



## Review Article

## Occupational Styrene Exposure on Auditory Function Among Adults: A Systematic Review of Selected Workers



Francis T. Pleban\*, Olutosin Oketope, Laxmi Shrestha

Department of Public Health, Health Administration, and Health Sciences, Tennessee State University, Avon Williams Campus, Nashville, TN, USA

## ARTICLE INFO

## Article history:

Received 12 August 2016

Received in revised form

30 December 2016

Accepted 11 January 2017

Available online 21 January 2017

## Keywords:

auditory system

human exposure

ototoxicity

styrene

## ABSTRACT

A review study was conducted to examine the adverse effects of styrene, styrene mixtures, or styrene and/or styrene mixtures and noise on the auditory system in humans employed in occupational settings. The search included peer-reviewed articles published in English language involving human volunteers spanning a 25-year period (1990–2015). Studies included peer review journals, case–control studies, and case reports. Animal studies were excluded. An initial search identified 40 studies. After screening for inclusion, 13 studies were retrieved for full journal detail examination and review. As a whole, the results range from no to mild associations between styrene exposure and auditory dysfunction, noting relatively small sample sizes. However, four studies investigating styrene with other organic solvent mixtures and noise suggested combined exposures to both styrene organic solvent mixtures may be more ototoxic than exposure to noise alone. There is little literature examining the effect of styrene on auditory functioning in humans. Nonetheless, findings suggest public health professionals and policy makers should be made aware of the future research needs pertaining to hearing impairment and ototoxicity from styrene. It is recommended that chronic styrene-exposed individuals be routinely evaluated with a comprehensive audiological test battery to detect early signs of auditory dysfunction.

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## 1. Introduction

Hearing involves the ear's ability to detect sounds and the brain's ability to interpret those sounds, principally speech. Hearing loss is a common problem caused—individually or collectively—by noise, aging, disease, and heredity. Two types of hearing loss may occur, conductive or sensory, with exposure duration to certain chemicals playing a role in the magnitude of auditory malfunctioning [1]. In the work setting, sensory or noise-induced hearing loss is one of the most common occupational diseases [2].

Toxicity from solvents may occur from accidental and/or deliberate inhalation of fumes, ingestion, or dermal absorption. Ototoxicity is commonly medication-induced; however, there are increasing scientific data indicating that exposure to some industrial solvents and other substances are associated with a risk of auditory loss in humans [3]. As well, the interaction of industrial chemicals, including styrene, and noise has traditionally received little empirical consideration [3].

The ear is a complex organ in support of hearing, transmitting sound information to the brain, where it is perceived and interpreted [4]. The ear has three main components: outer, middle, and inner. The outer ear consists of the pinna and external auditory canal. Both structures aid in collecting and transmitting amplified sound to the middle ear. The middle ear consists of tympanic membrane (eardrum) and three small bones—malleus, incus, and stapes—enhancing energy transfer from the outer to inner ear. The inner ear consists of sensory receptors [inner hair cells (IHCs) and outer hair cells (OHCs)], responsible for neural impulse initiation in the auditory nerve. Within the inner ear, the fluid-filled cochlea contains nerves specific for hearing. In coordination with other parts of the inner ear, the cochlea processes sound waves and transmits electrical signals, via nerves, to the brain. The inner ear component, the spiral-shaped cochlea—specifically the organ of Corti—is considered the target organ for solvents [5,6].

Styrene studied in rodents has been shown to cause a loss of auditory sensitivity in the midfrequency range and affect the OHCs, leaving the IHCs unaffected [7–9]. Styrene has been shown to cause

\* Corresponding author. Department of Public Health, Health Administration, and Health Sciences, Tennessee State University, Avon Williams Campus, 330 10<sup>th</sup> Avenue North, Suite D-413, Nashville, TN 37209-1561, USA.

E-mail address: [fpleban@tnstate.edu](mailto:fpleban@tnstate.edu) (F.T. Pleban).

the most damage to the OHCs along the basilar membrane [10]. With styrene concentrations of 600 ppm, substantial OHC loss occurs in the upper basilar membrane, leaving IHCs intact [11]. Investigators also concluded that at styrene concentration levels between 300 ppm and 600 ppm, a threshold for styrene ototoxicity in rats was apparent [11]. In rat models, Lataye et al [12] indicated an exposure duration of 3 months or more as a critical period for enhancing styrene ototoxicity.

Further research incorporating rat models indicate injury to the cochlea is also present with exposure to both noise and styrene [13]. At both low-intensity noise and low styrene concentrations, a potentiation risk of styrene-induced hearing loss by noise has also been documented [14]. Noise-induced hearing loss is due primarily to cilia damage, whereas styrene-induced hearing loss is caused by its toxic effect on the organ of Corti [8,13]. Campo et al [15] demonstrated that in exposed rats, cerebrospinal and inner ear fluids were free from detectable solvents, whereas the organ of Corti and associated nerves displayed levels of styrene contamination. Specifically, OHCs, when compared to IHCs, appeared to be the principal targets for industrial styrene within the organ of Corti. Styrene, transported by blood, diffuses via the stria vascularis to the OHC via the lipid-rich content of the membranes of outer sulcus cells (OSCs), modifying the membrane fluidity and structure. Disruption of the membranous OSC structures may be the genesis for cochlear injury, with further membranous impairments having mechanical insults on the organ of Corti [15]. Lataye et al [8] reported that the combined exposure to styrene and noise (8–16 kHz range) in rats demonstrated that threshold elevations and OHC losses exceeded the summed loss caused by styrene and noise alone. Their results suggest a permanent synergistic loss of auditory sensitivity with the combination of two ototoxic agents [8].

