The Combined Effects of Occupational Exposure to Noise and Other Risk Factors — A Systematic Review

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Abstract

Purpose: Noise-induced health effects exacerbate by many other risk factors. This systematic review aims at shedding light on the combined effects of co-exposure to occupational noise and other factors. Material and Methods: A literature search in Web of Science, Scopus, PubMed, Science Direct, and Google Scholar, with appropriate keywords on combined effects of occupational noise, and co-exposure to noise and other factors, revealed 7928 articles which were screened by two researchers. A total of 775 articles were reviewed in full text. We found 149 articles that were relevant and had sufficient quality for analysis. Results: We identified 16 risk factors that exacerbate occupational noise-induced health effects. These factors were classified into four groups: chemical (carbon monoxide (CO), solvents, heavy metals, and other chemicals), physical (lighting, heat, vibration, and cold), personal (age, gender, genetics, smoking, medication, contextual diseases) and occupational (workload and shift work). Hearing loss, hypertension, reduced performance, and cardiovascular strains, are the most important risk factors combined effects due to concurrent exposure to noise and other risk factors. Conclusion: Evidences of combined effects of solvents, vibration, heavy metals, CO, smoking, chemicals, aging, heat, and shiftwork were respectively stronger than for other factors. Most of the studies have investigated only the combined effects of risk factors on hearing, and the evidence for non-auditory effects is still limited, and more studies are warranted. Therefore, in the Hearing Conservation Programs, besides noise, aggravating factors of noise effects should also be taken into account.

Keywords: Aggravating factors, combined effects, combined exposure, noise effects, occupational exposure

INTRODUCTION

Noise-induced health effects exacerbate by many other risk factors. In other words, in the workplace, there are many risk factors in the combined exposure to noise. Combined exposures occur, for example, when steelworkers are exposed to blast furnace where noise and heat co-exist. Noise-induced hearing loss (NIHL) is the most frequently reported occupational disease in many studies. World Health Organization (WHO) estimated that about 45 million people suffer from mild to severe hearing loss in the occupational noise exposures. Non-auditory effects of exposure to noise include speech interference, sleep disturbance, cardiovascular and other physiological effects, psychological effects including those on cognitive performance and memory, effects on behavior, and annoyance, and side effects such as the increased risk of accidents. However, the health impact of the combined exposure to noise and other factors has been less investigated. In the workplace, workers are simultaneously exposed to several stressors that include a variety of physical, chemical, and biological, and psychological agents. Workers’ exposure to the combination of harmful factors in the workplace is associated with worse health consequences. Evaluation of occupational combined exposure to several risk factors, and

Access this article online

Quick Response Code:
Website: www.noiseandhealth.org
DOI: 10.4103/nah.NAH_4_18

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Received: 16 January 2018 Revised: 20 December 2019 Accepted: 3 January 2020 Published: 25 July 2020

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How to cite this article: Golmohammadi R, Darvishi E. The Combined Effects of Occupational Exposure to Noise and Other Risk Factors — A Systematic Review. Noise Health 2019;21:125-41.
also their interaction effects are very complex. Because in studies of specific effects due to noise, there are many confounding or aggravating factors.\(^1\) Effects due to combined exposure are exacerbating.\(^8\) Thus, a combined effect may be synergistic, additive, potentiation, or antagonism. Many occupational noise studies have considered the combined health effects of occupational exposure to noise and other risk factors.\(^3\),\(^9\) Hence, this paper reviews the literature on the combined effects of concurrent exposure to occupational noise and other factors.

**MATERIAL AND METHODS**

By reviewing the scientific literature, a systematic and critical analysis of the retrieved papers on the combined effects of occupational exposure to noise and intensifying factors was performed. The scientific literature search included the following databases: Web of Science (1950), Scopus (1995), MEDLINE (via PubMed) (1946), Science Direct (1985), and Google Scholar (1985), as well as Cochrane Collaboration Summaries. Also, a search strategy was developed for each database. We searched the following terms (MeSH) in the title and abstract using the Booleans connectors: “combined effects”, combined exposures, “occupational noise”, “exacerbating factors”, and “noise effects”. The search was completed in September 2019.

**Inclusion and exclusion criteria**

The inclusion criteria were exposure to occupational noise in combination with different kinds of risk factors which exacerbate the noise-induced health effects and the statistical association between the combined exposure and health outcomes. In this review, we have mainly focused on occupational, observational, and experimental studies, and also original articles in English and Persian journals. As to the present review, only articles regarding combined exposure to noise and other risk factors (i.e. co-exposure to noise and other physical or chemical agents) were included. Papers regarding environmental noise studies were excluded. All titles and abstracts from the literature search were assessed against the inclusion criteria. References that we judged to be potentially relevant were read in full and assessed for inclusion. For the assessment of studies’ methodology and quality, the comprehensive checklist of the National Institute of Occupational Health was used. The checklist was developed based on the Ariens\(^{10}\) and Hoogendoorn\(^{11}\) suggestions for observational studies. Therefore, the study population, noise exposure level (Equivalent Continuous Sound Level), data, and control of confounding factors was evaluated. We identified 149 articles that met the inclusion criteria and were eligible for this review. These were cross-sectional studies (\(N=93\)), longitudinal studies (\(N=22\)), experimental (\(N=26\)), and other (\(N=8\)). A flow chart of the selected studies is presented in Figure 1 (Prisma).

![Flow chart of the studies identification and selection process](image-url)
In the final, based on the literature review, a conceptual model for the combined effects was presented and examined concepts of stress and strain.

RESULTS

We identified 16 important risk factors (in four categories) in the workplace, which can intensify the noise-induced health effects during simultaneous exposure to noise and each of them. So, according to the literature review, we outlined four broad categories of risk factors that aggravate occupational noise effects: personal factors, occupational factors, physical agents, and chemical agents [Table 1]. The results of the review are presented based on these four categories. Also, in the end, the levels of evidence and risk of combined effects of each were determined based on the design and quality of articles reviewed. The level of evidence was determined based on the number of citations, methodological quality and design, validity, and applicability of studies results (Low – Medium– High). Moreover, the level of combined risk is the degree of effect intensification caused by the simultaneous presence of two factors or agents that was determined based on design and study type, the methodology, validity of data, and the study population. These effects include Additive, Synergistic, Potentiation, and Antagonism effects. An additive effect is the combined effect produced by the action of two or more agents, being equal to the sum of their separate effects. A synergistic effect is an effect arising between two or more agents or factors that is greater than the sum of their individual effects (2 + 2 = 25). The potentiation effect is an interaction between two factors (one with (2) and another without effect (0)) so that the no-effect agent enhances the total effect (0 + 2 = 10). Antagonism effect is when two or more agents in combination have an overall effect that is less than the sum of their individual effects. It is opposite to a synergistic effect (5 + 0 = 2).

