Safety and Health at Work 15 (2024) 382–395

Contents lists available at ScienceDirect

Safety and Health at Work

journal homepage: www.e-shaw.net

Review Article

Health Outcomes Related to Multiple Exposures in Occupational Settings: A Review

Cassandra Barbey [1,2], Nathalie Bonvallot [2], Frédéric Clerc [1,*]

[1] Department of Pollutant Metrology, French Research and Safety Institute for the Prevention of Occupational Accidents and Diseases (INRS), 54547 Vandœuvre-lès-Nancy, France

[2] Univ Rennes, Inserm, EHESP, Irset (Institut de recherche en santé, environnement et travail) - UMR_S 1085, F-35000 Rennes, France

ARTICLE INFO

Article history:
Received 18 March 2024
Received in revised form
14 September 2024
Accepted 21 October 2024
Available online 28 October 2024

Keywords:
Health effects
Multiple exposures
Occupational exposures
Occupational health
Occupational risk

ABSTRACT

Individuals are constantly exposed to hazardous factors that can affect their health, the hazards encountered in the workplace can lead to the development of occupational diseases. Risk mitigation measures help to reduce the risks, but they are often designed without consideration of interactions between occupational exposures. Therefore, there is a need for research and it resulted in international research plans and programmes. The aim of this scoping review is to provide an overview of the scientific results related to the link between multiple occupational exposures and human health outcomes. Sixty-three articles were reviewed. Research articles were included only if they mentioned: several combined exposures, the direct characterisation of each exposure, and exposure/health outcome associations. Seven activity sectors were identified: 'extraction and energy production and distribution', 'health care', 'banks, public administration and defence', 'chemical production', 'manufacturing industry', 'agriculture and food industry' and 'transport and logistics'. Six multiple exposures scenarios were identified: chemical ($n = 35$), chemical/physical-biomechanical ($n = 22$), chemical/psychosocial-organisational ($n = 6$), physical-biomechanical ($n = 9$), physical-biomechanical/psychosocial-organisational ($n = 13$), and psychosocial-organisational ($n = 12$). The health problems identified concern nervous, mental, respiratory, musculoskeletal, auditory and other systems. Eighty-eight of 97 (91%) multiple exposure/health problem associations were reported to be statistically significant. Twenty studies (32%) provided specific risk prevention advice for multiple exposures. Prevention aimed at reducing risks to workers' health is still underdeveloped, further research is needed to improve prevention methods. No study was related to biological risk, and some other multiple exposures known to have health effects were not identified as well. This highlights the need for more multiple exposures research.

1. Introduction

Every day, people are constantly exposed to numerous hazardous factors. These risks can influence health and lead to the onset of diseases with variable characteristics and effects. The effects induced can be linked to health determinants shared by a subset of the population, which may be systemically (education, social, health, etc.) or more contextually defined (legislative, economic, demographic, etc.). Alternatively, the cohort may be defined by individual characteristics (genetic, socioeconomic, lifestyle, etc.) or living environments (family, school, work, etc.) [1,2]. Public Health aims to study these determinants to implement a range of actions aimed to preventing disease and improving the health of the populations. Because work is recognised as a social and environmental determinant of health, occupational health is an important part of Public Health. Indeed, workers are exposed to several potential hazards at work: chemical (specific chemical products, particles, vapours, or fumes), physical (noise, vibrations, heat, etc.), biomechanical (posture, movement), biological (viruses, bacteria, fungi, etc.), psychosocial (stress, mental workload, relationship at

Cassandra Barbey: https://orcid.org/0009-0007-7017-9500; Nathalie Bonvallot: https://orcid.org/0000-0002-8070-6008; Frédéric Clerc: https://orcid.org/0000-0002-1058-800X

* Corresponding author. Department of Pollutant Metrology, French Research and Safety Institute for the Prevention of Occupational Accidents and Diseases (INRS), 54547 Vandœuvre-lès-Nancy, France.

E-mail address: frederic.clerc@inrs.fr (F. Clerc).

2093-7911/$ — see front matter
https://doi.org/10.1016/j.shaw.2024.10.004

work, etc.), and organisational (night work, shift work, lack of resources, etc.). These last two categories are often grouped together as organisational, relational, and ethical factors. Exposure to all of these occupational hazards has the potential to increase worker health risk. In 2016, global records indicate that around 1.9 million people died at work as a result of diseases and accidents [3].

To reduce the burden of occupational disease, safety measures are implemented based on occupational exposures' effects on individuals and corresponding risks. However, at present, this knowledge remains mainly 'mono-exposure' and does not sufficiently consider the possibility that exposure to several risk factors could have combined actions. These combined actions can lead to an increase or decrease of the impact of exposures, as defined by the concept of multiple exposures [4].

For several years in France, the concept of multiple exposures has become a central subject of study in public and occupational health thanks to the government's occupational health plans [5] (see for example the Ministry of labour website: https://travail-emploi.gouv.fr/sante-au-travail/plans-gouvernementaux-sante-au-travail/article/plans-sante-au-travail-pst). In this context, increasing numbers of studies deal with multiple exposure scenarios. For example, 12 homogeneous profiles of workers subject to multiple exposures were recently identified from responses to a French national questionnaire [6]. The responses also allowed 39 exposure indicators to be constructed for 5 types of occupational stress or exposure: relational, organisational, physical (including biomechanical exposures), chemical and biological.

International groups have also investigated multiple exposures, particularly co-exposure to chemicals. For example, in 2009, the International programme on chemical safety (IPCS) issued a report on combined exposures to multiple chemicals [7]. In addition, a series of publications assessing the risks of combined exposure to multiple chemicals was produced by the Inter-Organization Programme for the Sound Management of Chemicals (IOMC) [8]. However, the links with workers' health were not studied.

