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## **Solvent-Induced Hearing Loss from Occupational Exposure in Asia: A systematic review**

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### **Abstract**

Exposure to certain solvents in the workplace can cause hearing loss. This study aims to bring attention to the existing literature on the adverse effects of solvents on workers' auditory function in a diverse occupational setting. The literature search used in this study is PubMed and Web of Science. 87% of the selected studies reported that the highest prevalence of hearing loss was from solvents and noise-exposed groups. Evidence shows that interaction between the solvent and the noise could be both additive and synergistic. More epidemiology studies on solvent-induced hearing loss using diverse approaches are warranted in the Asia region.

**Keywords:** hearing loss; solvent; pure tone audiometry; chemical-induced hearing loss

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### **1.0 Introduction**

Hearing loss is the fourth highest cause of disability globally, with an approximate annual cost of over 750 billion dollars (Cunningham and Tucci, 2017). People with Occupational Noise-Related Hearing Disorders (ONRHD) are around 466 million people. Based on World Health Organization (WHO) projection, the number will increase up to 36% by 2030. Moreover, the number is expected to grow up to 900 million people by 2050 unless action is taken. Noise could not be assumed as the only ultimate risk factor that causes hearing loss as nowadays, chemicals are undeniably contributing to the current prevalence of hearing loss worldwide (WHO, 2018). According to Audiology Information Series (2015), certain chemicals could cause hazardous effects on hearing.

These chemicals are called ototoxic chemicals. The ototoxic substance includes solvent (organic and inorganic), pesticides, pharmaceuticals, asphyxiants, nitriles, heavy metals, and compounds (NIOSH Safety and Health Information Bulletin, 2018). When comparing solvent-exposed workers to non-exposed workers, human studies have found that solvent-exposed workers had a greater rate of hearing loss (Fuente & McPherson, 2012). Despite the existence of some data on ototoxic exposure in specific industries, little

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is known about who is the population at risk and more crucially, who is at a higher risk of co-exposure due to workplace noise (Lewkowski et al. 2019).

### 1.1 Purpose of the study

The purpose of this study was to highlight and provide the up-to-date current state of the research on solvent-induced hearing loss in Asia.

### 1.2 Objective of the study

The objective of this study was to explore the available scientific literature on the adverse effects of solvents on workers' auditory function in a diverse occupational setting in Asia. It examines the existing research in Asia on the impact of occupational exposure to solvents or solvent mixtures towards hearing impairment.

## 2.0 Literature Review

According to Kwon J.K & Lee J., (2021), the direct impact of solvents on the cells of the organ of Corti, resulting in the disruption of their membranous structures, would be the mechanism of acute damage, whereas the development of chemically and physiologically reactive intermediates might explain chronic ototoxic consequences.

Hemmativaghef (2020) also claimed that solvent could cause the formation of chemical and biological reactive intermediate, including reactive oxygen species, which may trigger the death of the organ of Corti. Therefore, when acoustic energy enters the cochlea with an organic solvent, it may be more damaging, resulting in high-tone sensorineural hearing loss. Chemical poisoning can occur when the solvents flow through the stria vascularis and reach the outer hair cells without creating mechanical stress. Loud noise, on the other hand, caused mechanical damage to the cochlea. The positive interaction effect between solvent and noise was due to the increased production of oxidative stress (Hsu et al. 2015).

Several studies have documented the ototoxicity of the solvent mixture, noise plus solvent mixture, and toluene plus noise (Hsu et al., 2015; Lewkowski et al., 2019; Staudt et al., 2019; Hemmativaghef, 2020). A study found a significant association between organic solvent (toluene, benzene, and ethylbenzene) and high-frequency hearing loss whereby the estimated effect is higher than the audiometrically assessed (Staudt et al. 2019).