PERSONAL FACTORS

Noise and age

Hearing loss is mainly related to increasing age. The interaction between noise exposure and aging on noise-induced hearing loss (NIHL) is complicated, and it might be an additive effect. Age-related hearing loss (ARHL) increases with age, but the NIHL begins after about 3–5 years of excessive exposure to high levels of noise. NIHL does not increase to the same extent in older persons as in younger persons because older persons already have ARHL. In frequencies that have already suffered severe hearing loss, age has a limited effect on NIHL. With aging, the death of hair cells increases in the cochlea. Also, other parts of the hearing apparatus such as the auditory nerve and cognitive functions might be affected with aging. Rubak et al. reported that in employees exposed to noise for more than 20 years compared to employees exposed less than 20 years, the risk of hearing loss was higher. In a cross-sectional study, Somma et al. compared the hearing of 184 male cement workers (daily noise exposure level >85 dB) with 98 non-exposed controls. They reported that a 5 dB hearing loss among the younger (age 21–30), and a 20 dB among the older workers (age 51–60), compared to the controls. Also, in another cross-sectional study, Loukzadeh et al. showed that with the increasing age and work experience, the mean hearing threshold in 4kHz and 8kHz frequencies significantly increased among 372 workers in a ceramic industry (mean age: 35±7.1 years). In another cross-sectional study, Golmohammadi et al. investigated the NIHL in 1062 tractor manufacturing workers (mean age 43.2 ±6.9 years and the Leq) was > 85 dB(A)). The study showed that hearing loss increased by age and work experience. Besides, they reported that regression coefficients (beta) of hearing loss were 0.303, 0.327, and 0.120 per one dB Leq, and per one year of work experience and age, respectively. Also, in a prospective, population-based, longitudinal study of individuals aged 70–75 years (432 men and 581 women) Hederstierna and Rosenhall reported an association between aging and NIHL. This study supports an additive model of NIHL and ARHL association. Overall, the literature suggests a correlation between NIHL and increasing age as an additive model so that aging increases NIHL compared to noise exposure alone (additive model).

Noise exposure and gender

Although, there are few studies concerning the role of gender in the occupational noise effects. However, it is probably an effective factor. In two cross-sectional studies of Beaver Dam, Wisconsin, Cruickshanks et al. (N = 3753) and Nash et al. (N = 3285) reported that hearing loss was associated with male gender, and occupational noise exposure. In a prospective study among 804,535 soldiers, Helfer reported that men lost hearing more than women after the same exposure to noise greater than 85 dB(A).

| Table 1: Aggravating risk factors of noise-induced health effects |
|---------------------------------------------------------------|
| Category | Aggravating risk factors |
|----------|--------------------------|
| Personal factors | Age, gender, genetic background, smoking, medication, contextual diseases |
| Chemical agents | Carbon monoxide, heavy metals, solvents, chemical substances |
| Physical agents | Lighting, heat, vibration, cold |
| Occupational factors | Workload, shift work |
In the field of non-auditory effects, in a laboratory study on 169 students (80 females and 89 male), Beheshti et al. (2019) reported that noise-induced annoyance among females was more frequent than among men. Röösli et al. (2023) examined sleep disturbances in 733 women and 533 men due to exposure to noise (Leq > 40 dB(A)). They suggested that noise-induced sleep disturbance in among men was greater than among women (at the same level of noise exposure). Girard et al. (2025) investigated cardiovascular disease among 8,910 retired workers exposed to occupational noise (≥80 dB (A)/8 h). They reported that the effect of noise on the prevalence of cardiovascular diseases was more pronounced among women compared to men.

**Noise and genetic background (genetic predisposition or heredity)**

Genetic or hereditary factors are a predisposing factor in noise effects, and there are several genetic studies of the relationship between genetic background and NIHL. Gates et al. (2031) confirmed that genetic background was very important for hearing. Konings et al. (2012) reported a correlation between exposure to noise and genetic variation in a survey of 1261 male noise-exposed workers (three occupational noise exposure categories, ≤85 dB(A), 86–91 dB(A), and ≥92 dB (A)) and they suggested that PCDH15 and MYH14 might be NIHL susceptibility genes. Also, Shen et al. (2013) suggested that GSTM1 polymorphism is associated with susceptibility to NIHL in a survey in 444 NIHL and 445 normal-hearing Chinese workers exposed to three occupational noise exposure categories: 85 dB(A) or less, 86 to 91 dB(A), and 92 dB (A)). NIHL is a sensorineural, rampant, and complex disease that can even result from the interaction of exposure to noise and genetic background. There are numerous studies on humans and animals showing that phenotypic variability may affect hearing. In another experimental study, Yousaf et al. (2036) reported that a phenotypic a phenotypic variability has a great variety of reasons, including physical agents at workplace (such as noise exposure). In a Chinese case-control study, Xu et al. (2037) studied ten single nucleotide polymorphisms in the genes POU4F3 and GRHL2 among 3790 workers who worked in a steel factory and exposed to occupational noise higher than 80 dB(A). They confirmed that genetic variations in POU4F3 and GRHL2 were associated with NIHL. Also, in a case-control study with 326 hearing loss cases and 326 controls of steelworkers, Yang et al. (2038) showed that EYA4 genetic variant and its interaction with noise (cumulative noise exposure ≥98 dB(A)) may have contributed to the NIHL. Shen et al. (2039) examined genetic variation in APE1 gene among 613 NIHL workers and 613 normal-hearing workers (age range 21–59 years) who were exposed to noise 85-92 dB(A). They found that the APE1-656 T>G polymorphism may have modified the susceptibility to NIHL. Overall, researchers from different countries have found that mutations of numerous genes were associated with hearing loss.

**Animal studies**

In an experimental study on a population of inbred mouse strains exposed to 10-kHz octave band noise at 108 dB sound pressure level during 5–6-weeks, Lavinsky et al. (2040) demonstrated that genetic architecture of NIHL provided strong evidence for gene-by-noise interactions in NIHL.