Rodent models also suggest that aging may also factor into additional hearing dysfunction when exposed to styrene. Campo et al [16] suggested that the presbycusis process may be enhanced with subsequent styrene exposure. Investigators cautioned that exposure results were not conclusive; however, further histopathological analysis showed an enhanced presbycusis [16].

Hearing loss and balance disturbances may occur in humans at levels below permitted levels of exposure to industrial solvents. Also, a synergistic effect of combined exposure to solvents and noise has been noted in humans, resulting in greater hearing losses than would be expected from exposure to noise and solvents alone [6]. Onset of hearing loss may be rapid or gradual, with severity related to the amount, time of exposure, and interactions with other physical or chemical agents. Cautionary consideration should be given to rodent studies, with higher styrene levels administration and lower timeframe exposures, than seen in human study data.

Styrene (CAS Reg. 100-42-5), also referred to by its trade names ethenyl benzene, vinyl benzene, phenylethylene, and styrol, is an organic compound. With a chemical formula of  $C_6H_5CH=CH_2$  or  $C_8H_8$ , styrene is an oily, colorless liquid that evaporates easily [17]. At low concentrations, styrene's odor presents as a sweet smell, although higher concentrations presents a less pleasing odor [17]. Styrene, a monomer, is the precursor to polystyrene, which can then be further molded and shaped. Adding a vinyl group to the monomer allows styrene to polymerize. Styrene, as a precursor for polystyrene plastics, has had commercially significant importance in the manufacturing of products including insulation, fiberglass, pipes, automobile and boat parts, food containers, and carpet backing [18,19]. However, the most significant use of—and subsequent occupational exposure to—styrene is as a cross-linking agent in polyester resins for the production of glass-fiber-reinforced plastic products, specific to gel coating and laminating operations [20,21]. Exposure to styrene may occur either in occupational and

nonoccupational settings; however, workers employed in certain occupations potentially are exposed to high levels of styrene compared with the general population [17]. Occupational exposure to styrene may occur during production of styrene monomer, polystyrene or styrene copolymers, glass-fiber-reinforced plastics, and styrene-butadiene rubber [17,22]. Exposure routes for styrene include inhalation, skin absorption, ingestion, and/or eye contact. Signs and symptoms of styrene exposure may consist of nose, eye, and respiratory irritation, headache, dizziness, confusion, drowsiness, unsteady gait, and contact dermatitis, with possible liver injury and reproductive effects [23,24]. Common health problems from extreme occupational exposure concentrations (e.g., levels 1,000 times higher than normal environmental levels) are specific to the nervous system [17]. Type and severity of health effects depends on several factors, including the amount of chemical an individual is exposed to, as well as length of exposure time [17]. Furthermore, important to this document, styrene has been shown to possibly disrupt the auditory system in both animals and humans [25]. The National Institute for Occupational Safety and Health (NIOSH)-recommended exposure limit for styrene is established at 50 ppm ( $215\text{ mg/m}^3$ ) as a time-weighted average (TWA). Also, 15 minutes as a short-term exposure limit (STEL) has been established by the NIOSH at 100 ppm ( $425\text{ mg/m}^3$ ). Conversely, the Occupational Safety and Health Administration (OSHA) permissible exposure limit for styrene is established at 100 ppm, as a TWA. As well, OSHA has also established a Ceiling (C) limit at 200 ppm, with a 600-ppm 5-minute maximum peak during any 3-hour timeframe [17]. Currently, styrene is classified by OSHA as a “Possible Select Carcinogen,” and by the International Agency for Research on Cancer as a “Group 2B Carcinogen,” possibly carcinogenic to humans [23,24]. The objective of this systematic review was to examine the adverse effects of the styrene auditory system in humans employed in various occupational settings, spanning the past 25 years (1990–2015). Studies referencing exposure to styrene or styrene and/or styrene mixtures with noise that negatively impact auditory functioning in humans were identified for review. These particular exposure scenarios tend to account for the majority of worker exposure to styrene in industrial settings [8,26].

## 2. Materials and methods

A systematic review of scientific literature was conducted detailing specific objectives, criteria for study selection, approach to abstracting data, and assessing study quality, outcomes, and research methods.

### 2.1. Review question

Does exposure to styrene or styrene and/or styrene mixtures with noise negatively impact auditory functioning in humans employed in certain industrial settings?

### 2.2. Criteria for considering studies and search strategy

Systematic search was conducted using Internet-based databases: GreenFILE, EBCOHOST, JSTOR, Academic Search Premier, and PubMed. The search included peer-reviewed articles published in the English language involving human volunteers spanning a 25-year period (1990–2016). Listed databases were used to retrieve abstracts and, if appropriate, full-text articles. The search terms included: styrene; “occupational workers” OR “factory workers”; and “ototoxicity” OR “ototoxic” OR “hearing loss” OR “hearing impairment” OR “auditory injury”. Results from each search were then combined to identify articles that included ototoxicity in

relationship with exposure to styrene, and any combination thereof.

The title and abstract of each identified study were reviewed. Studies were further included if they (1) appeared in peer-reviewed journals; (2) presented original data; (3) incorporated human volunteers; (4) published between the years 1990 and 2015; (5) reported occupational exposure; (6) were performed in developed countries; and (7) reported a minimum sample size of 10. Table 1 outlines the study inclusion and exclusion criteria. Results were grouped according to styrene, styrene mixtures, or styrene and/or styrene mixtures with noise, as well as occupational exposure; and discussed in narrative form.

