Published in final edited form as:

Otolaryngol Head Neck Surg. 2014 July ; 151(1): 29–41. doi:10.1177/0194599814526561.

Societal-level Risk Factors Associated with Pediatric Hearing Loss: A Systematic Review

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Abstract

Objective—To determine if the current body of evidence describes specific threshold values of concern for modifiable societal-level risk factors for pediatric hearing loss, with the overarching goal of providing actionable guidance for the prevention and screening of audiological deficits in children.

Data Sources—Three related systematic reviews were performed. Computerized PubMed, Embase, and Cochrane Library searches were performed from inception through October 2013 and were supplemented with manual searches.

Review Methods—Inclusion/exclusion criteria were designed to determine specific threshold values of societal-level risk factors on hearing loss in the pediatric population. Searches and data extraction were performed by independent reviewers.

Results—There were 20 criterion-meeting studies with 29,128 participants. Infants less than 2 standard deviations below standardized weight, length, or body mass index were at increased risk. Specific nutritional deficiencies related to iodine and thiamine may also increase risk, although data are limited and threshold values of concern have not been quantified. Blood lead levels above 10 µg/dL were significantly associated with pediatric sensorineural loss, and mixed findings were noted for other heavy metals. Hearing loss was also more prevalent among children of socioeconomically disadvantaged families, as measured by a poverty income ratio less than 0.3 to 1, higher deprivation category status, and head of household employment as a manual laborer.

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

Author Contributions

Adam P. Vasconcellos, acquisition of data, analysis and interpretation of data, drafting and editing manuscript, final approval; **Stephanie Colello**, acquisition of data, drafting of manuscript, final approval; **Meghann E. Kyle**, acquisition of data, analysis and interpretation of data, input into methods and results, final approval; **Jennifer J. Shin**, analysis and interpretation of data, acquisition of data, drafting and editing manuscript, final approval.

Disclosures

Competing interests: Jennifer J. Shin receives royalties from book publications: *Evidence-based Otolaryngology* (Springer International, 2008, 2010), *Otolaryngology Prep and Practice* (Plural Publishing, 2013).

Sponsorships: None.

Supplemental Material

Additional supporting information may be found at www.otojournal.org/supplemental

Conclusions—Increasing our understanding of specific thresholds of risk associated with causative factors forms the foundation for preventive and targeted screening programs as well as future research endeavors.

Keywords

hearing loss; child; infant; adolescent; pediatric; risk factor

Introduction

Hearing loss is the most common communicatively handicapping disorder and may potentiate delays in language, social, and behavioral development in children.¹ Associated needs for special education, amplification devices, and missed parental work have inevitable ramifications beyond the directly affected family unit,² and the expected lifetime cost for a single prelingually deafened child exceeds \$1,000,000.³ Even children who are not severely affected may have increased risk of grade failure, behavioral problems, and difficulty with interpersonal interactions and require a substantial financial investment.^{1,2,4} Thus, pediatric hearing loss has a large impact from both a societal and economic perspective.

Furthermore, the prevalence of hearing loss during childhood appears to be increasing over time,⁵⁻⁷ raising concern for an even larger societal and economic impact to come. Recent data from the National Health and Nutrition Examination Survey (NHANES) suggest that prevalence has increased from 15% to 20% over less than a decade. In addition, while risk may be elevated in some ethnic subgroups,^{8,9} hearing loss is a disorder that can affect any segment of the human population.

It would thus behoove us as a community to consider whether mechanisms exist whereby these effects might be mitigated through efforts to preempt or arrest the progression of audiological deficits. In other disorders, careful study of risk factors for disease has formed the foundation for highly successful preventive programs. For example, the incidence of goiter formation has been greatly diminished by the introduction of iodine into table salt,¹⁰ while dental public health has been markedly improved by widespread water fluoridation.¹¹ While we currently have limited capacity to change the inherent nature of genetics, certain sequelae of hearing-related infections, or the necessity for ototoxic but life-sparing medical interventions, other risk factors for hearing loss may be responsive to a preemptive approach.

With such future potential for preventive measures in mind, our goal was to determine what risk factors for hearing loss might ultimately be addressed in order to promote improvement in hearing-related pediatric health. We have therefore considered aspects that are modifiable at a personal and societal level via systematic review. Systematic reviews provide a reproducible, thorough method to evaluate the current best evidence regarding a specific clinical question and often constitute the highest level of evidence available.¹²⁻¹⁴ The current article focuses on risk factors that may require larger, society-level forces for modification, while personal-level factors have been addressed in a sister analysis.¹⁵ More specifically, this systematic review addresses the impact of quantifiable changes in nutrition, heavy metal exposure, and socioeconomic status.