## 3.0 Methodology

### 3.1 Data sources

Two search engines PubMed and Web of Science (WoS) were used in this review. The search included peer-reviewed articles published in English from the year 2000 until 2021. The literature search was done with the following keywords: solvent OR chemical AND (Hearing loss) OR (hearing impairment) OR (hearing disorder) OR (auditory dysfunction) AND (Occupational exposure) OR workers OR employee OR workplace AND Ototoxicity OR Ototoxicant OR cochleotoxicants OR vestibulotoxicants). Reference from identified studies was scanned to identify any other relevant research. A set of criteria was established to select relevant studies (Table 1).

Table 1. Inclusion and exclusion criteria

Criterion	Inclusion	Exclusion
Time	Year 2000 onwards	Year 1999 and below
Article type	Peer-reviewed	Non-peer reviewed
Language setting	English	Non-English
Exposure setting	Occupational	Non-occupational
Type of study	Human studies	Animal studies
Hazard exposure	Solvent exposure	Heavy metal, pharmaceutical drugs, asphyxiants, nitriles.
Participant	Occupational workers	Non-occupational workers
Country	Asia	Other than Asia countries

## 4.0 Findings

### 4.1 Description of excluded studies

Initial keyword search identified 125 studies (see Figure 1). A total of 61 studies were excluded composed of duplicate studies (n=43), systematic review, letter, book chapter, case report, case series (n=15), non-occupational exposure studies (n=3). After initial exclusion, a total of 64 studies were retrieved for further screening. The inclusion and exclusion criteria specified in Table 1 were not met by 49 of the 64 studies. Full-text copies from the fifteen remaining studies were used in this study, and the following data were extracted: hazard exposure, study design, sample size, industrial setting, audiological procedure, and the outcome.