### 3. Results

The initial search identified 40 studies. Of the 40 studies initially identified, a total of five studies were excluded. The five excluded studies were composed of three duplicate studies, one nonoccupational worker exposure population, and one systematic review. After initial exclusion, a total of 35 abstracts were retrieved for further examination. Of the 35 abstracts screened, 22 did not meet the inclusion and exclusion criteria outlined in Table 1. The 22 excluded studies comprised 15 animal studies [7–14,16,26–31], two studies using special populations [32,33], four studies investigating heavy metal or pharmacological exposure [34–37], and one study investigating the protective effects for hearing loss [38]. From the remaining 13 studies meeting the inclusion criteria, the following data were extracted: hazard exposure(s), exposure level(s), study design, sample size, industry setting(s), assessment method(s), and outcome(s). Of the 13 remaining abstracts, all 13 articles were retrieved for full journal detail examination. Of the 13 articles retrieved, and after detailed examination, all 13 studies were used in the systematic review (Fig. 1).

#### 3.1. Description and methodological quality of excluded studies

Of the 22 excluded studies (Fig. 1), 15 studies were excluded because they featured data collection using animals. The excluded animal studies included those conducted by Lataye et al [7,8], Crofton et al [9], Gagnaire and Langlais [10], Mäkitie et al [11], Lataye et al [12], Pouyatos et al [13], Lataye et al [14], Campo et al [16], Harvilchuck [26], Pouyatos et al [27], Chen et al [28], Loquet et al [29], Pouyatos et al [30], and Lund and Kristiansen [31].

Two studies were excluded on the basis of data from special population participants other than workers occupationally exposed to styrene, styrene mixtures, or styrene and/or styrene mixtures

with noise; the excluded special population participants included children [32] and military personnel [33].

Four studies were excluded because of other occupational exposures in addition to styrene, styrene mixtures, or styrene and/or styrene mixtures with noise (Fig. 1). The excluded occupational exposures in addition to styrene include heavy metals [34,35] and pharmacological drugs [36,37].

One study was excluded because it investigated the protective effect of amino acid *N*-acetyl-L-cysteine (Fig. 1). Excluded protective effects of amino acid *N*-acetyl-L-cysteine [38].

#### 3.2. Description and methodological quality of included studies

##### 3.2.1. Study design

This review included two prospective cohort studies [25,39] and nine case–control studies [40–50] (Table 2).

##### 3.2.2. Participants

For the included studies, sample sizes ranged from 18 participants to 1,620 participants. Study sample sizes were reported as follows:  $n = 18$  [39];  $n = 20$  [25];  $n = 28$  [45];  $n = 32$  [40];  $n = 93$  [43];  $n = 101$  [48];  $n = 299$  [44];  $n = 313$  [41,42];  $n = 700$ ;  $n = 513$  [47];  $n = 1,117$  [48]; and  $n = 1,620$  [50].

##### 3.2.3. Exposure setting

Eight of the 13 studies included in the systematic review ( $n = 4$ ) included participants who were occupationally exposed to styrene, styrene mixtures, or styrene and/or styrene mixtures with noise in: plastic button manufacturing and fiber-reinforced bath manufacturing ( $n = 2$ ), yacht shipyard and plastic factory ( $n = 1$ ), and paint and varnish industry ( $n = 1$ ) (Table 2): fiber glass manufacturing ( $n = 6$ ) [25,41,42,45,46,49]; boat building construction ( $n = 3$ ) [39,40,50]; and other occupational settings ( $n = 4$ ): plastic button manufacturing and fiber-reinforced bath manufacturing [43,44], yacht shipyard and plastic factory [47], and paint and varnish industry [48].

##### 3.2.4. Outcome assessment

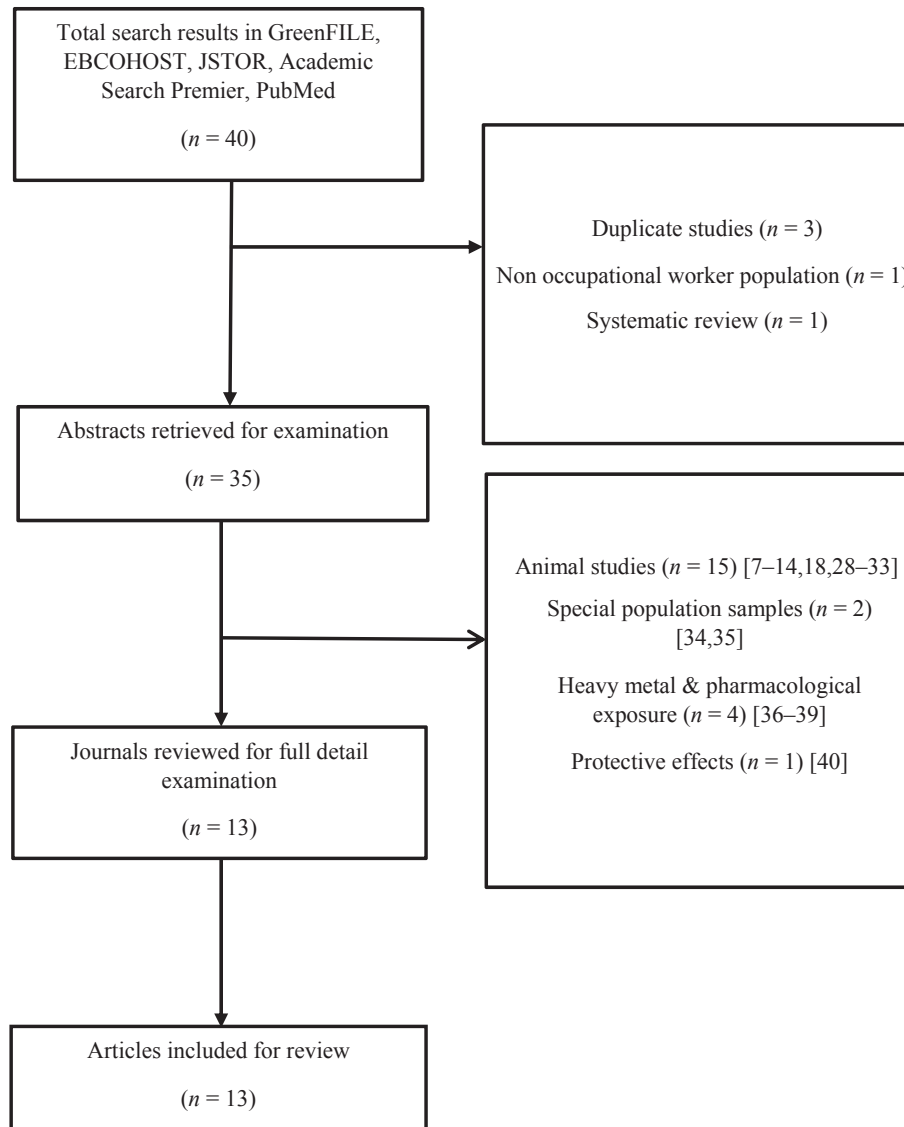
The included literature revealed little or no evidence for ototoxicity to significant auditory effects to styrene, styrene mixtures, or styrene and/or styrene mixtures with noise. Hazard exposure outcomes were classified as follows: (1) exposed to styrene only (15–600 ppm), (2) styrene (50–200 ppm or 0–309 mg/m<sup>3</sup> and noise (>69 dBA), and (3) styrene and/or other solvents (0.2–450.0 mg/m<sup>3</sup>) and noise (> 64 dBA).