Methods

Search Strategy

A series of computerized searches were performed to identify all relevant data. At the outset, a computerized PubMed search of MEDLINE (1966 to February 2013) was performed to evaluate studies assessing risk factors for hearing loss in children in overview. Articles that mapped to the medical subject heading *hearing loss* (exploded) or contained *hearing loss* in the title were collected into one group. Next, articles mapping to the medical subject headings *risk factors* (exploded) or *longitudinal studies* (exploded) or containing the keywords *risk* or *prospective* were collected in a second group. Articles that mapped to the medical subject headings *child*, *infant*, *adolescent*, or *pediatrics* (all exploded) or contained these terms in any field collected into a third group. The 3 groups were then cross-referenced and limited to those with human subjects and English language. The studies were then limited to those that utilized the word cohort and did not focus solely on cochlear implant recipients. This initial computerized search yielded 2942 studies, which were reviewed to determine which risk factors warranted additional dedicated study.

Based on the results of the aforementioned review, subsequent computerized searches of PubMed, Embase, and the Cochrane Library (inception to October 2013) were performed that focused on the specific areas of nutrition, lead and other heavy metal exposure, and socioeconomic status. Within PubMed, the following search strategy was utilized: Articles that mapped to the medical subject heading *hearing loss* (exploded) or contained *hearing loss* in the title were collected into one group. Articles that mapped to the exploded medical subject headings nutritional status; nutritional deficiencies; vitamins; heavy metal poisoning, nervous system; poisoning; or *socioeconomic status* (all exploded) were collected into a second group. Articles that mapped to the exploded medical subject headings or text words *child*, *infant*, *adolescent*, or *pediatrics* or contained these terms in any field were collected into a third group. The 3 groups were then cross-referenced and limited to those with human subjects and English language. Studies that focused solely on outcomes after cochlear implant were not included. Parallel searches were performed in Embase and the Cochrane Library. Independent searches were performed in duplicate among 3 separate reviewers. This search yielded 5928 studies.

The titles of all of the studies from these combined search methods were evaluated according to the a priori inclusion/exclusion criteria described in the following. This title evaluation then yielded 148 potential abstracts, which were reviewed in more detail according to the same criteria. Subsequently, 44 full articles were evaluated against a priori criteria in detail (**Figure 1**).

Inclusion and Exclusion Criteria

The articles identified by the computerized search strategy described previously were evaluated to identify those that met the following inclusion criteria: (1) average study participant age 18 years or younger, (2) risk factors for permanent hearing loss evaluated (nutrition, lead and other heavy metals, and/or socioeconomic status), (3) comparison made between exposure to environmental risk factor and no/minimal exposure, and (4) hearing

loss clearly defined (mild, moderate, severe, or profound; unilateral or bilateral). Articles were excluded if (1) adults and pediatric data were combined such that pediatric data could not be reviewed distinctly; (2) age at the time of analysis was not specifically described; (3) nonpermanent hearing loss was primarily assessed, such as hearing loss from acute otitis media, otitis media with effusion, or recent trauma; (4) hearing loss was not clearly defined, such as parent surveys to assess possible hearing impairment of their children without accompanying audiological measurements; or (5) exposures found to be a result of receiving indicated medical treatment, such as receipt of ototoxic medications, hearing loss attributed to a stay in the neonatal intensive care unit, or receipt of extracorporeal membrane oxygenation.

The socioeconomic metric was selected a priori as a standard measure defined by the Centers for Disease Control and utilized by the World Health Organization and the US Department of Health and Human Service's *Healthy People 2020*. It is defined as “a composite measure that typically incorporates economic, social, and work status. Economic status is measured by income. Social status is measured by education, and work status is measured by occupation. Each status is considered an indicator.”¹⁶

Data Extraction

Data extraction was focused on items relevant to the study results, potential sources of heterogeneity among those results, and study identification (author, year of publication, full reference citation). Extracted data included (1) the number of subjects in each group, (2) the number/percentage with hearing loss in each group, and (3) the *P*-value, confidence interval, or descriptive statistics reported. In addition, potential sources of heterogeneity among studies were included: (1) age at outcome of measurement, (2) definition of environmental risk factor assessed, (3) definition of any relevant control group, (4) audiological criteria used for stratification of data, and (5) study design. Two reviewers experienced in systematic reviews evaluated the data independently using standardized tables. In the instance of multiple studies emanating from a common database, the sample size from the study with the largest number of subjects was utilized toward the total patient count estimate, so as to avoid duplicate counts.

Quantitative Data Analysis

The primary outcome measure was risk of pediatric hearing loss as associated with nutrition, lead and other heavy metals, and/or low socioeconomic status. An a priori plan was made to perform a meta-analysis if study designs and outcome measures had sufficient homogeneity. The final results set, however, had too much heterogeneity to support numerical pooling of data.

Results

Study Characteristics

This search criteria yielded 20 criterion-meeting papers ($n = 29,128$ subjects) that assessed the potential impact of nutrition and vitamin deficits, lead and additional heavy metals exposure, and/or low socioeconomic status on pediatric hearing loss. These eligible studies

included 15 cross-sectional studies, 3 cohort studies, 1 prospective observational random population sample, and 1 case series. Exposure to a given risk factor was assessed by quantitative measurements in 13 studies and by self-report in 7 studies.