**Noise and smoking**

Smoking is potentially relevant for hearing loss and all of the studies we identified suggest that smoking is an exacerbating risk factor for NIHL. Starck et al. (2047) found that combined exposure to noise and smoking contributed significantly to NIHL among 199 professional forest workers (exposed to the noise level of 95 dB(A)) and 171 shipyard workers (exposed to the noise level of 86 dB (A)). In a cross-sectional study, Mehrparvar et al. (2048) evaluated the combined effects of noise exposure and smoking (at least 1 pack/year) on pure tone audiometry (PTA) and distortion product otoacoustic emissions (DP-OAEs) on 224 workers (105 smokers and 119 nonsmokers) exposed to noise (Leq = 91 dB(A)) in the tile and ceramic industry. They reported that mean DP-OAE response amplitude at frequencies higher than 1000 Hz was significantly higher in smokers compared to non-smokers. Also, in two cross-sectional studies, with 8543 subjects (3593 smokers and 4950 non-smokers) exposed to occupational noise (>85dB(A)) and with 622 male workers (252 smokers and 370 non-smokers) exposed to occupational noise (Leq = 91 dB(A)) Sung et al. (2049) and Mohammadi et al. (2050) showed that smoking accompanied by noise exposure had an interactive effect on hearing loss. Also, the hearing thresholds of workers exposed to noise were significantly influenced by smoking. In a cross-sectional study of 270 male workers of rubber factory (135 smokers and 135 non-smokers) revealed that hearing loss was significantly associated with co-exposure to noise (L_Aeq,8h ≥ 85 dB(A)) and smoking. In another cross-sectional study, Tao et al. (2052) examined the effect of smoking on NIHL in 517 male workers (199 nonsmokers and 318 smokers) exposed to L_Aeq,8h ≥ 90 dB(A). The study suggested that interaction between smoking and occupational noise exposure may have been additive (hearing loss was 1.94 times more frequent than with noise alone). In a population-based cross-sectional study among 1723 women exposed to noise > 85 dB(A), Ferrite et al. (2053) suggested a dose–response relationship between smoking and noise on hearing loss.

In investigating the effect of smoking on hearing loss of 150 male workers from a refractory factory (55 smokers and 95 non-smokers), who were exposed to occupational noise levels of 89±3 dB(A), Mofateh et al. (2054) emphasized that smoking had an additive role in hearing loss of workers exposed to noise. Additionally, two studies were found in the field of non-auditory effects of noise. In a retrospective study, Alimohammadi and Danesh (2055) evaluated the combined
The synergistic interaction of cisplatin and noise has been investigated since the 1960s. Gannon and Tso [61] reported aminoglycoside-induced ototoxicity by concurrent exposure to noise and furosemide (100 mg/kg) and salicylic acid (350 mg/kg) has an additive effect with noise. All of the research literature on the combined effects of drugs and noise is based on experimental work on laboratory animals. In an experimental study, Bombard et al. [59] found the combined effect of noise (Leq = 85–95 dB(A)) and gentamicin on hearing of 89 albino’s male guinea pigs. Cisplatin (antineoplastic drugs) is a chemotherapeutic against malignancies. However, its ototoxic effect is relatively strong. In an experimental study, DeBacker [60] confirmed the synergistic interaction of cisplatin and noise (SPL = 90–110 dB(A)) on hearing loss of rats. Potentiation of aminoglycoside-induced ototoxicity by concurrent exposure to noise has been investigated since the 1960s. Gannon and Tso [61] reported aminoglycoside-induced ototoxicity. In a study on guinea pigs study, Vernon et al. [62] confirmed a prominent synergistic effect of noise (45 dB SPL) and neomycin (200 mg/kg/day). Collins [63] also reported that the combination of gentamicin (50 mg/kg/day for 10 days) and noise (116 dB SPL for 1 hour) caused a considerable hair cell loss that surpassed a simple summation due to each factor alone. In another study, Tan et al. (2001) reported that exposure to aminoglycoside antibiotics (100 mg/kg/day) aggravated a noise-induced cochlear damage. [64] In another animal study, Ryan and Bone [65] discovered that hearing threshold increased with the combined exposure to noise (100 dB SPL) and aminoglycoside antibiotics (150 mg/kg/day). Also, in another experimental study on normal hearing albino mice (N = 39), De Jong et al. [66] reported that a combination of exposure to noise (Laeq > 113 dB(A)) and furosemide (100 mg/kg) and salicylic acid (350 mg/kg) increased the hearing loss compared with exposure to noise alone. Hence, NIOSH (The National Institute for Occupational Safety and Health) and ACOEM (American College of Occupational and Environmental Medicine) have recommended hearing protection programs and risk assessment for exposure to ototoxic drugs and chemical substances. [67] Also, OSHA (Occupational Safety and Health Administration) has recommended hearing testing of workers exposed to ototoxic medications regularly. [68]

**Animal studies**

Habylabady et al. [57] investigated the combined effect of exposure to cigarette smoke and noise on hearing loss of three groups of male rats, during 10 days, 8 hours daily. They observed the permanent change in rats’ hearing. It can be concluded that smoking significantly exacerbates NIHL and has an additive effect with noise.

**Noise and medication (drugs)**

It has been found that several medications have toxic effects on the hearing (ototoxic). Gentamicin toxicity is the most common single known cause of bilateral vestibulopathy. [58] All of the research literature on the combined effects of drugs and noise is based on experimental work on laboratory animals. In an experimental study, Bombard et al. [59] found the combined effect of noise (Leq = 85–95 dB(A)) and gentamicin on hearing of 89 albino’s male guinea pigs. Cisplatin (antineoplastic drugs) is a chemotherapeutic against malignancies. However, its ototoxic effect is relatively strong. In an experimental study, DeBacker [60] confirmed the synergistic interaction of cisplatin and noise (SPL = 90–110 dB(A)) on hearing loss of rats. Potentiation of aminoglycoside-induced ototoxicity by concurrent exposure to noise has been investigated since the 1960s. Gannon and Tso [61] reported aminoglycoside-induced ototoxicity. In a study on guinea pigs study, Vernon et al. [62] confirmed a prominent synergistic effect of noise (45 dB SPL) and neomycin (200 mg/kg/day). Collins [63] also reported that the combination of gentamicin (50 mg/kg/day for 10 days) and noise (116 dB SPL for 1 hour) caused a considerable hair cell loss that surpassed a simple summation due to each factor alone. In another study, Tan et al. (2001) reported that exposure to aminoglycoside antibiotics (100 mg/kg/day) aggravated a noise-induced cochlear damage. [64] In another animal study, Ryan and Bone [65] discovered that hearing threshold increased with the combined exposure to noise (100 dB SPL) and aminoglycoside antibiotics (150 mg/kg/day). Also, in another experimental study on normal hearing albino mice (N = 39), De Jong et al. [66] reported that a combination of exposure to noise (Laeq > 113 dB(A)) and furosemide (100 mg/kg) and salicylic acid (350 mg/kg) increased the hearing loss compared with exposure to noise alone. Hence, NIOSH (The National Institute for Occupational Safety and Health) and ACOEM (American College of Occupational and Environmental Medicine) have recommended hearing protection programs and risk assessment for exposure to ototoxic drugs and chemical substances. [67] Also, OSHA (Occupational Safety and Health Administration) has recommended hearing testing of workers exposed to ototoxic medications regularly. [68]

**Noise and contextual diseases**

Studies have shown that noise exposure exacerbates contextual diseases. And vice versa suffering from a contextual disease aggravates the noise effects (such as hearing loss). [13] According to various studies, cardiovascular diseases and hypertension, diabetes, increased cholesterol and triglycerides are significantly associated with NIHL. [69] In a cohort study of occupational noise exposure and diabetes (N = 245), Ishii et al. [70] reported that the incidence of type 2 diabetes was associated with hearing loss. In an occupational cohort of 665 workers at an American university, Fuortes et al. [71] reported that hearing loss was associated with high cholesterolemia and high blood pressure. Also, in a population-based cohort study of 1189 men, Yoshioka et al. [72] reported that arterial sclerosis could intensify deleterious effects of noise and exacerbate NIHL. In a cross-sectional multicenter study (N = 4083) of the impaired hearing due to a number of factors, such as occupational noise, cholesterol, diabetes, heart disease, and hypertension, Fransen et al. [73] concluded that NIHL might be associated with cardiovascular disease. In general, more longitudinal studies are needed on the combined effects of contextual diseases at workplaces. Table 2 shows a summary of the results of the literature review about the combined effects of personal factors and noise and also the level of risk and evidence.