**3.2.4.1. Exposure to styrene only ( $n = 4$ ).** One study revealed no effect on hearing; however, it documented an impact on the vestibular system at the subclinical effect level [25]. Hoffman et al [40] reported that styrene exposure did not have any effect on measured hearing levels, primarily because of a small sample size ( $n = 32$ ) and exposure of controls to low styrene levels. One study revealed effects on the auditory and balance systems after low-level exposure to styrene [39]. Finally, Triebig et al [50] referenced an increase in hearing thresholds at chronic and intense styrene exposure, with improvements in hearing thresholds during work and exposure-free periods.

**3.2.4.2. Exposure to styrene and noise ( $n = 5$ ).** Four of five studies investigating the joint effects of styrene and noise reported some level of auditory dysfunction. Johnson et al [41], Morata et al [42], Morata et al [49], and Sass-Kortsak et al [44] reported auditory system effects and poorer audiometric thresholds of exposed individuals. One study [45] reported no conclusive evidence for chronic styrene induced reduced hearing acuity, when accounting

**Table 1**  
Review inclusion and exclusion criteria

Criterion	Inclusion	Exclusion
Time	1990–2015 (past 25 y)	Historical data
Article type	Peer-reviewed original data	Nonpeer-reviewed
Sample size	≥10	<10
Language	English	Non-English
Exposure Setting	Occupational	Nonoccupational
Hazard exposure	Styrene, styrene mixtures, or styrene &/or styrene mixtures & noise	Other chemical, biological, & physical hazards
Types of study	Human studies	Animal studies
Participants	Occupational workers	Nonoccupational persons
Country composite statistic—Human Development Index (HDI)	Developed countries	Developing countries



**Fig. 1.** Study selection flow diagram for systematic review of published research on ototoxicity of styrene in occupational work settings.

for both noise and styrene. To note, of the five studies subdivided into styrene and noise exposures, Sisto et al et al [45] incorporated the fewest reported study samples ( $n = 28$ ).

**3.2.4.3. Exposure to styrene and/or other solvents with noise ( $n = 4$ ).** Four studies investigated styrene with other organic solvent mixtures with noise on auditory function. Two of the four studies [43,48] reported upper limit hearing reduction and sensorineural high frequency hearing loss, respectively. Sliwinska-Kowalska et al [46,47] reported that combined exposures to both styrene organic solvent mixtures may be more ototoxic than exposure to noise alone.

### 3.2.5. Interventions

For included studies, performance-processing evaluation was generally based on several assessment methods: (1) personal sampling; (2) measures of hearing thresholds; (3) transient evoked otoacoustic emissions [28,45,50]; and (4) otoneurological test battery including measures of pure tone audiometry, speech discrimination, interrupted speech, distortion product otoacoustic emissions, and cortical response audiometry [39,41–44,46,47,49], or

pure tone audiometry and stapedius reflex measurements, vestibule-ocular reflex test, and rotating chair test [25,48]. Four studies [25,40,45,50] also included biological monitoring in assessment. Across most studies, pure tone audiometry was one of the primary hearing assessment methods. Studies by Möller et al [39] and Hoffman et al [40] stressed the importance of incorporating larger sample sizes.

## 4. Discussion

Styrene studied in rodents have been shown to cause a loss of auditory sensitivity in the midfrequency range and affecting the OHCs, leaving IHCs unaffected [7–9]. Research incorporating rat models and styrene have documented: (1) a possible threshold level (300 ppm and 600 ppm) [11]; (2) exposure duration (3 months or more) [12]; (3) synergistic effects of low-intensity noise and low styrene concentrations [8,14]; and (4) presbycusis as a possible additional factor for hearing loss, with styrene exposure [16].