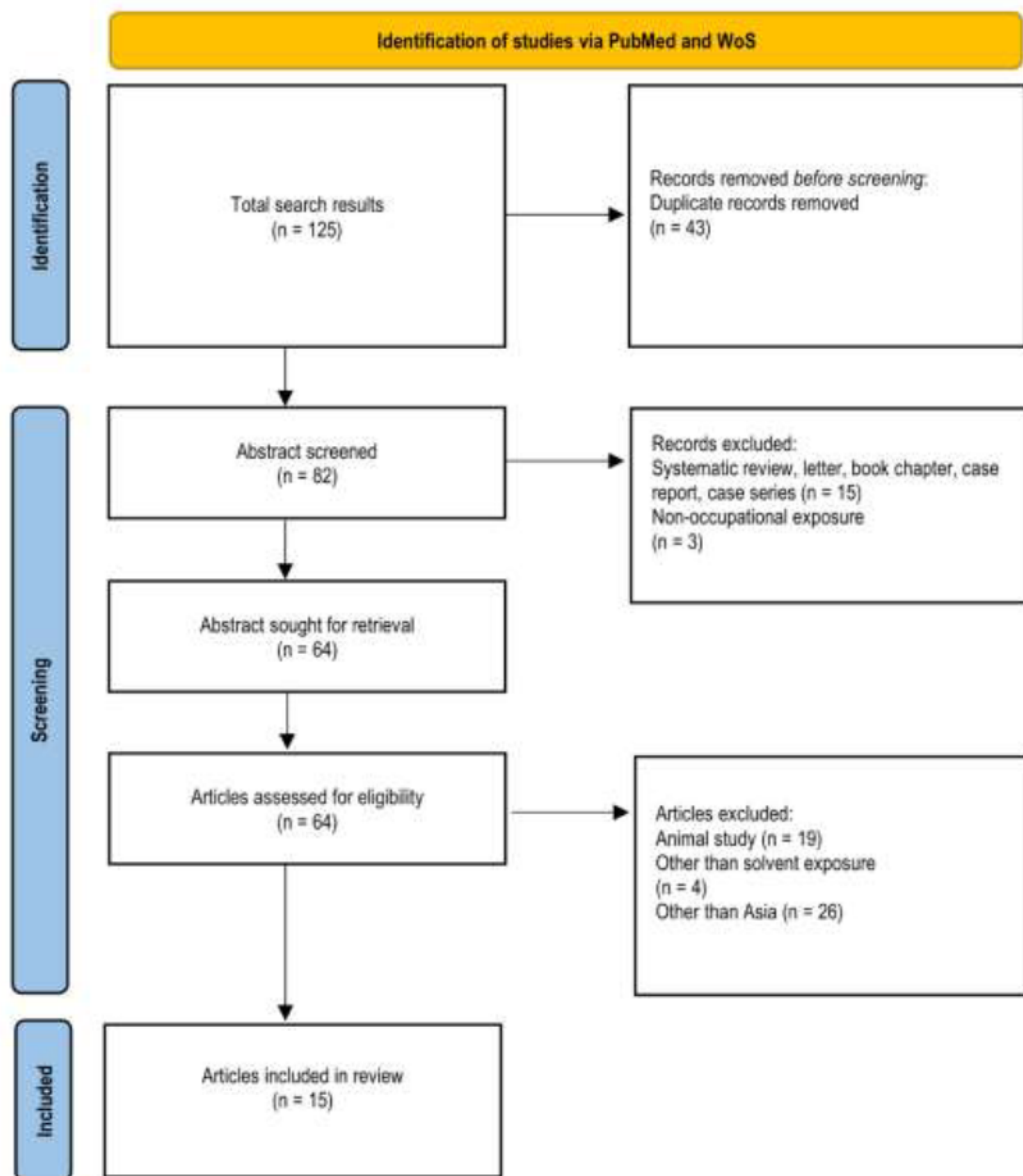


Fig 1: Flow chart of the studies identification and selection process.

## 4.2 Description of selected studies

### 4.2.1 Study design

This review consists of fifteen studies from various occupational settings that were eligible for final review composed of twelve (n=12) cross-sectional studies (Morioka I. et al. 2000; Chang et al. 2003; Kim J. et al. 2005; Chang et al. 2006; Mohammadi S. et al. 2010; Beshir, Elserougy & Amer 2011; Zhang et al. 2013; Choi Y.H & Kim K. 2014; Loukzedeh Z. et al. 2014; Kaewboonchoo et al. 2014; Yang H.Y et al. 2016; Choochouy et al. 2019). Three (n=3) retrospective case-control studies (Rizk and Sharaf, 2010; Metwally et al. 2011; Unlu et al. 2014).

### 4.2.2 Industrial setting

The selected studies in this review were from Plastic button factory (Morioka I. et al. 2000); viscose rayon plant (Chang et al. 2003); aviation industry (Kim J. et al. 2005); adhesive material manufacturing industry (Chang et al. 2006); automobile plant (Mohammadi S. et al. 2010) and (Unlu et al. 2014); fermentation plant factory (Rizk and Sharaf, 2010); ceramic factory (Beshir, Elserougy & Amer 2011); paint industry (Metwally et al. 2011); petrochemical industry (Zhang et al. 2013); nationwide industrial workers (Choi Y.H & Kim

K. 2014); petroleum-distillate-producing industry (Loukzedeh Z. et al. 2014); Naval Officer (Kaewboonchoo et al. 2014); stone processing industry (Yang H.Y et al. 2016); conventional farmers and organic farmers (Choochouy et al. 2019).

### 4.2.3 Auditory Assessment method

Exposure to all substances studied primarily uses Pure Tone Audiometry (PTA; n=15), Otoscopic Examination (n=2), Otopharyngeal Examination (n=1) to measure the study's outcome.