Impact of Nutrition on Pediatric Hearing Loss

Generalized undernutrition—Two cross-sectional studies explored undernutrition as a risk factor for pediatric hearing loss (**Table 1** and appendix at www.otojournal.org).^{17,18} The first assessed hearing loss in a population of infants (n = 3386) ages 0 to 3 months in inner-city Lagos, Nigeria. The authors defined undernutrition as an infant having a z-score <2 standard deviations below any of 3 indices (weight-for-age, length-for-age, or body mass index for age) and hearing loss as a threshold of >30 dB in at least 1 ear. Infants with any undernourished physical state were significantly more likely to have severe-profound sensori-neural hearing loss than infants without any undernourishment.¹⁷ The second publication built upon these results and added weight-for-length as a fourth index. It also encompassed a larger total study population (n = 6585) and also demonstrated that early-onset permanent hearing loss was significantly more prevalent among undernourished infants.¹⁸

Iodine and thiamine deficiencies—One cross-sectional study and 1 case series explored specific nutritional deficiencies and their potential impact on pediatric hearing loss (**Table 2** and appendix at www.otojournal.org). The cross-sectional study suggested that hearing thresholds were worse among children at risk of mild to moderate iodine deficiency, with a statistically significant correlation between hearing at 4000 Hz and urine iodine levels.¹⁹ The case series was small (n = 11) and examined infants with thiamine deficiency resulting in pediatric intensive care unit admission. This retrospective study suggested a prevalence of hearing loss and auditory neuropathy of 27.3% to 45.5% among affected infants.²⁰ These patients were treated with thiamine supplementation and their postintervention hearing was evaluated in comparison, showing improvement to bilateral normal audiometry in 5 of 11 cases.

Impact of Lead and Other Heavy Metals on Pediatric Hearing Loss

Lead exposure—Five cross-sectional studies and 1 prospective observational random population sample assessed the impact of lead exposure on pediatric hearing loss (**Table 3** and appendix at www.otojournal.org). All studies assessed the relationship between blood lead levels (BLL) and hearing thresholds, and the preponderance of data suggest a significant association.

One study reported data from the Hispanic Health and Nutrition Examination Survey (HHANES) of children ages 6 to 19 (n = 3262) and demonstrated an associated risk of worse hearing thresholds at all frequencies tested in the left ear and all but 4000 Hz in the right ear²¹; an increase in BLL from 6 µg/dL to 18 µg/dL was associated with a small but measureable hearing loss in all frequencies, and there was a 15% additional risk for hearing threshold compromise at 2000 Hz. In a second publication, adolescents from NHANES 2005-2006 and 2007-2008 (n = 2535) demonstrated an increased odds of high frequency hearing loss if BLL were higher than 2 µg/dL. There was, however, no association between

BLL by quartile in either low or high frequency hearing loss, suggesting that the response may not be overtly dose-dependent.²² The third cross-sectional study showed that children with BLL ≥ 10 $\mu\text{g}/\text{dL}$ had a significantly higher hearing threshold than those with BLL <10 $\mu\text{g}/\text{dL}$.²³ The fourth cross-sectional study correlated increasing BLL with worse pan-frequency hearing thresholds in children on multivariate analysis ($P < .001$). When only children with BLL below 100 $\mu\text{g}/\text{L}$ were analyzed, increased lead levels continued to have a significant impact on the hearing thresholds in all multiple regression models ($P < .001$ -.012, left ear: $P < .001$ -.015, right ear).²⁴ The fifth cross-sectional study was small ($n = 14$) and compared audiologic results in pediatric patients with BLL ranging 33.4 to 118.2 $\mu\text{g}/\text{dL}$ as compared to a historical control and noted a tendency toward diminished distortion product otoacoustic emissions (DPOAEs) with high BLL, but consistent correlations were not observed.²⁵

The single prospective observational study concluded that there was no difference between BLL and hearing thresholds.²⁶ The study population consisted of Ecuadorian children (age 4-15 years) living in a lead-contaminated area, as compared to a control region. The median lead level for the exposure group was 52.6 $\mu\text{g}/\text{dL}$ (range, 9.9-110.0), while it was 6.4 $\mu\text{g}/\text{dL}$ (range, 3.9-12.0) in the control group. Thus, the exposure level in the control group overlaps that of the exposure groups in several of the aforementioned cross-sectional studies.

Other heavy metals exposure.—One cross-sectional study, 1 prospective cohort, 1 prospective observational random population sample, and 1 retrospective cohort assessed the effect of other heavy metals such as mercury, arsenic, and cadmium (Table 4 and the appendix at www.otojournal.org). Data regarding mercury were mixed. In a cross-sectional study of NHANES 2005-2006 ($n = 2535$, ages 12-19 years), blood mercury levels were not significantly associated with hearing loss.²² In contrast, a prospective cohort study ($n = 859$) measured intrauterine methylmercury levels via cord blood and auditory thresholds at 14 years of age and demonstrated a significant association between intrauterine mercury exposure and elevated hearing thresholds at 4 kHz, as well as auditory brainstem response (ABR) latencies (peaks III and V).²⁷ Meanwhile, a prospective observational random population sample ($n = 62$) of children (ages 4-15 years) observed no correlation between high frequency auditory thresholds and blood mercury levels.²⁶