In humans, low-level styrene exposure may have impacts on the auditory and vestibular systems [25,39,50]. A synergistic effect of

**Table 2**  
Exposure to styrene and hearing loss in industry settings

Author(s)	Hazard exposure(s)	Exposure level(s)	Study design	Sample size	Industry setting(s)	Outcome(s)
Calabrese et al [25]	Styrene	< 54 ppm	Prospective Cohort	20	Fiberglass manufacturing	No effect in hearing test 17 workers showed abnormalities in vestibular test (subclinical effect)
Möller et al [39]	Styrene	15–35 ppm	Prospective Cohort	18	Boat construction	Effects on auditory system after low-level exposure
Hoffman et al [40]	Styrene	300–600 ppm	Case-control	32	Boat construction	No relationship between occupational exposure to styrene & hearing loss
Triebig et al [50]	Styrene	30–50 ppm	Cross-sectional	700	Boat construction	Elevated risk for impaired hearing expected at chronic & extensive exposure
Johnson et al [41]	Styrene & low-level noise	Styrene (90 mg/m <sup>3</sup> ) Noise (69–108 dBA)	Case-control	313	Fiberglass manufacturing	Auditory (peripheral & central) effects with low-level styrene exposure
Morata et al [42]	Styrene & low-level noise	Styrene (11–38 ppm; 120 ppm max) Noise (69–108 dBA)	Case-control	313	Fiberglass manufacturing	Auditory system effects with low-level styrene exposure
Morata et al [49]	Styrene & low-level noise	Styrene (0–309 mg/m <sup>3</sup> ) Noise (<85 dBA & >85 dBA)	Cross-sectional	1,620	Fiberglass manufacturing	Exposed audiometric threshold poorer than the published standard Significant interaction between styrene & noise
Sisto et al [45]	Styrene & noise	Styrene (4.9–150 mg/m <sup>3</sup> ) Noise (<85 dBA & >85 dBA)	Case-control	28	Fiberglass manufacturing	Significant negative correlation found between otoacoustic emission levels & urinary styrene metabolites Participants exposed to styrene & noise, reported negative cochlear functionality
Sass-Kortsak et al [44]	Styrene & noise	Styrene (73.5 mg/m <sup>3</sup> (ave) Noise (>80 dBA)	Case-control	299	Fiber-reinforced plastic manufacturing	No conclusive evidence for chronic styrene induced reduced hearing acuity, accounting for both noise & styrene
Morioka et al [43]	Styrene, organic solvent mixture & noise	Styrene (50–200 ppm) Noise (53.0–95.0 dBA)	Case-control	93	Plastic buttons & fiber-reinforced bath manufacturing	Reduction of the upper limit of hearing with 5+ y of environmental organic solvent exposure
Sliwinska-Kowalska et al [46]	Styrene, styrene mixture & noise	Styrene (0.2–198.4 mg/m <sup>3</sup> ) Noise (>85 dBA)	Case-control	513	Fiberglass manufacturing	Occupational exposure to styrene is related to increased odds risk of hearing loss Combined noise & styrene exposure may be more ototoxic than exposure to noise alone
Sliwinska-Kowalska et al [47]	Solvents & noise	Solvents (0.2–450.0 mg/m <sup>3</sup> ) Noise (64–100 dBA)	Case-control	1,117	Yacht shipyard & plastic factory	Simultaneous organic solvents & noise exposure appears to enhance hearing deficit, compared to isolated exposures
Sulkowski et al [48]	Organic solvent mixture & low-level noise	Solvents (1.40–68.40 mg/m <sup>3</sup> ) Noise (<85 dBA)	Case-control	101	Paint & varnish industry	Vestibular dysfunction, sensorineural high frequency hearing loss

combined exposure to solvents and noise has also been noted in humans, resulting in greater hearing losses than would be expected from exposure to noise and solvents alone [6]. Four of five studies investigating the joint effects of styrene and noise reported some level of auditory dysfunction [41,42,44,49]. Finally, exposure to styrene and/or other solvents and noise may affect upper limit hearing and sensorineural high frequency hearing [43,48].

#### 4.1. Ototoxicity and hearing loss in workers exposed to styrene

Calabrese et al [25] revealed no effect on hearing; however, they documented an impact on the vestibular system at the subclinical effect level [25]. Hoffman et al [40] reported that styrene exposure did not have any effect on measured hearing levels, primarily because of a small sample size ( $n = 32$ ) and exposure of controls to low styrene levels. One study revealed effects on the auditory and balance systems after low-level exposure to styrene [39]. Finally, Triebig et al [50] referenced an increase in hearing thresholds at chronic and intense styrene exposure, with improvements in hearing thresholds during work and exposure-free periods. However, Möller et al [39] stated that it was not feasible to demonstrate a dose–response relationship owing to (1) a relatively small sample size and (2) difficulty in distinguishing pure tone audiometry results for styrene exposure and effects caused by noise or age, individually or collectively. As well, referencing sample size, Hoffmann et al [40] reported styrene exposure having no effect on measured hearing levels, primarily because of a small sample size.

#### 4.2. Ototoxicity and hearing loss in workers exposed to styrene and noise

Johnson et al [41], Morata et al [42], Sass-Kortsak et al [44], and Morata et al [49] reported auditory system effects and poorer audiometric thresholds in exposed individuals. One study [45] reported no conclusive evidence for chronic styrene induced reduced hearing acuity, when accounting for both noise and styrene. It should be noted that Sisto et al [45] incorporated the fewest reported study samples ( $n = 28$ ) of all of the five studies subdivided by styrene and noise criteria. Four of the five studies investigating the joint effects of styrene and noise reported some level of auditory dysfunction.

#### 4.3. Ototoxicity and hearing loss in workers exposed to styrene and/or other solvents with noise

Four studies investigated styrene with other organic solvent mixtures with noise on auditory function. Sliwinska-Kowalska et al [46,47] reported that combined exposures to both styrene organic solvent mixtures may be more ototoxic than exposure to noise alone. Morioka et al [43] and Sułkowski et al [48] reported upper limit hearing reduction and sensorineural high frequency hearing loss, respectively.