### 4.2.4 Hazard exposure and the Outcome

Eleven (n=11) studies evaluated the combined auditory effect of noise and organic solvents mixture (Morioka I. et al. 2000; Kim J. et al. 2005; Mohammadi S. et al. 2010; Rizk and Sharaf 2010; Beshir, Elserougy & Amer 2011; Metwally et al. 2011; Unlu et al. 2014; Kaewboonchoo et al. 2014; Loukzedeh Z. et al. 2014; Yang H.Y et al. 2016; Choochouy et al. 2019). One study (n=1) evaluated the combined effect of noise, organic solvents mixture, and a mixture of heavy metals (Choi Y.H & Kim K. 2014). The rest of the studies evaluated the combined effect of noise and carbon disulfide, CS<sub>2</sub> (Chang et al. 2003), toluene (Chang et al. 2006), and ethylbenzene (Zhang et al. 2013) individually.

Thirteen out of 15 studies (n=13) demonstrate a significant increase in hearing loss from the exposure of "solvent and noise", "solvent mixture and noise" and "solvent mixture, heavy metal mixture, and noise" compared with the control groups (Morioka I. et al. 2000; Chang et al. 2003; Kim J. et al. 2005; Chang et al. 2006; Mohammadi S. et al. 2010; Rizk et al. 2010; Metwally et al. 2011; Beshir, Elserougy & Amer 2011; Zhang et al. 2013; Unlu et al. 2014; Choi Y.H & Kim K. 2014; Yang H.Y et al. 2016; Choochouy et al. 2019).

Two (n=2) studies related to organic solvent mixture found no association between the organic solvent mixture and hearing impairment (Loukzedeh Z. et al. 2014; Kaewboonchoo et al. 2014). Table 2 shows the highlighted part of the research, hazard exposure, study design, sample size, industrial setting, audiological procedure, and the outcomes.

Table 2. Highlighted part of the research.

Author	Hazard exposure	Study place / design	No. of participants	Industrial setting	Audiological procedure	Outcome
Morioka I. et al. (2000)	Styrene 3.7-46.3 ppm; methanol 2.9-135ppm; methyl acetate 2.5-93.8ppm; Noise 58-92dB(A)	Japan / cross-sectional study	Total: 54	Plastic button factory	PTA 0.5-8kHz	The combined group had a significantly greater prevalence of hearing loss (25%) than the noise-only group and the control group.
Chang et al. (2003)	Carbon disulphide 1.6-20.1ppm. Noise 80-91dB(A)	Taiwan / cross-sectional study	Total: 346	Viscose rayon plant	PTA 0.5-6kHz	Hearing loss >25dB is more common in rayon workers (67.9%) than in administrative (23.6%) and electronic employees (32.4%).  Hearing loss showed the most severe at frequency 6kHz and the least at 2kHz.
Kim J. et al. (2005)	Organic solvent (toluene, xylene, etc.) Noise 85 - 101dB(A)	Korea / cross-sectional study	Total: 328	Aviation industry	PTA 0.5-8kHz	Prevalence of hearing loss of noise plus solvent-exposed group (54.9%) was higher than other groups; 6% unexposed, 17.1% noise only, 27.8% solvent only.  RR 8.1 (noise plus solvent group), 4.3 (noise-only group), 2.6 (solvent-only group).
Chang et al. (2006)	Toluene 33-164.6 ppm Noise 69.9 - 90.1 dB(A).	Taiwan / cross-sectional study	Total: 174	Adhesive material manufacturing workers.	PTA 0.5-6kHz Otopharyngeal examination	The prevalence of hearing loss >25dB in the toluene plus noise group (86.2%) was significantly higher than in the noise only (44.8%) and administrative personnel groups (5%).  Poorest hearing threshold 4-6kHz
Rizk and Sharaf (2010)	Toluene, xylene, butyl acetate, ethyl alcohol Noise 54-107.5dB(A)	Egypt / retrospective case-control study	Total: 140	Fermentation plant factory	PTA 4kHz v-notch	36% exposed group suffered hearing loss compared to the control group (33%), p<0.001.

