had substantially shorter

duration of deafness than those with congenital SSD, suggesting that longer duration of deafness may be associated with the worse patient-reported outcomes in the congenital SSD group. Early auditory stimulation is important in the development and maturation of the auditory cortex; with lack of appropriate stimulation, children with long duration of congenital deafness show abnormal cortical response latencies when they undergo cochlear implantation.[51,52] Patients with acquired hearing loss likely have shorter duration of hearing loss and more timely intervention compared with patients with congenital hearing loss.[28,31] Subsequently, with known worse implant performance in long-standing untreated congenital hearing loss, it is not too surprising that patients with acquired hearing loss performed better on auditory performance questionnaires in the studies we reviewed. As a correlate, results of this study show that children with longer duration of deafness were more likely to be nonusers of implants. Because longer duration of deafness was associated with inferior outcomes, children likely perceived less value, which may have been a factor in nonuse. Half of the nonusers in this review cited the lack of improvement as a reason for not using their device.

An overarching theme suggested by these findings is that shorter duration of deafness, ranging from less than 4 to 7 years, is associated with greater postimplantation improvement in both audiological and patient-reported outcomes in children with SSD. These findings are comparable to results in children with bilateral congenital deafness. Ample data and an overall agreement support that children with bilateral congenital deafness gain the most advantage when cochlear implantation occurs within a sensitive period of central auditory development, during which auditory neuronal pathways are at maximal plasticity.[53,54] Cortical auditory responses were shown to reach normal range in children who received an implant before age 3.5 years, and abnormal responses were observed in children who received an implant after age 7 years, even after long-term implant use.[53,55-58] These electrophysiological findings also correlate with speech and language performance studies that found children who underwent cochlear implantation before age 3 to 4 years, or those with shorter duration of deafness, achieved substantially better speech perception scores and language skills vs children who received an implant after age 5 to 7 years.[59-62]

However, data on the association of implantation age and duration of deafness with auditory pathway reorganization, as well as with audiological outcomes, after cochlear implantation in children with unilateral hearing loss are limited and inconclusive. Polonenko et al[39] identified restored cortical organization after implantation, and 6 months of device use, before age 3.6 years in 5 children with CMV- and enlarged vestibular aqueduct–related SSD. Sharma et al[63] also reported cortical reorganization in a child with progressive idiopathic SSD from age 5 who underwent cochlear implantation at age 9.86 years. These authors[39,63] hypothesized that either the patient's prior experience with sound in the deaf ear (owing to the progressive nature of the hearing loss) or stimulation through crossed pathways from the normal hearing ear would explain the favorable results at this late age. Neither of these 2 studies offered definitive conclusions regarding the optimal age or duration of deafness for implantation.

A 2018 systematic review of 8 studies that included 78 adults with postlingual SSD concluded that longer duration of deafness had a substantial negative correlation with speech perception outcomes.[64] Although a lack of postimplantation improvement after 10 years of deafness was witnessed, only 5 patients were followed for that length of time, and the authors concluded that no specific time cutoffs for cochlear implantation could be inferred.[64] The present study emphasizes the need for more robust research that seeks to identify the optimal cochlear implantation age and the duration of deafness that could prohibit favorable outcomes in children with SSD.

Limitations

This study has limitations. It selected studies with small sample sizes. It also was unable to control for the heterogeneity of the pediatric SSD population, including deafness cause, onset and duration, age at implantation, device manufacturers, and extent and availability of social and rehabilitative support systems. The limitations of the quantitative syntheses included the use of study-level data when individual patient data were not available. The use of variable tests and configurations to evaluate audiological outcomes suggests further between-study heterogeneity. However, only studies with comparable outcomes and design were included in the meta-analysis. This approach, although not free from pitfalls, allowed a clearer result interpretation than could be achieved with a qualitative review and was used in previous meta-analyses of adults with hearing loss.[65,66] In addition, previous works have suggested that, other than duration of deafness and implantation timing (which are 2 of the most important outcome determinants in pediatric cochlear implant recipients[62,67,68]), comorbid conditions, such as inner ear malformations and genetic mutations, have implications for the outcomes.[69-72] Unfortunately, inconsistent reporting of comorbidities and their direct association with outcomes and device use rates in the studies that we examined precluded us from offering a comorbidity analysis. With sufficient sample size, this topic should be analyzed in future research on the cochlear implant SSD pediatric population.

Conclusions

This systematic review and meta-analysis found that, among children with SSD, cochlear implantation was associated with improved objective and subjective auditory outcomes. Children with acquired SSD and shorter durations of deafness, however, reported experiencing greater advantages and were less likely to become nonusers of implant devices. These results can be used to guide research efforts, refine cochlear implantation candidacy criteria, and aid in family counseling and shared decision-making. The heterogeneity and small sample sizes of the included studies emphasize the need for robust clinical studies.

ARTICLE INFORMATION

Accepted for Publication: August 30, 2020.

Published Online: November 5, 2020. doi:10.1001/jamaoto.2020.3852

Author Contributions: Drs Cohen and Benchetrit had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Benchetrit, Ronner, Cohen.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Benchetrit, Ronner.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Benchetrit, Ronner.
Obtained funding: Benchetrit.
Administrative, technical, or material support: Benchetrit.
Supervision: Benchetrit, Anne, Cohen.

Conflict of Interest Disclosures: Dr Cohen reported receiving grants from MED-EL outside the submitted work. No other disclosures were reported.

Disclaimer: Dr Anne is Patient Page Section Editor of *JAMA Otolaryngology–Head & Neck Surgery* but was not involved in any of the decisions regarding review of the manuscript or its acceptance.

Additional Contributions: Judy Spak, MS, Yale University School of Medicine, provided assistance with building the literature search strategy and conducting the search. She received no additional compensation, outside of her usual salary, for her contributions.

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