#### 4.4. Hazard assessment

Although current recommendations have examined the hearing of workers exposed to potentially ototoxic chemicals [23,25], currently there are no regulations requiring such monitoring. As a result, there may be a number of workers exposed to potentially ototoxic chemicals in the presence of background noise, and few workers will be required to have regular hearing prevention tests because noise exposure levels may not exceed established regulatory noise guidelines [16]. Although there is information that exposure to certain chemicals alone or in combination with noise can produce auditory failure, it is likely that present hearing loss

recognition and prevention practices are not sufficient to protect the worker [16]. Other hazard recognition issues include: the adequacy of pure tone audiometry testing in screening ototoxic chemically exposed workers, the appropriateness of the current styrene threshold limits when certain hazards occur simultaneously in the work place, and the role of hearing recognition and assessment as applied to the early identification of ototoxicity.

#### 4.5. Implications for practice

As a whole, results range from no association between styrene and hearing loss to a low association between styrene and hearing loss due to styrene and other potential confounders. Also, this review notes the examination of relatively small sample sizes as a possible contributing factor for the lack of association.

Confounders such as exposure to excessive noise, both in and outside of the occupational environment, could significantly contribute to decreased hearing in workers. In most occupational settings, noise exposures occur in proximity of solvent exposures, with hearing losses observed. In these situations, hearing loss is often attributed to noise exposure, without regard to solvent exposure. In addition, rudimentary observation of a pure tone audiogram does not determine the etiology of an auditory disorder. Visually, the audiometric configuration of noise-induced hearing loss and ototoxic-induced hearing loss may be indistinguishable [16]. Additionally, variability among exposure hearing assessments between studies makes outcome comparison problematic. Medical surveillance of workers exposed to noise may also need to include those workers exposed to styrene and other organic solvents associated with ototoxicity. Morata and Campo [51] suggest proposing a strategy for preventing chemical-induced hearing loss by analyzing further work site data that relates other potentially ototoxic exposure conditions to hearing loss.

Existing exposure limits for styrene may not be sufficient for preventing styrene-induced hearing loss. Alternatively, there is a possibility that peak significant exposures to styrene may be significantly contributing to causing styrene-induced hearing loss. Morata and Campo [51] further stated that it is common to observe high peak exposures in the work environment owing to the misuse of solvents rather than typical exposures over an 8-hour working day (20 ppm TWA) [52]. For worker protection, styrene standards for occupational environments are 20 ppm averaged over an 8-hour working day (20 ppm TWA) with an STEL of 40 ppm [52].

However, findings suggest clinicians, researchers, industrial hygienists, and policy makers should be made aware of the future research needs pertaining to hearing impairment and ototoxicity from styrene exposure. It is recommended that styrene-exposed individuals be routinely evaluated with a comprehensive audiological test battery on a regular basis, to detect early signs of auditory dysfunction. Further investigation identifying auditory dysfunction and occupational styrene exposure in workers employed in boat construction and fiberglass manufacturing is required so as to better assess sufficiency of the current recommended styrene exposure limits.

Factoring for noise, consideration should be given to workers in noise-producing environments, particularly when noise levels approach 85 dBA or higher. At levels of 85 dBA or higher, appropriate engineering controls (i.e., modifying or replacing equipment, or making other related physical changes at the noise source) and/or administrative controls (i.e., changes in the workplace, schedule, and/or distance) should be first explored as options to reduce or eliminate worker exposure to noise. To note, doubling the distance between the noise source and worker decreases noise exposures by 6 dBA. Finally, personal protective equipment may also be used,

either alone or to complement engineering and administrative controls, for noise reduction.

#### 4.6. Considerations for future research

Because of multiple confounding factors, assessment of solvent ototoxicity, in general, and styrene, in particular, is difficult. To accurately assess any relationship, multiple hearing assessment measures are necessary. Confounders such as noise, age, and sex warrant longitudinal case/control study exploration, with the inclusion or larger, random samples. Confounders such as noise, age, and sex require further longitudinal case–control study exploration, with the inclusion or larger, random samples. Referencing noise, studies including low (< 85 dBA) and high (> 85 dBA) environmental conditions should also be considered. The acquisition of comprehensive baseline historical participant data should also be a consideration for future research. Finally, prior to further study initiation, biases, specifically surveyor and health worker effect also need to be considered.

#### Conflicts of interest

All authors have no conflicts of interest to declare.