**CHEMICAL AGENTS**

**Noise and carbon monoxide (CO)**

Carbon monoxide is a toxic asphyxiant that impairs the oxygen exchange to tissues by producing carboxyhemoglobin (COHb). [74] International commission on biological effects of noise (ICBEN) has reported that carbon monoxide exacerbates effects of exposure to occupational noise on hearing. [75] Studies show that CO can reduce oxygen levels in the cochlea (cochlear hypoxia) particularly in the basal region. [76] Noise exposure also induces cochlear hypoxia. [77] Thus, chronic cochlear hypoxia caused by concurrent exposure to noise and CO can lead to significant effects on hearing of workers at workplaces such as the steel industry. [78] Lacerda and Leroux [79] compared the hearing thresholds of a group of workers exposed to noise (90 dB(A)) and CO, with another group of workers exposed only to noise (90 dB(A)). The results revealed that hearing thresholds (at high frequencies 3, 4, and 6 kHz) was significantly higher in the “noise + CO group” compared to the “noise group”. In an observational
In a retrospective and cross-sectional study, Concerning the non-auditory effects of CO, we identified compared to the 2 noise group. More frequent by 12% among the 2 noise + CO group workers in a steel plant. They concluded that hearing loss was (ppm)) and noise (range of 87–93 dB(A)) among 80 male workers in a steel plant. They concluded that hearing loss was more frequent by 12% among the 2 noise + CO group compared to the 2 noise group.

Concerning the non-auditory effects of CO, we identified only one study. In a retrospective and cross-sectional study, Zeigelboim et al. [81] evaluated the neurological symptoms in 30 Brazilian fishermen exposed to a combination of CO (100 ppm) and noise (97 dB(A)). The results revealed that neurological symptoms (fatigue, dizziness, anxiety, mental impairment, and depression) were significantly more among workers exposed to a combination of noise and CO than among those exposed only to noise.

Animal studies

In an experimental study, Young et al. [78] examined the combined effects of exposure to noise (L_{Aeq} = 90\,\text{dB(A)}) and CO (1200 ppm) on hearing of 16 male Long-Evans hooded rats. They reported that CO potentiated high-frequency auditory threshold shifts induced by noise.

| Personal factors | The level of combined risk | Level of evidence | Effects | Comments | Study |
|------------------|----------------------------|-------------------|---------|----------|-------|
| Noise & aging    | Exposure to Leq > 85 dB(A) and age (mean) > 45 years, exposure (mean) > 3–5 years | Additive | High | Hearing loss | Aging high age is strongly related to hearing loss |
|                  | Exposure to Leq > 80 dB(A) and male gender | Potentiation | High | Hearing loss, sleep disturbance | Men lose hearing more frequent than women and women are more vulnerable to non-auditory effects |
| Noise & genetic background | Exposure to Leq > 80 dB(A) and genes POU4F3 | Potentiation | Medium | Hearing loss | Genetic background predisposes for NIHL (explains a great part of the individual variation in hearing loss) |
| Noise & smoking  | Exposure to Leq > 85 dB(A) and smoking (a pack per month during 5 years) | Additive | High | Hearing loss, hypertension, | Smokers have NIHL higher than non-smokers |
| Noise & medication | Exposure to Leq > 85 dB(A) and permanent drug intake (at least 3–5 years) | Both synergistic and antagonism | High | Hearing loss | Aminoglycoside, cisplatin, and gentamycin have a synergistic effect. Cysteine and Ginseng have an antagonistic effect on NIHL |
| Noise & contextual disease | Suffering from disease and exposure to Leq > 85 dB(A) simultaneously | Additive | Medium | Hearing loss and other diseases | Ear disease, diabetes mellitus, and hypertension are significantly associated with NIHL but cholesterol and triglycerides relation to NIHL is uncertain |

Level of evidence: was determined based on the number of citations, methodological quality and design, validity, and applicability of obtained results (Low – Medium – High). The Level of combined risk: The degree of effect intensification caused by the simultaneous presence of two factors or agents that was determined based on design and study type, the methodological, validity of data, and the study population. Additive effect: The combined effect produced by the action of two or more agents, being equal to the sum of their separate effects (2+2=4). Synergistic effects: An effect arising between two or more agents, or factors, that produces an effect greater than the sum of their individual effects (2 + 2 = 25). Potentiation effects: The combination of a factor or agent that has no effect (0) with a factor or agent that has some effect (2) equals the combined effect (10) greater than the sum of the effects of each one alone (0 + 2 = 10). Antagonistic effects: Two or more agents in combination have an overall effect that is less than the sum of their individual effects (5 + 0 = 2).

Study, Ferreira et al. [80] investigated hearing effects induced by simultaneous exposure to CO (ranged from 200 to 700 (ppm)) and noise (range of 87–93 dB(A)) among 80 male workers in a steel plant. They concluded that hearing loss was more frequent by 12% among the 2 noise + CO group compared to the 2 noise group.