Mohammadi S. et al. (2010)	Toluene 19-31 mg/m <sup>3</sup> ; xylene 137-388 mg/m <sup>3</sup> ; benzene 0.003 – 2.012mg/m <sup>3</sup>  Noise 75-88dB(A)	Tehran / cross-sectional study	Total: 441	Automobile plant	PTA 0.5-8kHz	A significant association between hearing loss and mix organic solvent even within recommended exposure limit.  High-frequency hearing loss range 4,6 and 8kHz.
Metwally et al. (2011)	Toluene 142- 182 mg/m <sup>3</sup> ; xylene 232-314 mg/m <sup>3</sup> ; other solvents  Noise 68.2- 87.1dB(A)	Egypt / Retrospective case-control study	Total: 222	Paint industry	PTA 0.5-8kHz	Statistically significant different hearing loss between study groups ( $p < 0.01$ ).  The noise plus solvent group had a higher prevalence of sensory neural hearing loss (43%) than the noise-only group (23.4%).
Beshir, Elserougy & Amer (2011)	Organic solvent mixture Toluene, xylene, acetone, ethanol, butanol, ethyl acetate, isopropanolol  Noise 48-83dB(A)	Egypt / Cross-sectional study	Total: 204	Ceramic factory	PTA 0.25-8kHz	Solvent plus noise-exposed group significantly higher auditory threshold compared to control group.  At high frequencies (4 and 8 kHz), the solvent group exhibited a strong positive connection with the exposure time.
Zhang et al. (2013)	Ethylbenzene 122.83-134.64 mg/m <sup>3</sup>  Noise 67.3.- 84.3dB(A)	China / cross-sectional study	Total: 1170	Petrol chemical plant	PTA 0.5-8kHz Otosopic examination	The prevalence of hearing loss is much higher in petrol chemical groups (78.4% and 80.1%) than in the power station (56.9%) and control group (5.2%).  Compared with the control group, OR petrochemical groups were 107 (95% CI = 17.1 to 358) and 114 (95% CI = 34.2 to 343), about four times higher than that of 27.5 (95% CI = 6.4 to 63.2) in the power station group, respectively.
Choi Y.H & Kim K. (2014)	Mixture / individual Organic solvent (toluene, isopropyl alcohol, xylene).  Mixture heavy metal (lead, cadmium, mercury, chrome, manganese)  Noise >80 dB(A)	Korea /cross-sectional study	Total: 30,072	Industrial workers	PTA 0.5-6KHz	Individuals exposed to heavy metal plus organic solvent had 1.64 to 2.15 times higher PTA increment with occupational noise exposure.  Higher increment organic solvent at 3,4 and 6 kHz; heavy metal exposed group at 2 and 3kHz.

Loukzede Z. et al. (2014)	Organic solvent (toluene, xylene, benzene)  Noise <75dB(A)	Iran / Cross-sectional study	Total: 182	Petroleum-distillate-producing industry	PTA 0.5-8kHz	No significant association between solvent exposure and hearing loss.
Unlu et al. (2014)	Toluene 26-33mg/m <sup>3</sup> , benzene 0.98-1.86mg/m <sup>3</sup> , xylene 265-411mg/m <sup>3</sup> , tetrachloroethylene 43-51 mg/m <sup>3</sup> , acetone 98-182 mg/m <sup>3</sup> .  Noise 78-87dB(A)	Turkey / Retrospective case-control study	Total: 588	Bus and truck manufacturing plant.	PTA 0.5-8kHz.	Hearing loss was increased in the solvent plus noise-exposed group in the range 2-8kHz.  The prevalence of hearing loss is higher in the solvent plus noise group compared to other groups.
Kaewboonchoo et al. (2014)	Organic solvent mixture; toluene 0.18-0.32 ppm; xylene 0.12-0.15 ppm, ethyl acetate 0.40-0.70ppm, butyl acetate 0.09-0.11ppm, and cyclohexanone 0.13-0.29ppm  Noise 62.2-104.7 dB(A)	Thailand / cross-sectional study	Total: 149	Naval Officers	PTA 0.5-8kHz	39.6% of Naval Officers had hearing loss.  Hearing loss was linked to people who were over 39 years old and had more than 8 years of job experience.