Data regarding arsenic were also nonuniform. Data from the NHANES study ($n = 875$, 2005-2006 and 2007-2008) showed no association between urine arsenic and hearing loss.²² A retrospective cohort study ($n = 107$, ages 9.5-11 years) showed contrasting results; children residing near a power plant that burned coal with high arsenic content demonstrated significantly higher rates of hearing loss at multiple frequencies, as compared to a control group of age-matched children living outside the polluted area.²⁸

The aforementioned NHANES study also examined cadmium ($n = 878$) levels in quartiles in children 12 to 19 years of age. The highest quartile of cadmium exposure was associated with a significantly increased risk of low frequency hearing loss.²²

Impact of Socioeconomic Factors on Pediatric Hearing Loss

Nine cross-sectional studies and 1 prospective cohort study assessed the impact of socioeconomic factors on pediatric hearing loss.

Poverty income ratio—The poverty income ratio (PIR) is defined as the total family income divided by the poverty threshold as determined by the United States Bureau of the Census for the year of interview. Three reports of cross-sectional studies analyzed PIR in NHANES data, while 1 evaluated data from HHANES (**Table 5** and appendix at www.otojournal.org). A 1998 cross-sectional study of NHANES 1988-1994 explored the impact of poverty levels on pure tone averages (n = 6166, age 6-19 years), separating PIR into low (< 0.3, eligible for government food assistance benefits), middle (1.3 < PIR ≤ 3.5), and high (>3.5) strata. Low-income families had a statistically significant increased prevalence of high frequency hearing loss (16.3%, 95% CI, 13.6%-18.9%) as compared with children of families in the high income bracket (7.9%, 95% CI, 5.1%-10.7%).²⁹ A 2010 study also performed a cross-sectional analysis of NHANES 1988-1994 but defined poverty as PIR <1; utilizing this higher PIR cutoff, this analysis found no significant association between poverty and high frequency hearing loss (OR, 1.37; 95% CI, 0.97-1.93).⁷

A similar analysis using NHANES 2005-2006 (n = 1771), however, did demonstrate a significant association between PIR <1 and increased odds of any hearing loss (23.7% vs 18.4%; OR, 1.60, 95% CI, 1.10-2.32).⁷ An additional study of the NHANES 2005-2006 data set evaluated the risk associated with PIR ≥ 1 in the subset of adolescents with available serum cotinine levels (the study was primarily designed to assess risk of secondhand smoke in youth, n = 1475). Among this subgroup, a bivariate analysis demonstrated no significant association between PIR ≥ 1 and either low or high frequency unilateral or bilateral hearing loss.³⁰

A cross-sectional study analyzing HHANES 1982-1984 data (ages 6-19 years, n = 3262) presented a linear regression model associating family income level with hearing thresholds. Lower family income was associated with elevated hearing thresholds at 4000 Hz for both ears, although not for either ear at 500 Hz. Findings were inconsistent at other frequencies.²¹

Additional socioeconomic measures—A number of other socioeconomic markers were assessed in related studies; 4 of these demonstrated a significant association with hearing loss, while 2 did not (**Table 6** and appendix at www.oto-journal.org). One cross-sectional study (n = 124, age 0-80 months) separated households into “deprivation categories” specific to car ownership, male unemployment, overcrowding, and social class, and a significant association between higher deprivation categories and congenital hearing impairment was reported. The authors suggested these findings could be due to the higher incidence of prematurity and low birth weight found in deprived families, as well as a greater likelihood for families with many hearing-impaired members to be economically disadvantaged.³¹ A second cross-sectional study (n = 145) defined social class by occupation of head of household and demonstrated that lower classes had a significantly higher risk of births with sensorineural hearing loss, particularly among families of manual workers.³² A third cross-sectional study (n = 237, ages 10-17 years) linked household

income of <\$100,000 per year with worse hearing thresholds at 2000 Hz in the left ear and at high frequency pure tone averages in the right ear.³³ A fourth cross-sectional study compared high frequency pure tone averages in impoverished Peruvian schoolchildren (n = 335, ages 6-19 years) with age-matched schoolchildren in the United States and Japan and found that the impoverished group was 4 to 7 times more likely to have hearing loss.³⁴

In contrast, a prospective cohort study observing hearing thresholds at ages 7, 9, and 11 years showed no significant association between “low” housing level (housing obtained via council or via other means, not owned or mortgaged) and mild or high frequency hearing loss. There was also no statistically significant association between maternal social class as defined by maternal occupation (manual vs non-manual labor) and hearing loss.³⁵ Likewise, a 2011 cross-sectional study of infants demonstrated no significant association between early-onset permanent hearing loss and low maternal education level or shared sanitation residence.¹⁸

Discussion

The preponderance of data in this systematic review suggest that there is a significant association between hearing loss and nutritional deficits, elevated blood lead levels, and socioeconomic status. The related results describing specific thresholds of risk factors are limited, but may ultimately help formulate future preventive and management strategies and guide additional related research.