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Noise and solvents

We identified 21 studies describing the combined effects of occupational exposure to noise and solvents. Solvent exposure is associated with hearing loss.[82,83] Morata et al. [84] reported that the combination of noise (88–97 dB (A)) and solvents (370 ppm) increased the hearing loss compared with exposure to noise and solvents separately (a synergistic effect). Sliwinska-Kowalska et al. [85] studied the combined effects of noise and solvents, such as styrene, xylene, n-hexane, and toluene on hearing loss of 1117 workers from different industries. They reported that the combination of noise (Leq > 85 dB(A)) and solvents caused a greater hearing loss than exposure only to noise. Kim et al. [86] examined the toxic effect of mixed solvents on the auditory system of 542 male workers in the aviation industry, who were exposed to noise (levels ranged from 85 dB(A) to 101 dB(A)). They suggested that the prevalence of hearing loss was higher in the group exposed to noise and mixed solvents simultaneously (54.9%) than among those exposed only to noise (6%). Jacobsen et al. [87] in a Danish cross-sectional study on 3282 men (exposed to both noise>86 dB(A) and solvents), Botelho et al. [88] in a study on 155
Brazilian steel workers exposed to both toluene and noise (70–95 dB(A)), Mohammadi et al.\textsuperscript{[9]} in an cross-sectional study included 411 workers exposed to both mixed solvents and noise (79 dB(A) to 86 dB(A)), Metwally et al.\textsuperscript{[90]} in an retrospective case-control study of 223 workers in a painting production factory (exposed to both noise of Leq=90 dB(A) and toluene and ethanol, hexane, xylene, acetone, butanol), Unlu et al.\textsuperscript{[91]} in an case-control study on 469 truck plant workers exposed to noise level >85dB(A) and styrene (30 ppm), and Chang et al.\textsuperscript{[92]} in a case-control study on 58 workers exposed to both toluene and noise (Leq=79–87 dB(A))) studied the effects of occupational noise and organic solvents on hearing loss. They reported that combined exposure to mixed solvents and occupational noise could exacerbate hearing loss in workers. Also, in another cross-sectional study on 1029 workers of a tire manufacturing company, Pourzarea et al.\textsuperscript{[93]} estimated that co-exposure to mixed solvents and noise (Leq=85dB(A)) could reduce the frequency of hearing impairment 1.74 times more than noise alone. In a transversal retrospective cohort study on 198 workers in a metal graphics company, Lobato et al.\textsuperscript{[94]} indicated that combined exposure to solvents (aromatic hydrocarbons, toluene, xylene, turpentine, oils, greases, lead chromates, and molybdate) and noise (Leq=85 to 93 dB(A)) could damage the peripheral auditory system. Also, Sliwińska-Kowalska et al.\textsuperscript{[85]} compared hearing loss in 290 workers exposed to styrene (average concentration 6.2 ± 52 mg/m³) and noise (range SPL=71–93 dB(A)) and 213 workers exposed only to noise (range SPL= 70–97 dB(A)) from a plastic boat factory. The study revealed that combined exposures to noise and styrene seemed to be more ototoxic than exposure to noise alone and that the effects were at least additive, if not synergistic. In the study of 701 shipyard workers, the same authors reported that the combination of exposures to noise, and xylene and toluene was additive.\textsuperscript{[94]} Also, in a study on rayon wool workers (105 exposed to noise (80–90 dB(A) and 132 exposed to a combination of noise (80–90 dB(A) and carbon disulfide), Chang et al.\textsuperscript{[96]} reported that the hearing loss was higher among workers exposed to carbon-disulfide and noise compared to those exposed to noise alone.

Concerning the non-auditory effects, the combined effects of occupational noise and solvents on blood pressure have also been studied. In a cross-sectional study, Attarchi et al.\textsuperscript{[97]} demonstrated that co-exposure to noise (SPL>85 dB(A)) and mixed organic solvents (benzene, toluene, xylene, and acetone) had an additive effect on the prevalence of hypertension.

**Animal studies**

Styrene is a cochleotoxic chemical. In an experimental study on adult male Brown-Norway (n = 114) rats weighing over 300 g, Campo et al.\textsuperscript{[98]} revealed that a co-exposure to impulsive noise (85 dB SPL) and styrene (300-ppm) 6 h per day, 5 days per week, for four weeks was more damaging on the organ of Corti than exposure to continuous noise alone or co-exposure to continuous noise and styrene. In an experimental study, Fetonì et al.\textsuperscript{[99]} found that styrene enhanced a noise-induced oxidative stress in the cochlea and affected mechano-sensory and supporting cells.

**Noise and heavy metals**

We identified 21 studies on this topic. Lead, mercury, cadmium, and arsenic are likely to exacerbate noise effects.\textsuperscript{[100]} The evidences of ototoxic effects of noise have been published.\textsuperscript{[100]} Wu et al.\textsuperscript{[101]} examined a hearing loss in 220 employees exposed to high levels of lead (56.9 ug/dL) and noise (Leq=86 dB(A)) simultaneously, in a lead battery manufacturing plant. They showed that the hearing threshold increased at 4 kHz with combined exposure. Also, in a study on 412 Taiwanese steelworkers, Hwang et al.\textsuperscript{[102]} reported an association between lead in blood and hearing loss. Moreover, Farahat et al., Bleecker et al., and Forst et al.\textsuperscript{[105]} confirmed a significant correlation between current blood lead levels and occupational noise on hearing thresholds of the exposed workers. Mercury and mercury compounds (methyl mercury chloride, mercuric sulfide) have often been reported as ototoxic.\textsuperscript{[106]} Several studies have been conducted regarding the effects of mercury on the auditory system. Studies of Discalzi et al.,\textsuperscript{[107]} and Shlomo et al.\textsuperscript{[108]} showed that industrial exposure to inorganic mercury and noise could cause auditory impairments. Cadmium can also cause hearing loss, and the synergistic effect of cadmium fumes and occupational noise on NIHL has been found.\textsuperscript{[109]} Ozcaglar et al.\textsuperscript{[110]} examined the effect of exposure to noise (SPL=87 dB(A)) and cadmium (2 mg/kg) fumes and showed that hearing loss at 4 kHz and 6 kHz was more severe with combined exposure.

Concerning the non-auditory effects, several studies have explored the risk of hypertension due to occupational exposure to lead (Pb) and noise simultaneously. In a cross-sectional study, Rapisarda et al.\textsuperscript{[111]} examined the relationship between occupational exposure to lead (Pb = 0.05 mg/m³) and noise (SPL >80 dB(A)) and the risk of hypertension in 105 workers of a battery recycling plant. They concluded that a simultaneous occupational exposure to lead and noise was associated with increased systolic and diastolic blood pressure (OR = 1.2).

**Animal studies**

The combined effect of manganese has also been examined in an experimental study on hearing loss of rats exposed to noise (SPL=90 dB for 8 h/d) and manganese (moderate levels=10 mg MnCl₂/liter water) for 90 days. The results indicated that manganese and noise had a minor combined effect on auditory system.\textsuperscript{[112]} Also, Kesici\textsuperscript{[113]} reported that arsenic could cause hearing loss at frequencies of 125, 250, and 8000 Hz.
Table 3: Summary of the results of the literature review of the combined effects of noise and chemical agents