Yang H.Y et al. (2016)	78 Volatile organic solvent (toluene, acetate, butane, etc.)  Noise 87.7dB(A)	Taiwan / cross-sectional study	Total: 314	Stone processing industry workers.	PTA 0.2-20kHz	Prevalence of hearing loss increase in the epoxy exposed group (42%) compared to the non-epoxy exposed group (21%), administrative staff group (9.3%).  Significantly increased risk of hearing loss in the epoxy adhesive exposed group between 2-6kHz (interaction observed at 3,4, & 6kHz.)
Choochouy et al. (2019)	Insecticide 0.07, >2.407 (score-year)  Organophosphate 0.09, >1.118 (score-year)  Noise 61.8-92.7dB(A)	Thailand / Cross-sectional study	Total: 335	Conventional farmers and organic farmers	PTA 0.5-6kHz Otoscopy examination	Cumulative exposure from groups insecticide, organophosphate, and noise was associated with an increased high-frequency hearing threshold in conventional farmers.  Prevalence abnormal hearing (>25dB) is higher in the high-frequency band (3-6kHz) than in the lower band (0.5-2kHz).

## 5.0 Discussion

### 5.1 Exposure of Workers to Solvent and Noise

The prevalence of hearing loss of  $\geq 25$  dB in the group with concurrent exposure to noise and CS<sub>2</sub> (Chang et al. 2003), toluene (Chang et al. 2006), and ethylbenzene (Zhang et al. 2013) was considerably higher in the solvent-exposed group than that in the two comparison groups, the noise-only group, and the control group.

Studies have proven that the noise plus solvent mixture exposed group seem to have the highest rate of hearing loss compared to the solvent only and unexposed groups, despite the level of noise (Metwally et al. 2011; Unlu et al. 2014) level of each organic solvent (Kim J. et al. 2005; Morioka I. et al. 2000; Metwally et al. 2011; Unlu et al. 2014; Yang H.Y et al. 2016) lower than the level recommended limit and threshold limit value (TLV). There was also a significantly higher auditory threshold shift in the solvent and noise-exposed group than the control group, although the concentration solvent mixture was lower than the level recommended limit and threshold limit value (TLV) (Beshir, Elserougy & Amer, 2011).

On the contrary, Kaewboonchoo et al. (2014) reported that only age and service experience were significantly associated with hearing loss. This is due to the fact the highest exposure solvent level was only 1.6% from the exposure limit. A similar finding was also reported by Loukzede Z. et al. (2014), who pointed that there was no significant association between solvent exposure and high-frequency and low-frequency hearing loss. This might be due to the noise level at all sites was 75dB, much lower than the permissible exposure limit and the mean work duration was less than four years. M. Śliwińska-Kowalska et al. (2005) also found that the risk of hearing loss was not increased by short-term (four years) exposure to a low-concentration mixture of chemicals.

Ten reported studies (n=10) confirmed a synergistic effect of solvent and noise exposure (Morioka I. et al. 2000; Chang et al. 2003; Kim J. et al. 2005; Chang et al. 2006; Mohammadi S. et al. 2010; Rizk and Sharaf 2010; Metwally et al. 2011; Zhang et al. 2013; Unlu et al. 2014; Yang H.Y et al. 2016). These studies confirmed an increased effect of combined exposure of noise and solvent compared to noise alone. Similarly, Kim J. et al. (2005) concluded that noise and solvent have a multiplicative synergistic effect.

Two studies (n=2) confirmed that there was an additive effect of solvent exposure and noise. Choochouy et al. (2019) claimed that there was an additive effect between pesticide and noise exposure since the model in this study did not show any synergistic effect. The same results were also obtained by Choi Y.H. and Kim K. (2014), who claimed that noise exposure is the main cause of hearing loss and the ototoxic chemicals may have an additional impact in low-noise environments. However, there was no accessible measurable data for the solvent and heavy metal in that study as they were classed as exposed or not exposed.