#### References

- [1] De Barba MC, Jurkiewicz AL, Zeigelboim BS, de Oliveira LA, Belle AP. Audiometric findings in petrochemical workers exposed to noise and chemical agents. *Noise Health* 2005;7:7–11.
- [2] Loukazadeh Z, Shojaoddiny-Ardekani A, Mehrparvar AH, Yazdi Z, Mollasadeghi A. Effect of exposure to a mixture of organic solvents on hearing thresholds in petrochemical industry workers. *Iran J Otorhinolaryngol* 2014;26:235–43.
- [3] Vyskocil A, Truchon G, Leroux T, Lemay F, Gendron M, Gagnon F, Majidi N, Boudjerida A, Lim S, Émond C, Viau C. A weight of evidence approach for the assessment of the ototoxic potential of industrial chemicals. *Toxicol Ind Health* 2012;28:796–819.
- [4] Berger EH, Royster LH, Royster JD, Driscoll DP, Layne ML. The noise manual. 5th ed. Akron (OH): American Industrial Hygiene Association (US); 2000. 795 p.
- [5] Campo P, Maguin K. Solvent-induced hearing loss: mechanisms and prevention strategy. *Int J Occup Med Environ Health* 2007;20:265–70.
- [6] Hodgkinson L, Prasher D. Effects of industrial solvents on hearing and balance: a review. *Noise Health* 2006;8:114–33.
- [7] Lataye R, Campo P, Pouyatos B, Cossec B, Blachère V, Morel G. Solvent ototoxicity in the rat and guinea pig. *Neurotoxicol Teratol* 2003;25:39–50.
- [8] Lataye R, Campo P, Loquet G. Combined effects of noise and styrene exposure on hearing function in the rat. *Hear Res* 2000;139:89–96.
- [9] Crofton KM, Lassiter TL, Rebert CS. Solvent-induced ototoxicity in rats: An atypical selective mid-frequency hearing deficit. *Hear Res* 1994;80:25–30.
- [10] Gagnaire F, Langlais C. Relative ototoxicity of 21 aromatic solvents. *Arch Toxicol* 2005;79:346–54.
- [11] Mäkitie A, Pirvola U, Pyykkö I, Sakakibara H, Riihimäki V, Ylikoski J. Functional and morphological effects of styrene on the auditory system of the rat. *Arch Toxicol* 2002;76:40–7.
- [12] Lataye R, Pouyatos B, Campo P, Lambert A, Morel G. Critical period for styrene ototoxicity in the rat. *Noise Health* 2004;7:1–10.
- [13] Pouyatos B, Morel G, Lambert-Xolin A, Maguin K, Campo P. Consequences of noise- or styrene-induced cochlear damages on glutamate decarboxylase levels in the rat inferior colliculus. *Hear Res* 2004;189:83–91.
- [14] Lataye R, Campo P, Loquet G, Morel G. Combined effects of noise and styrene on hearing: comparison between active and sedentary rats. *Noise Health* 2005;7:49–64.
- [15] Campo P, Lataye R, Loquet G, Bonnet P. Styrene-induced hearing loss: a membrane insult. *Hear Res* 2001;54:170–80.
- [16] Campo P, Venet T, Rumeau C, Thomas A, Rieger B, Cour C, Cosnier F, Parietti-Winkler C. Impact of noise or styrene exposure on the kinetics of presbycusis. *Hear Res* 2011;280:122–32.
- [17] Toxicological profile for styrene [Internet]. Atlanta (GA): Department of Health and Human Services, Public Health Service. 2010 [cited 2016 Jun 16]. Available from: <http://www.atsdr.cdc.gov/toxprofiles/tp53.pdf>.
- [18] Boffetta P, Adami HO, Cole P, Trichopoulos D, Mandel JS. Epidemiologic studies of styrene and cancer: A review of the literature. *J Occup Environ Med* 2009;51:1275–87.
- [19] Cohen JT, Carlson G, Charnley G, Coggon D, Delzell E, Graham JD. A comprehensive evaluation of the potential health risks associated with occupational and environmental exposure to styrene. *J Toxicol Environ Health B Crit Rev* 2002;5:1–263.
- [20] Miller RR, Newhook R, Poole A. Styrene production, use, and human exposure. *Crit Rev Toxicol* 1994;24:S1–10.
- [21] National Toxicology Program (NTP). Report on carcinogens, Fourteenth Edition [Internet]. Research Triangle Park, NC: U.S. Department of Health and Human Services, Public Health Service. 2016 1997 [cited 2017 Feb 02]. Available from: <http://ntp.niehs.nih.gov/go/roc14/>.
- [22] International Agency for Research on Cancer (IARC). Some traditional herbal medicines, some mycotoxins, naphthalene and styrene. *IARC Monogr Eval Carcinogen Risk Hum* 2002;82:590.
- [23] Styrene. SDS No. 1907/2006. [Internet]. SPA styrene safety data sheet. Auderghem, Belgium: The European Chemical Industry Council; 2011 [cited 2016 Jun 5]. Available from: <http://www.styrenemonomer.org/Styrene-SPA-SDS-14-12-2011.pdf>.
- [24] Department of Health and Human Services (DHHS), National Institute for Occupational Safety and Health. Criteria for a recommended standard: Occupational noise exposure [Internet]. Cincinnati (OH): National Institute for Occupational Safety and Health (US); 1983 [cited 2016 Jun 16]. Available from: <https://www.cdc.gov/niosh/docs/83-119/83-119.pdf>.
- [25] Calabrese G, Martini A, Sessa G, Cellini M, Bartolucci GB, Marcuzzo G, De Rosa E. Otoneurological study in workers exposed to styrene in the fiberglass industry. *Int Arch Occup Environ Health* 1996;68(4):219–23.
- [26] Harvilchuck JA. Toxicity of styrene and its metabolites styrene oxide and 4-vinylphenol on mouse clara cells [Internet]. West Lafayette, Indiana, USA: Purdue University Libraries; Purdue e-Pubs 2009 [cited 2016 Nov 05]. Available from: <http://docs.lib.purdue.edu/dissertations/AI13378761/>.
- [27] Pouyatos B, Campo P, Lataye R. Influence of age on noise- and styrene-induced hearing loss in the Long–Evans rat. *Environ Toxicol Pharmacol* 2005;19:561–70.
- [28] Chen G, Tanaka C, Henderson D. Relation between outer hair cell loss and hearing loss in rats exposed to styrene. *Hear Res* 2008;243:28–34.
- [29] Loquet G, Campo P, Lataye R, Cossec B, Bonnet P. Combined effects of exposure to styrene and ethanol on the auditory function in the rat. *Hear Res* 2000;148:173–80.
- [30] Pouyatos B, Campo P, Lataye R. Use of DPOAEs for assessing hearing loss caused by styrene in the rat. *Hear Res* 2002;165:156–64.
- [31] Lund SP, Kristiansen GB. Hazards to hearing from combined exposure to toluene and noise in rats. *Int J Occup Med Environ Health* 2008;21:47–57.
- [32] Corne S. Children of microelectronics workers: a follow-up study of prenatal occupational solvent exposure and child neuropsychological performance [Internet]. Ann Arbor, Michigan, USA: ProQuest Dissertations Publishing. ProQuest Dissertations. 1991 [cited 2016 Nov 05]. Available from: <http://search.proquest.com/docview/303927941/8CD897504DB241C3PQ/1?accountid=14275>.
- [33] Hughes H. Evaluation of the effects of exposure to organic solvents and hazardous noise among U.S. air force reserve personnel [Internet]. Ann Arbor, Michigan, USA: ProQuest Dissertations Publishing. ProQuest Dissertations. 2011 [cited 2016 Nov 05]. Available from: <http://search.proquest.com/docview/864566181/867DA6C0424945ECPQ/1?accountid=14275>.
- [34] Choi Y-H, Kim K. Noise-Induced Hearing Loss in Korean Workers: Co-Exposure to Organic Solvents and Heavy Metals in Nationwide Industries. Matsui JI, ed. *PLoS ONE* 2014;9:e97538.
- [35] Schaal NC (2016). Effects of heavy metal exposure on hearing loss among shipyard personnel [Internet]. Ann Arbor, Michigan, USA: ProQuest Dissertations Publishing. ProQuest Dissertations. 2016 [cited 2016 Nov 05]. Available from: <http://search.proquest.com/docview/1781592023>.
- [36] Brown JJ, Brummett RE, Fox KE, Bendrick TW. Combined effects of noise and kanamycin cochlear pathology and pharmacology. *Arch Otolaryngol* 1980;106:744–50.
- [37] Li H, Steyger P. Synergistic ototoxicity due to noise exposure and aminoglycoside antibiotics. *Noise Health* 2009;11:26–32.
- [38] Yang WP, Hu BH, Di Chen G, Bielefeld EC, Henderson D. Protective effect of N-acetyl-L-cysteine (L-NAC) against styrene-induced cochlear injuries. *Acta Otolaryngol* 2009;129:1036–43.
- [39] Möller C, Ödqvist L, Larsby B, Tham R, Ledin T, Bergholtz LM. Otoneurological findings in workers exposed to styrene. *Scand J Work Environ Health* 1990;16:189–94.
- [40] Hoffmann J, Ihrig A, Hoth S, Triebig G. Field study to explore possible effects of styrene on auditory function in exposed workers. *Ind Health* 2006;44:283–6.
- [41] Johnson AC, Morata TC, Lindblad AC, Nylén P, Svensson EB, Krieg E, Aksentijevic A, Prasher D. Audiological findings in workers exposed to styrene alone or in concert with noise. *Noise Health* 2006;8:45–57.
- [42] Morata TC, Johnson AC, Nylén P, Svensson EB, Cheng J, Krieg EK, Lindblad AC, Ernstgård L, Franks J. Audiometric findings in workers exposed to low levels of styrene and noise. *J Occup Environ Med* 2002;44:806–14.
- [43] Morioka I, Kuroda M, Miyashita K, Takeda S. Evaluation of organic solvent ototoxicity by the upper limit of hearing. *Arch Environ Occup Health* 1999;54:341–6.
- [44] Sass-Kortsak AM, Corey PN, Robertson JM. An investigation of the association between exposure to styrene and hearing loss. *Ann Epidemiol* 1995;5:15–24.
- [45] Sisto R, Cerini L, Gatto MP, Gherardi M, Gordiani A, Sanjust F, Paci E, Tranfo G, Moleti A. Otoacoustic emission sensitivity to exposure to styrene and noise. *J Acoust Soc Am* 2013;134:3739–48.
- [46] Sliwiska-Kowalska M, Zamysłowska-Szymtke E, Szymczak W, Pawlarczyk-Luszczynska M. Ototoxic effects of occupational exposure to styrene and co-exposure to styrene and noise. *J Occup Environ Med* 2003;45:15–24.