| Chemical agents                  | The level of combined risk | Level of evidence | Effects                                      | Comments                                      | Study                                           |
|----------------------------------|----------------------------|-------------------|---------------------------------------------|-----------------------------------------------|------------------------------------------------|
| Noise & CO                        | Exposure to Leq > 80dBA and CO concentration > 200 ppm | Additive          | High                                        | Hearing loss, fatigue, impaired cognitive performance,NIHL | [74], [75], [76], [77], [78], [79], [80], and [81] |
| Noise & solvents                 | Exposure to Leq > 80 dBA and concentrations equal to 50–300 ppm | Synergistic        | High                                        | Hypertension, Styrene, toluene, hexane, xylene, acetone, butanol, trichloroethylene, and ethanol have combined effects with noise | [82], [83], [84], [85], [86], [87], [88], [89], [90], [91], [92], [93], [94], [95], [96], [97], [98], and [99] |
| Noise & heavy metals             | Exposure to Leq = 80–95dBA and lead (Pb = 0.05 mg/m³), (manganese = 10 mg MnCl₂/liter water), cadmium (2 mg/kg) | Synergistic        | High                                        | Hearing loss, Lead, mercury, arsenic, cadmium have combined effects with noise | [100], [101], [102], [103], [104], [105], [106], [107], [108], [109], [110], [111], [112], and [113] |
| Noise & other chemical           | Exposure to Leq > 80 dBA | Additive          | Medium                                      | Hearing loss, Epoxy adhesives and organophosphate pesticides have combined effects with noise | [114], [115], and [116] |

**Level of evidence**: was determined based on the number of citations, methodological quality and design, validity, and applicability of studies results (Low – Medium – High). The **Level of combined risk**: The degree of effect intensification caused by the simultaneous presence of two factors or agents that was determined based on the design and study type, the methodological, validity of data, and the study population. **Additive effect**: The combined effect produced by the action of two or more agents, being equal to the sum of their separate effects (2+2=4). **Synergistic effects**: An effect arising between two or more agents, or factors, that produces an effect greater than the sum of their individual effects (2+2=5). **Potentiation effects**: The combination of a factor or agent that has no effect (0) with a factor or agent that has some effect (2) is equal to the combined effect (10) greater than the sum of the effects of each one alone (0+2 = 10). **Antagonism effect**: Two or more combined agents have an overall effect that is less than the sum of their individual effects (5+0 = 2).

**Noise and other chemicals substances**

In addition to solvents, several chemical substances can cause hearing loss. We have found three papers on this topic. In a follow-up study of 14229 male applicators from 1999 to 2003, Crawford et al. 2003, Crawford et al. 2003, Crawford et al. 2003 reported that the interaction between noise and organo-phosphorous pesticides significantly reduced the hearing on 8kHz among farm-workers. In a cross-sectional study on 300 workers in a rubber factory, Niranjana et al. concluded that simultaneous exposure to ototoxic chemicals (phosphorous compounds, cyanides, and hydrogen cyanide (HCN)) and noise (> 85 dB (A)) increased the frequency of hearing loss (with an OR of 1.7). Also, in another cross-sectional study, Yang et al. compared the prevalence of NIHL in 182 stoneworkers exposed to epoxy adhesive and noise (88 dB(A)) with 133 workers exposed to noise alone. They reported that the prevalence of NIHL was significantly higher in the “epoxy adhesives and noise group” (42%) compared to the “noise group” (21%). Table 3 shows a summary of the results of the literature review about the combined effects of chemical agents and noise.

**PHYSICAL FACTORS**

Noise and lighting (illuminance)

Few studies have showed the combined effects of unfavorable lighting and noise. The most important combined effect of noise and unfavorable lighting at workplaces are impaired visual function. All of the research literature is based on experimental work. In an experimental study of 12 desk workers the subjects who conducted the tests of letter cancellation, hand precision, two-hand coordination, and tweezers dexterity, Bhattacharya et al. reported the interactive negative effects of noise and bad illumination on the speed and efficacy of performance. In another experimental study, the same authors confirmed increased performance error by combinations of good illumination and quiet (60 dB(A)) and noise (100 dB(A)) on neuropsychological performance capability of 20 male college students. In another experimental study, Gorai et al. found that bad illumination had a combined negative effect with noise on operators’ performance. Mangipudy also suggested that the combined effect of noise and light seemed to be a potential source of extrinsic cognitive load on students’ achievement. Moreover, in another experimental study, Liebl et al. found an interaction effect between noise and lighting on cognitive performance and well-being of healthy young subjects. In another study, Amiri et al. examined the effects of combined exposure to noise and lighting on cognitive performance of healthy young subjects. They suggested that combined exposure to noise (SPL=95 dB (A)), and unfavorable lighting (20 Lux) had adverse effects on cognitive performance (working memory,
attention, and concentration). The study of the combined effects of more than two physical factors on humans is very complex. In an analytical-descriptive study, Golbabaei et al.\textsuperscript{[125]} examined the combined effects of noise, unfavorable lighting and heat stress on job performance using manual and mental tests among 30 employees of the auto parts manufacturer. Their results indicated that simultaneous exposure to noise and high thermal stress and low lighting increased the duration of manual and mental tests and reduced accuracy compared to the effect of each agent alone. Also, they pointed out that background noise can impair short-term memory.

Cross-modal effects of noise and noise type music, water babble and fan) and illuminance were investigated indoors among 60 university students (30 men and 30 women). The findings revealed that the acoustic conditions affected visual relaxation. The illuminance conditions did not affect acoustic perception. Cross-modal interactions were asymmetric between sound and illuminance in indoor environmental settings. Women were more sensitive to the perception of both acoustic and illuminance stimuli than men at a high level of stimulation\textsuperscript{[126]} In another empirical study, Liu et al.\textsuperscript{[127]} investigated the effects of noise type, and intensity and illumination intensity on reading performance. They reported that illumination intensity (too high or too low) combined with a high noise level, impaired reading performance more compared to noise or illumination alone.

**Noise and heat**

Heat stress is also an environmental factor that can exacerbate noise-induced health effects.\textsuperscript{[128]} In a cross-sectional study, Singh et al.\textsuperscript{[129]} confirmed combined effects of noise and heat stress on hearing loss in 350 male workers of the casting industry. Also, in an experimental study, Chen et al.\textsuperscript{[130]} examined the combined exposure to noise and temperature on auditory fatigue of 14 healthy young subjects in a climatic chamber. They concluded that heat stress enhanced noise-induced temporary threshold shift.

Concerning the non-auditory effects, several studies have investigated the combined effects of noise and heat stress. In an experimental study, Witterseh et al.\textsuperscript{[131]} confirmed the interaction effect of increasing temperatures and noise on the pronunciation of subjective distress and fatigue among male employees in an open-plan office. In another experimental study, Pellerin and Candas\textsuperscript{[128]} examined the combined effects of noise and temperature on the discomfort of 108 lightly clothed subjects (54 male and 54 female). They suggested that noise may altered thermal pleasantness in warm conditions. Moreover, in an experimental study, Tiller et al.\textsuperscript{[132]} examined the combined effects of noise and heat stress on comfort and performance of 30 healthy young subjects (16 females, 14 males). They found that thermal comfort was strongly affected by noise.