High-frequency hearing loss is more common in the solvent plus noise-exposed group compared to noise only and solvent only group (Morioka I. et al. 2000; Kim J. et al. 2005; Mohammadi S. et al. 2010; Metwally et al. 2011; Beshir, Elserougy & Amer, 2011; Choi Y.H. and Kim K. (2014); Unlu et al. 2014). Loukzede Z. et al. (2014). Beshir, Elserougy & Amer (2011) reported that when comparing the solvent group and the noise group, hearing loss is more common at 8 kHz than 4 kHz in the solvent group, while in the noise group, 4 kHz is more common than 8 kHz. Rizk and Sharaf (2010) who studied workers in a fermentation plant factory revealed that there was a significantly higher proportion of v-notch among solvent mixture and noise group than the non-exposed at 4k Hz. On the other hand,

two studies claimed that there was a significant interaction between solvent mixture and noise were observed in mid and high frequency (3-6 kHz) (Yang H.Y et al. 2016; Choochouy et al. 2019).

The pattern of hearing impairment associated with concurrent exposure of noise and CS<sub>2</sub> (Chang et al. 2003) and toluene (Chang et al. 2006) were similar. Both investigations discovered that the most significant effect at lower frequencies of 0.5 to 2 kHz. When compared to noise alone, both solvent-exposed groups show a more significant impact on speech frequency. However, the results were most likely caused by conductive hearing loss as sound may not reach the inner ear due to an obstruction or damage to the outer or middle ear that prevents sound from being conducted to the inner ear.

### 5.2 Implication and the Knowledge Gaps.

Only 27% of studies have conducted pure-tone air and bone conduction audiometry, capable of distinguishing between conductive and sensorineural hearing loss. Therefore, most studies could not truly confirm that the hearing losses were due to solvent exposure. Due to this fact, this is a systematic review with the diversity of outcome measures within the Asia region, the potential underlying reason should have come into consideration.

Understanding the type of hearing loss and the equipment required to improve auditory reception is critical in addressing hearing loss. One way to distinguish between conductive and sensorineural hearing loss is by comparing air-conduction and bone-conduction hearing threshold levels. According to Rowe & O'Leary (2014), air-conduction thresholds provide only limited information on auditory disorders. The bone-conduction testing thresholds are needed to determine whether an auditory impairment is conductive or cochlear (sensorineural) or both (mixed).

Since air conduction audiometry is the most widely used audiometry test for screening occupational hearing loss, it is insufficient to use results based on this screening audiometry to diagnose the type of hearing loss. Thus, air-conduction audiometry should always be complemented with bone-conduction audiometry to critically distinguish between conductive and sensorineural hearing loss. Researchers could also consider a more sensitive test, the Otoacoustic Emission to complement PTA. This test can detect hearing loss one phase earlier compared to PTA and could differentiate whether it is a sensory hearing disorder or neural hearing disorder.

## 6.0 Conclusion & Recommendations

It can be concluded that concurrent exposure of solvent and noise might cause synergistic and additive interaction. Therefore, in the case of a combination of exposure, the permissible exposure limit for each noise and solvent should be lowered than the existing permissible limit. Employees exposed to ototoxic solvents must be included in the Hearing Conservation Program (HCP). However, it is also important to note that in most of the reported cases where potential ototoxic was identified, the actual sensorineural diagnosis could not be made certain as the studies did not mention specific bone conduction tests being done in the methodology. More epidemiology studies on the hearing effect from solvent exposure using a diverse approach are warranted to let the underlying cause of the problem be diagnosed.

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## Paper Contribution to Related Field of Study

This study provided the up-to-date current state of the research on solvent-induced hearing loss in Asia and analyzed the interaction effect of simultaneous noise and solvent exposure.

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