Nutrition

The evidence suggests that generalized undernutrition and iodine deficiency are associated with an increased risk of hearing loss. In addition, thiamine deficiency is likely associated with risk of infantile sensorineural loss, but these data are at a more preliminary stage.

Specific targets have been suggested by studies evaluating general undernutrition. Infants less than 2 standard deviations below mean weight-for-age, length-for-age, body mass index, or weight-for-length have demonstrated risk and may therefore be worthy of more diligent screening or preventive programs.

Hearing-specific targets regarding specific nutritional deficits, however, are not clearly delineated by available evidence. The study evaluating the impact of iodine deficiency utilized urinary levels for screening, so it is difficult to target intake levels directly based on these data. General pediatric daily iodine intake recommendations range from 90 to 150 µg, depending on age,³⁶ and related screening or preventive strategies would currently be limited to targeting these already accepted values. Similarly, the recommended daily thiamine intake in children ranges from 0.2 mg/day in early infancy to 1.2 mg/day for adolescent boys.³⁷ Based on current data, specific thiamine intake goals would be limited to these suggested levels as well.

The data in the current review arise from a variety of national and international study groups and research designs, and it is thus unclear exactly how applicable the results are to patients outside of the populations included in the investigations. The analyses by mean body indices

may be more widely applicable, since sex-specific *z*-scores for nutritional indices were obtained from the World Health Organization Multicentre Growth references.^{17,18,38}

The mechanism by which undernutrition compromises the auditory system has not been firmly established. The specific effects on early onset permanent hearing loss remain largely unstudied, although specific nutritional deficiencies are well documented to cause other sensory impairments (eg, vitamin A deficiency and visual loss).^{17,39} With regard to the mechanism by which iodine deficiency affects hearing, it may be related to neurological development as mild iodine deficits can have subtle effects on the neurologic system.^{19,36} General neurologic and cardiovascular sequelae of thiamine deficiency are well established^{20,40} and may underlie any potential effects on hearing. Limited data have suggested an association between micronutrient or vitamin deficiencies and middle ear disease.⁴¹

Lead and Additional Heavy Metals

The cumulative data support an association between BLL and elevated hearing thresholds, with the majority of studies suggesting a causative relationship, particularly with high frequency hearing loss.²¹⁻²⁵ Data from cross-sectional studies suggest that worse hearing thresholds may occur at BLL below the previous recommended standard of 10 µg/dL.^{21,22} A significant increase in incidence of high frequency hearing loss was noted in adolescents with BLL of at least 2 µg/dL, as compared to those with less than 1 µg/dL in a multivariate analysis.²² Consistent results such as these might ultimately raise the question of whether a lower recommended threshold might be warranted.

One study, a prospective observational analysis, reported no association between high BLL and hearing loss.²⁶ Differences in methodology may account for the prospective observational study's contrasting findings; this study based exposure on a geographic sampling in Peru and utilized a 25 dB threshold for abnormal hearing. There were also higher levels of exposure in the control group, and it was among the smaller of the related studies.

The effect of mercury and arsenic on hearing loss remains unclear as data are mixed. Only one cross-sectional study assessed impact of cadmium exposure on pediatric hearing loss; while the highest quartile of cadmium exposure was associated with a significantly increased risk of low frequency hearing loss, no significant dose response relationship was ultimately observed ($P = .13$).²² These data are also somewhat difficult to place in context as the mean urinary cadmium noted in the US population is more than double the levels measured in the adolescent age group in this cross-sectional study.²²

Limitations in these data include an association of lead exposure with poorer, inner-city children and possible concurrent noise exposure. In addition, data from the NHANES and HHANES cross-sectional studies included measurements of air conduction, under the assumption that high frequency hearing loss noted in the 12- to 19-year-old age group likely represents acquired sensorineural impairment, rather than transient conductive loss from fluid or Eustachian tube dysfunction. In addition, BLL, blood mercury levels, and urine cadmium and arsenic measurements were limited to single spot results, which may not

reflect longitudinal exposure. Sample sizes and associated power are also limited in some studies.

The neurotoxic effects of lead have been widely acknowledged, as demonstrated in studies of IQ and school performance.⁴² While the specific mechanism by which lead affects hearing has not been clearly elucidated, such data suggest it may occur by a neurologic mechanism. Arsenic and cadmium likewise have described general neurotoxic effects, which range from oxidative damage to alteration of synaptic function,⁴³⁻⁴⁹ although the hearing-specific effects have likewise not been mechanistically determined.

Socioeconomic Status

Data regarding socioeconomic status and hearing loss are mixed, but the majority of studies report a significant association between these 2 variables. Reported values suggest that there is an increased risk specifically with PIR of less than 0.3 to 1, higher deprivation categories, household income less than \$100,000, and head of household employment as a manual laborer. In addition, infants born in impoverished countries may be nearly twice as likely to demonstrate hearing loss on screening exams as those born in more developed countries.^{34,50,51}

Multiple authors suggest that lower income or social status may not directly cause hearing loss but be representative of a number of additional confounding factors.⁵¹ Disadvantaged families may also have a higher incidence of prematurity, low birth weight, or undernutrition. In addition, families with many hearing-impaired members may be more likely to be economically disadvantaged due to associated employment limitations, incorporating a potential genetic confounder. There may also be associated disparities in race and maternal age,^{31,32,34} and some authors suggest that children of low socioeconomic status have more “positive attitudes” toward intense levels of sound and did not use hearing protection as frequently.⁵³ In addition, there could be additional related exposure to tobacco, heavy metals, and pollutants.