In a cross-sectional study in an iron foundry, Sen et al.\textsuperscript{[133]} reported that co-exposure to noise and heat stress increased the health risk of workers and consequently reduced the efficiency and the production. Moreover, the study of the combined effect of noise and heat stress on the metabolic syndrome of 590 steelworkers, it was demonstrated that the prevalence of metabolic syndrome in the “noise and heat group” was 1.12 times higher than in the “noise alone group”.\textsuperscript{[134]}

In an experimental study, Dehghani et al.\textsuperscript{[135]} examined the combined effect of noise and heat stress on hypertension among 14 healthy young subjects in a climatic chamber. They reported that heat intensified noise-induced hypertension, and blood pressure under concomitant exposure to noise and heat was significantly higher compared to noise alone. Fouladi Dehghi et al.\textsuperscript{[136]} reported that the combined effect of noise and high thermal stress significantly decreased the VO2 max value (maximal aerobic capacity) in 50 students compared to combined noisy and the lower heat conditions.

**Noise and vibration**

Vibration can affect physical and mental performance.\textsuperscript{[137,138]} Sleep disorders,\textsuperscript{[139]} difficulty in concentration,\textsuperscript{[138]} fatigue,\textsuperscript{[138]} depression,\textsuperscript{[140]} irritability,\textsuperscript{[140]} shock,\textsuperscript{[140]} loss of grip strength, blanching (white finger), and anxiety are health effects that were reported due to vibration. Numerous studies have reported the combined effects of noise and vibration, and for many years vibration and vibration-induced effects, with combined exposure to noise, have been considered as possible risk factors for developing hearing loss.\textsuperscript{[7,138,139,141,142]} We identified 11 studies describing the combined effects of occupational exposure to noise and vibration. In an experimental study of healthy young subjects, Zhu et al.\textsuperscript{[143]} reported that combined exposure to noise and hand-arm vibration caused a greater temporary hearing loss than exposure to noise alone. In a cohort study of hearing loss in 15757 mining and forestry male workers who suffered from white finger and had combined exposure to noise and a whole-body vibration, Turcot et al.\textsuperscript{[144]} reported that in workers with vibration-induced white fingers (VWF), hearing loss at low and high frequencies was higher compared to workers without VWF. Also, in a longitudinal study, Iki et al.\textsuperscript{[142]} reported that hearing loss in the 2–4-kHz range was more frequent in among individuals with VWF exposed to occupational noise than among controls exposed to noise alone. Pykkö et al.\textsuperscript{[145]} studied the shipyard workers, forestry workers, metal workers, and patients referred to a clinic. They reported that workers with Raynaud disease (due to vibration) were more susceptible to hearing loss at 4 kHz than workers exposed to noise alone. In a cohort study, Pettersson\textsuperscript{[14]} examined the risk of NIHL in 276 workers exposed to noise and hand-arm vibration (HAV) in a heavy engineering industry. Exposure to noise and machine-induced hand. They found that HAV increased the risk of NIHL. Also, in an experimental study, Sisto et al.\textsuperscript{[146]} investigated the combined effect of exposure to noise and HAV (0.5 m/s\textsuperscript{2}), on the distortion product otoacoustic emission (DPOAE) level in 12 volunteers. They found a
synergistic adverse effect of co-exposure to noise and HAV on the cochlear function. Generally, studies have confirmed synergistic effects of HAV and noise on the cochlear function.

Concerning the non-auditory effects, in an experimental study, Huang and Griffin\cite{147} presented a regression model to predict the discomfort caused by simultaneous exposure to noise and whole-body vibration in 24 healthy young subjects (12 males and 12 female). They concluded that discomfort caused by a combination of noise and vibration was greater than under each factor each alone. Besides, noise had a masking effect about the judgment on the discomfort caused by vibration. In summary, in all experimental studies, the psychological effects of combined noise and vibration include increased stress, annoyance, and discomfort, decreased performance and alertness.\cite{137} It is worth noting that the effects of combined exposure to noise and vibration have been reported at low levels of noise.\cite{138} Also, in a cross-sectional study, Dzhambov and Dimitrova\cite{148} studied the synergistic effects of co-exposure to noise and a whole-body vibration and the risk of heart diseases in 3149 workers in Bulgaria. The found that whole-body vibration raised the risk of heart diseases among workers exposed to noise.

**Noise and cold**

Exposure to cold causes reduction of nerve and muscle functionality, frostbite, and chilblain.\cite{140,149} Few studies reported combined health effects of simultaneous exposure to low temperature and noise.\cite{140,150} In an experimental study, Chao et al. (2013) studied the combined effects of noise and cold and HAV on the physiological parameters of 23 healthy young subjects using the Taguchi Method.\cite{8} The study showed that the combination of noise, cold, and HAV might lead to permanent threshold shift and white finger syndrome. More studies on the combined effects of low temperature and occupational noise are warranted.

Table 4 shows a summary of the results of the literature review about the combined effects of physical agents and noise and also the level of risk and evidence.

**OCCUPATIONAL FACTORS**

**Noise and workload**

Mental workload is defined as the expenses imposed on the operator to achieve a certain level of performance.\cite{151} High mental and physical workload causes fatigue, decreased performance, memory loss, impaired cognitive function, and irritability.\cite{152} Also, the low mental workload can lead to depression and cognitive performance decline.\cite{153} The studies show that exposure to occupational noise can increase mental workload.\cite{154,155} On the other hand, high mental workload exacerbates noise effects.\cite{156} We have found only one study on the exposure to a combination of occupational noise and high workload. In an experimental study of 14 healthy young subjects, Chen et al. (2007) investigated the combined effects of noise and workload on noise-induced hearing temporary threshold shift (NITTS).\cite{130} The results showed that workload enhanced NITTS.

Concerning the non-auditory effects, in a follow-up study comprised 1502 middle-aged industrial workers, Koskinen et al.\cite{157} reported that occupational noise globus and physical workload concurrently were associated with increased levels of blood pressure and the risk of coronary heart disease (RR = 2.19) compared to noise. In another cohort study on 14 healthy young subjects, Dehghan et al.\cite{159} reported that exposure to noise globus and high workload in a favourable thermal condition increased the heart rate. In an experimental study on work memory of 31 healthy subjects, Golmohammadi et al.\cite{160} reported an increased noise-induced impairment of cognitive function under a higher workload.

**Noise and shift work**

Shift work is probably a risk factor for noise-induced health effects. Health effects that include fatigue, insomnia, gastrointestinal problems, cardiovascular disease, and decreased cognitive performance are associated with night work.\cite{161} Therefore, it may be expected that night work aggravates the noise-induced health effects.