- [47] Sliwiska-Kowalska M, Zamysłowska-Szmytke E, Szymczak W, Kotyło P, Fiszer M, Wesolowski W, Pawlaczyk-Luszczynska M. Exacerbation of noise-induced hearing loss by co-exposure to workplace chemicals. *Environ Toxicol Pharmacol* 2005;19:547–53.
- [48] Sułkowski WJ, Kowalska S, Matyja W, Guzek W, Wesolowski W, Szymczak W, Kostrzewski P. Effects of occupational exposure to a mixture of solvents on the inner ear: a field study. *Int J Occup Med Environ Health* 2002;15:247–56.
- [49] Morata TC, Sliwiska-Kowalska M, Johnson AC, Starck J, Pawlas K, Zamysłowska-Szmytke E, Nylén P, Toppila E, Krieg E, Pawlas N, Prasher D. A multicenter study on the audiometric findings of styrene-exposed workers. *Int J Audiol* 2011;50:652–60.
- [50] Triebig G, Bruckner T, Seeber A. Occupational styrene exposure and hearing loss: a cohort study with repeated measurements. *Int Arch Occup Environ Health* 2009;82:463–80.
- [51] Morata TC, Campo P. Ototoxic effects of styrene alone or in concert with other agents: a review. *Noise Health* 2002;4:15–24.
- [52] ACGIH. 2013 TLVs and BEIs. Cincinnati (OH): ACGIH Signature Publications; 2013. 242 p.