While the socioeconomic variable itself may be affected by such related confounders, not all studies account for these potential effects through well-described multivariate analyses. In addition, with the exception of PIR, standardized metrics for socioeconomic status were not utilized across studies, limiting direct comparisons. The smaller sample sizes in some reports may also raise concern for limited power, but these analyses actually demonstrated significantly positive results.³¹⁻³⁴

Exploring further specifics within this large category of potential risk might ultimately facilitate guidance in caring for children from disadvantaged families by determining whether they would benefit from more diligent audiology monitoring, educational programs, or other hearing-related interventions.

Summary and Conclusions

Modifiable societal-level risk factors for pediatric hearing loss include nutritional deficiencies, elevated blood lead levels, and disadvantaged socioeconomic status. The current data to support actionable guidance for preventive measures are limited. Establishing

concrete targets to guide primary prevention strategies and screening programs might ultimately include nutritional “checkpoints” in infancy, “hearing-safe” standards for blood lead levels, and a higher index of suspicion or more intensive screening for children from high-risk groups.

Acknowledgments

JJS would like to thank Thomas Y. Lin and the C.H.E.E.R. Network for support during the preparation of this manuscript.

Funding source: None.

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Figure 1.
Flow diagram showing the stages of the identification of studies for the systematic review.

Table 1

Impact of Undernutrition on Pediatric Hearing Loss.

Author, Year	Study Design (sample size)	Age	Nutrition Indicator	Hearing Evaluation	Follow-up Time	Results/Conclusions	Additional Comments
Olusanya, 2011 ¹⁸	Cross-sectional (n = 6585)	0-3 months	z-score less than -2 for any of: weight-for-age, length-for-age, weight-for-length, body mass index	TEOAE, ABR	N/A	Undernourished infants have a significantly higher risk of early onset permanent hearing loss.	Chi-square test, adjusted odds ratio, 95% confidence interval
Olusanya, 2010 ¹⁷	Cross-sectional (n = 3386)	0-3 months	z-score less than -2 for any of: weight-for-age, BMI-for-age, length-for-age	TEOAE, ABR	N/A	Infants with any undernourished physical state were significantly more likely to have severe-profound SNHL than infants without any undernourishment.	Odds ratio, 95% confidence interval, <i>t</i> test

Abbreviations: TEOAE, transient evoked otoacoustic emissions; ABR, auditory brainstem response.

Table 2

Impact of Nutritional Deficiencies on Pediatric Hearing Loss.

Author, Year	Study Design (sample size)	Age	Nutritional Deficiency	Hearing Evaluation	Follow-up Time	Results/Conclusions	Additional Comments
Valeix, 1994 ¹⁹	Cross-sectional (n = 1222)	10 months, 2 yrs, 4 yrs	Iodine	Audiometric threshold PTA	N/A	Hearing loss at 4000 Hz and PTA were more severe among children at risk of mild to moderate iodine deficiency; statistically significant positive correlation between hearing at 4000 Hz and urine iodine levels.	<i>t</i> test
Attias, 2012 ²⁰	Case series (n = 11)	2-5 months	Thiamine	ABR; audiometric threshold PTA	6-8 yrs	Human infantile thiamine deficiency may be uniquely associated with dysfunctions of the cochlea or auditory nerve, and/or auditory brain stem pathways.	Five of 11 exposed infants had transient auditory neuropathy; 3 of 11 children on follow-up had persistent auditory neuropathy

Abbreviations: PTA, pure tone audiometry; ABR, auditory brainstem response.

Table 3

Impact of Lead Exposure on Pediatric Hearing Loss.