In a cross-sectional study, Chou et al.\cite{162} compared the hearing loss of 218 male workers (146 workers had an 8-hour work schedule, and 72 workers had a 12-hour work schedule) exposed to noise levels exceeding 85 dB(A) in a semiconductor factory. They reported that the hearing loss in shift workers with a 12-hour work schedule was significantly lower compared to shift workers with an 8-hour work schedule. The number of studies on this topic is limited, but it appears that shift workers are more prone to hearing loss than non-shift workers.

Concerning the non-auditory effects, we identified several studies on this topic. In a study on 254 workers in a chemical plant (including 188 shift workers and 66-day workers exposed to noise (Leq, 8 hr was >85 dB), Saremi et al.\cite{163} reported that mean level of noise-induced fatigue in shift workers was more pronounced compared to day workers. They suggested that the combined effect of shift work and noise on fatigue was synergistic. In a follow-up study of 1804 middle-aged male workers exposed to occupational noise and shift work Virkkunen et al.\cite{158} concluded that these two factors were associated with an excess risk of the coronary heart disease. In a cross-sectional study, Attarchi et al.\cite{164} investigated the combined effects of noise and shift work on blood pressure of 331 workers in a rubber manufacturing company. Their study showed an additive effect of noise and shift work on systolic and diastolic blood pressure.
risk factors can exacerbate the noise-induced health effects. These factors include aging and smoking (personal factors), vibration and heat (physical agents), chemicals, solvents, CO, and metals (chemical agents) and shift work (occupational factor).

Hearing loss is mainly related to increasing age. Men lose hearing more than women do. Heredity also plays a role. Smoking seems to be a certain intensifying factor for NIHL. Moreover, the combined effects of solvents (toluene, styrene, and trichloroethylene), CO, metals, and chemicals with noise on hearing are evident. The research findings on other solvents and trichloroethylene, CO, and metals (chemical agents) and shift work (occupational factor).

However, the evidence of the combined effects of occupational noise and gender, heredity, medication, lighting, cold, and workload are weaker and further studies are needed. Besides, it is necessary to consider the effect of confounding factors. Diabetes, hypertension, and cholesterol seem to affect

**DISCUSSION**

This systematic review focused on the combined effects of occupational noise and other occupational risk factors. The majority of the included studies had a cross-sectional design. We believe that these studies provide valid data because field measurements of noise and other risk factors were performed. Most of the studies we identified have investigated only combined effects of risk factors on hearing, and the evidence for non-auditory effects is still limited. Further studies are needed in the field of non-auditory effects due to concurrent exposure to noise and other risk factors. Another limitation is that in some studies, the degree of combined effects was not clearly expressed. Overall, we assessed the level of combined risk for each risk factor based on study type, the method, validity of data, and the investigated population. Moreover, in a study of combined effects in occupational environments, there are many confounding factors, making such studies rather years complicated.

According to the literature review and the level of evidence, 16 risk factors can exacerbate the noise-induced health effects. These factors include aging and smoking (personal factors), vibration and heat (physical agents), chemicals, solvents, CO, and metals (chemical agents) and shift work (occupational factor).
NIHL, but the evidence of noise-induced non-hearing effects is still limited.

According to the results of the literature review and the general adaptation syndrome,[165] a concurrent exposure to multiple stressors leads to a three-stage bodily response. Therefore, upon perceiving a stressor (such as noise), the sympathetic nervous system is stimulated, and the body’s resources mobilize to meet the danger. The result of this reaction is a “fight-or-flight” response. Stress is the organism’s reaction of neurologic and endocrinologic systems to environmental demands or pressures. The body makes an effort to limit stress. If a stressor persists, the body focuses on resources and resists against the stress and remains on alert. The result of this resistance is a response named strain. The strain is deformation, disturbance, or deflection of physiological in the body due to the persistence of stress. In other words, the strain is an unstable physiological response to get rid of the stressor. Hence, the parasympathetic nervous system is stimulated and attempts to return many physiological functions to normal levels. The strain is directly proportional to stress and is a load applied to a proportional limit. Upon the stressor is removed, stress is back to normal, and the strain also becomes zero. These actions are taken to avoid the noise and are called coping. But, if the exposure to stressor or stressors continues beyond the body’s capacity, the resources become exhausted, the body strains beyond the proportional limit and is susceptible

Table 5: Summary of the results of the literature review of the combined effects of noise and occupational factors

| Occupational factors | The level of combined risk | Level of evidence | Effects | Comments | Study |
|----------------------|---------------------------|-------------------|---------|----------|-------|
| Noise & workload     | Exposure to Leq > 75 dBA, and score of workload > 50/100 | Additive          | Low     | Hearing loss, fatigue, disturbance | Workload may aggravate health complaints due to noise [130], [155], [156], [157], [158], [159], and [160] |
| Noise & shiftwork    | Exposure to Leq > 80 dBA, and 8 h night work during >5 years | Both additive and synergistic | Medium   | Cardiovascular effects, hypertension, fatigue | Shiftwork is strongly related to cardiovascular diseases and hearing loss and aggravates this effect when combined with noise [158], [162], [163], and [164] |

Level of evidence: Level of evidence was determined based on the number of citations, methodological quality and design, validity, and applicability of studies results (Low – Medium – High). The Level of combined risk: The degree of effect intensification caused by the simultaneous presence of two factors or agents that was determined based on design and study type, the methodological, validity of data, and the study population. Additive effect: The combined effect produced by the action of two or more agents, being equal to the sum of their separate effects (2+2=4). Synergistic effects: An effect arising between two or more agents, or factors, that produces an effect greater than the sum of their individual effects (2 + 2 = 25). Potentiation effects: The combination of a factor or agent that has no effect (0) with a factor or agent that has effect (2) is equal to the combined effect (10) greater than the sum of the effects of each one alone (0 + 2 = 10). Antagonism effects: Two or more combined agents have an overall effect that is less than the sum of their individual effects (5 + 0 = 2).

Figure 2: Conceptual model of the combined effects of occupational exposure to noise and other risk factors.
to disease. Based on the results of this literature review, we have developed a conceptual model to explain the combined effects of occupational exposure to noise and other risk factors [Figure 2].

As shown in Figure 2, in addition to combined exposure to noise and each of the 16 risk factors; 1), there are five endogenous and subjective factors, including noise sensitivity, disturbance (disruption in communication, cognitive function, and sleep), annoyance, noise-induced health complaints and coping with stress and strain due to noise. Finally, the model output is the incidence of the combined effects. Hearing loss, hypertension, cardiovascular effects, psychological effects, and sleep disorder are the most important combined effects due to occupational exposure to noise and other factors. Studies on combined effects in various occupations suggest that hearing loss is the most important health outcome. Research findings on non-auditory effects are more uncertain.

Generally, it can be concluded that solvents, vibration, age, heavy metals, CO, smoking, chemicals, heat, and shift work show the strongest combined effects with noise. Therefore, in addition to the hearing conservation programs, preventive programs against each of the aggravating factors of noise effects should also be implemented at workplaces.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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