Author, Year	Study Design (sample size)	Age	Lead Exposure Measurement	Hearing Evaluation	Follow-up Time	Results/Conclusions	Additional Comments
Counter, 1997 ²⁶	Prospective observational random sample (n = 62)	4-15yrs	Blood lead levels	Audiometric threshold PTA	N/A	There was no significant relationship between SNHL and elevated blood lead levels.	t test; median blood lead level 52.6 µg/dl (range, 9.9-110.0 µg/dl)
Schwartz, 1991 ²¹	Cross-sectional (n = 3262)	6-19 yrs HHANES (1982-1984)	Blood lead levels	Audiometric threshold PTA	N/A	Lead is associated with increased risk of hearing loss at all frequencies in the left ear and all but 4000 Hz in the right ear.	Multiple logistic regression analysis
Shargorodsky, 2011 ²²	Cross-sectional (n = 2535)	12-19 yrs NHANES (2005-2006, 2007-2008)	Blood lead levels	Audiometric threshold PTA	N/A	There is no significant association between individual quartiles of lead exposure and any low or high frequency hearing loss.	Multivariate odds ratio; quartile median values (µg/dL): Q1: 0.47, Q2: 0.67, Q3: 0.94, Q4: 1.59
Abdel Rasoul, 2012 ²³	Cross-sectional (n = 190)	Primary school (specific age not reported)	Blood lead levels	Audiometric threshold PTA	N/A	Students with BLL > 10 µg/dL had significantly higher hearing threshold than those with BLL < 10 µg/dL.	Chi-square test; t test
Osman, 1999 ²⁴	Cross-sectional (n = 155)	4-14 yrs	Blood lead levels	Audiometric threshold PTA	N/A	Hearing thresholds increased significantly with increasing blood lead levels at all frequencies.	Multivariate association; subgroup analysis
Buchanan, 1999 ²⁵	Cross-sectional with historical control (n = 14)	5-14 yrs	Blood lead levels	DPOAE	N/A	There was a tendency toward diminished DPOAEs with high blood lead levels but no consistent correlation was found.	t test comparing DPOAEs of lead exposure group to age-matched controls; blood lead levels range. 33.4-118.2 µg/dl (mean 51.5)

Abbreviations: PTA, pure tone audiometry; SNHL, sensorineural hearing loss; HHANES, Hispanic Health and Nutrition Examination Survey; NHANES, National Health and Nutrition Examination Survey; BLL, blood lead levels; DPOAEs, distortion product otoacoustic emissions.

Table 4

Impact of Other Heavy Metals Exposure on Pediatric Hearing Loss.

Author, Year	Study Design (sample size)	Age	Heavy Metal Exposure Measurement	Hearing Evaluation	Follow-up Time	Results/Conclusions	Additional Comments
Murata, 2004 ²⁷	Prospective cohort (n = 859)	14 yrs	Methylmercury, concentration as measured in cord blood, maternal hair, child's hair	ABR; audiometric threshold PTA	7 yrs, 14 yrs	Intrauterine MeHg exposure was significantly associated at several BAEP latencies, especially peaks III and V Regression coefficients suggested an effect of recent MeHg exposure mainly on III-V interpeak interval. Persistence of prolonged I-III interpeak intervals suggests some neurotoxic effects from intrauterine MeHg exposure are irreversible. Hearing thresholds were associated with in utero MeHg exposure exclusively at 4 kHz in the right ear.	Regression analysis; hearing loss as determined at follow-up examination at age 14 yrs
Counter, 1997 ²⁶	Prospective observational random population sample (n = 62)	4-15 yrs	Mercury, blood levels	Audiometric threshold PTA	N/A	The average high frequency auditory threshold measured at 2, 3, 4, 6, and 8 kHz measured as a function of blood mercury level indicated no correlation between blood mercury level and hearing acuity for either ear.	<i>t</i> test; median blood mercury level 0.16 µg/dl (range, 0.04-0.58)
Shargorodsky, 2011 ²²	Cross-sectional (n = 2535)	12-19 yrs NHANES (2005-2006, 2007-2008)	Mercury, blood levels	Audiometric threshold PTA	N/A	There is no significant association between individual quartiles of mercury exposure and any low or high frequency hearing loss.	Multivariate odds ratio, 95% confidence interval; quartile median values (µg/L): Q1: 0.20, Q2: 0.39, Q3: 0.63, Q4: 1.28
	Cross-sectional (n = 878)	12-19 yrs NHANES (2005-2006, 2007-2008)	Cadmium, urinary levels	Audiometric threshold PTA	N/A	The highest quartile of cadmium exposure was associated with significantly increased risk of low frequency hearing loss.	Multivariate odds ratio, 95% confidence interval; quartile median values (µg/g of creatinine): Q1: 0.04, Q2: 0.07, Q3: 0.10, Q4: 0.15
	Cross-sectional (n = 875)	12-19 yrs NHANES (2005-2006, 2007-2008)	Arsenic, urinary levels	Audiometric threshold PTA	N/A	There is no significant association between individual quartiles of arsenic exposure and any low or high frequency hearing loss.	Multivariate odds ratio, 95% confidence interval; quartile median values (µg/g of creatinine): Q1: 2.8, Q2: 4.29, Q3: 6.33, Q4: 14.75
Bencko, 1977 ²⁸	Retrospective cohort (n = 107)	9.5-11 yrs	Arsenic, concentration in hair samples	Audiometric threshold PTA	N/A	Significant hearing losses were observed at multiple frequency levels with respect to both air and bone conduction, associating arsenic exposure with hearing loss.	Chi-square test; exposed group: residence near coal-burning power plant

Abbreviations: ABR, auditory brainstem response; PTA, pure tone audiometry; BAER brainstem auditory evoked potential; NHANES, National Health and Nutrition Examination Survey.

Table 5
Impact of Socioeconomic Status by Poverty Income Ratio on Pediatric Hearing Loss.

Author, Year	Study Design (sample size)	Patient Description	Socioeconomic Indicator	Hearing Evaluation	Follow-up Time	Results/Conclusions	Additional Comments
Niskar, 1998 ²⁹	Cross-sectional (n = 6166)	Age 6-19 yrs NHANES (1988-1994)	Poverty income ratio	Audiometric threshold PTA	N/A	Children from low-income families had a statistically significantly increased prevalence of HFHL (16.3%), as compared to either children from middle-income families (12.7%) or high-income families (7.9%).	No family income data available for 8.6% (n = 529) of children tested
Lalwani, 2011 ³⁰	Cross-sectional (n = 1475)	Age 12-19 yrs NHANES (2005-2006)	Poverty income ratio	Audiometric threshold PTA	N/A	The data do not suggest a strong association between adolescent hearing loss and poverty as defined by poverty income ratio.	Secondary outcome measurement for a study with primary outcome of assessing secondhand smoke and hearing loss in adolescents
Shargorodsky, 2010 ⁷	Cross-sectional (n = 1771)	Age 12-19 yrs NHANES (2005-2006)	Poverty income ratio	Audiometric threshold PTA	N/A	A PIR < 1 was significantly associated with increased odds of any hearing loss as compared with a PIR of 1 or greater.	Multivariate logistic regression analysis
Shargorodsky, 2010 ⁷	Cross-sectional (n = 2928)	Age 12-19 yrs NHANES (1988-1994)	Poverty income ratio	Audiometric threshold PTA	N/A	There was no significant association between PIR and hearing loss.	Multivariate logistic regression analysis

Abbreviations: NHANES, National Health and Nutrition Examination Survey; PTA, pure tone audiometry; HFHL, high frequency hearing loss; PIR, poverty income ratio.

Table 6

Impact of Socioeconomic Status (by other measures) on Pediatric Hearing Loss.

Author, Year	Study Design (sample size)	Patient Description	Socioeconomic Indicator	Hearing Evaluation	Follow-up Time	Results/Conclusions	Additional Comments
Hall, 2011 ³⁵	Prospective cohort (n = 4257, maternal social class; n = 4901 housing level)	Age 11 yrs	Maternal social class Housing level	Audiometric threshold PTA	2 yrs, 4 yrs	No statistically significant association between mild or high frequency hearing loss and maternal social class (defined by occupation: manual or non-manual labor) or housing level.	Hearing loss had to be present at each time point measured or the last 2 time points
Schwartz, 1991 ²¹	Cross-sectional (n = 3262)	Age 6-19 yrs HHANES (1982-1984)	Family income levels	Hearing thresholds, ANSI standard	N/A	Family income was associated with worse thresholds at 4 kHz for both ears, not for either ear at 500 Hz, and inconsistent at other frequencies.	Linear regression analysis
Olusanya, 2011 ¹⁸	Cross-sectional (n = 2254)	Age 0-3 months	Low maternal education level Shared sanitation residence	TEOAE, ABR; visual response audiometry	N/A	No significant association between low maternal education level or shared sanitation residence and EPHL among an undernourished newborn population in inner-city Lagos, Nigeria.	Undernourished defined as z-score < -2 for weight-for-age, length-for-age, weight-for-length, or body mass index
Sutton, 1997 ³²	Cross-sectional (n = 145)	Specific age range not specified; approximately ages 0-6 yrs	Social class as per head of household	Audiometric threshold PTA	N/A	Lower social classes had significantly higher risk of SNHL; more SNHL births were observed in families of semi-skilled and skilled manual workers in comparison to the reference population.	Significant confounding associations included Asian ethnicity, maternal age.
Marcoux, 2012 ³³	Cross-sectional (n = 237)	Age 10-17 yrs	Household income	Audiometric threshold PTA	N/A	Household income of < \$100,000/yr was statistically significantly associated with worse hearing thresholds at 2 kHz in the left ear and at HFPTA in the right ear.	N = 187 analyzed at HFPTA; n = 184 analyzed at 2 kHz
Kubba, 2004 ³¹	Cross-sectional (n = 124)	Age 0 to approximately 80 months	Poverty defined by 7 "deprivation categories"	Audiometric threshold PTA	N/A	Deprivation was significantly associated	Family history of deafness, low birth weight, and

Author, Year	Study Design (sample size)	Patient Description	Socioeconomic Indicator	Hearing Evaluation	Follow-up Time	Results/Conclusions	Additional Comments
Czechowicz, 2010 ³⁴	Cross-sectional (n = 335)	Age 6-19 yrs	Living in an impoverished Peruvian district, compared to US and Japan	Audiometric threshold PTA	N/A	with congenital hearing impairment. Impoverished Peruvian schoolchildren were 4 to 7 times more likely to experience hearing loss than children living in higher-income countries.	prematurity were associated with worse deprivation Hearing loss totals include sensorineural, mixed, and conductive hearing loss

Abbreviations: PTA, pure tone audiometry; HHANES, Hispanic Health and Nutrition Examination Survey; ANSI, American National Standards Institute (threshold of 0 = ANSI standard level); TEOAE, transient evoked otoacoustic emissions; ABR, auditory brainstem response; EPHL, early-onset permanent hearing loss; SNHL, sensorineural hearing loss; HFPTA, high frequency pure tone average.