The aim of this article is to review specifically the links between occupational multiple exposures and workers' health with the scoping review, in order to gain a better understanding of how such exposures affect health.

2. Materials and methods

This scoping review covered the period from 1991 to 2024. Studies were selected using a three-step iterative process (see Fig. 1):

1) The PubMed and Web of Science databases were used the following query: "occupational ((health OR patholog*) AND (risk* factor OR exposure* OR co-exposure* OR coexposure)) AND (multiple OR combined OR cumulative) effect* AND work*". Although this query was effective with the Web of Science database, it was too broad for the PubMed database. Indeed, around 97% of the studies proposed did not correspond to the initial selection criteria. The term 'assessment' was therefore added to the PubMed query. These search queries were designed in November 2022 and updated in August 2024. Three types of studies were excluded because they were considered beyond the scope of this review: First, laboratory *in vivo* or *in vitro* research studies. Second, studies focusing specifically on populations under 18 years of age. This population is only marginally represented among workers. Third, studies involving pregnant women were excluded. Pregnancy at work is an

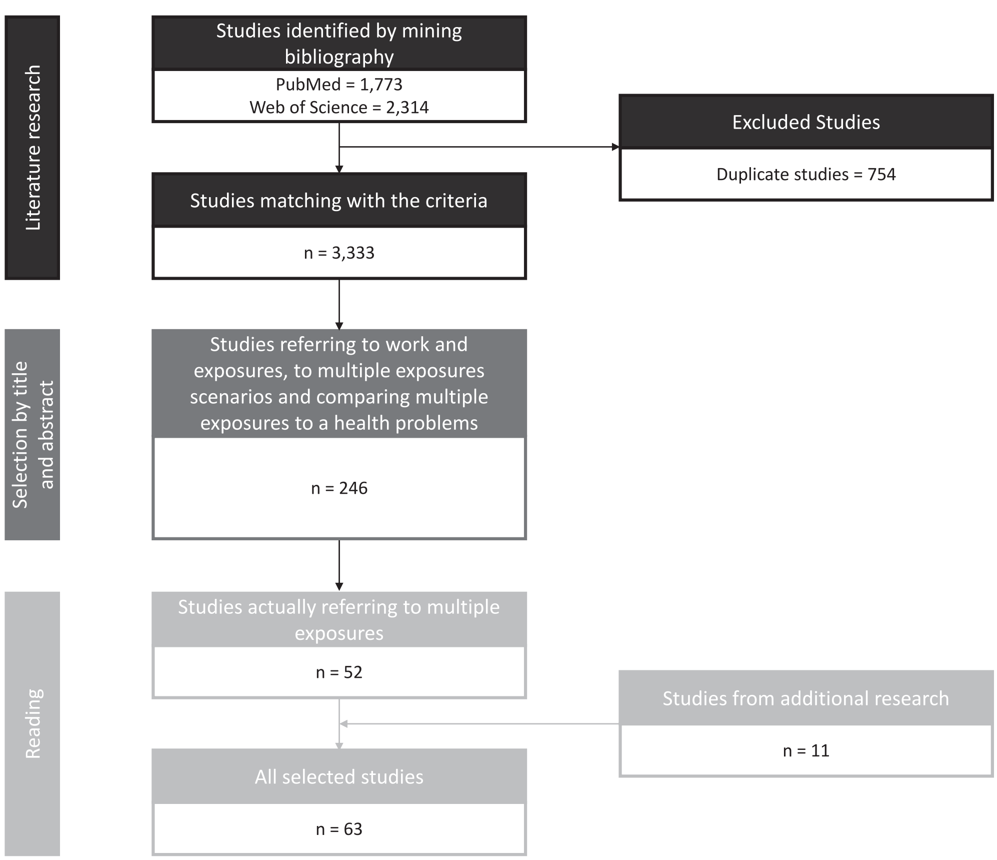

Fig. 1. Study-selection flow chart.

important and complex subject for occupational health. Few studies have been conducted on this subject, and most of them were interested in child development during and after the pregnancy, but not directly in the woman's health. Duplicate studies were also excluded. Review and meta-analysis meeting the selection criteria were excluded from the articles retained, but were included in the discussion.

2) Selected studies were screened based on the subject-title match: the studies were retained if the title mentioned workplace and exposures as well as a possible combined action of several exposures. The abstracts of the remaining studies were read. Those indicating a link between different types of exposure and a health issue were selected. To be selected, studies also had to mention a combined action between the different exposure scenarios, and not only an individual relation between each exposure and the health problem.
3) Inclusion was validated by reading the entire publication. The reading validation step made it possible to exclude all studies that did not mention a real association between the combinations of exposures and the chosen health problem, whether statistically significant or not.

Following, the application of these criteria, 52 studies had been selected. The reference lists of these studies were mined for additional articles, if relevant (meeting the inclusion criteria). Following this step, a total of 63 studies were included for review.

For each publication, the following items were extracted for further description: information about population (nation, gender, average age, number of people, activity sector or occupation), information about exposure (type, name, measurement method) and information about health problem (name and assessment method). Any information related to confounding factors and statistical analysis methods was also collected.

3. Results

3.1. Populations

The worker populations studied were predominantly European and Asian, particularly from France and the United States of America (USA). Many populations came from China, Republic of Korea, and Canada. Other countries (South Africa, Mexico, Germany, Finland, etc.) were less represented, with only one study for each, either alone or studied with other countries or nations). Forty-five studies involved both men and women workers, while 16 and 2 studies focused solely on men and women workers respectively. The period covered by these studies ranged from 1942 to 2023, with several worker populations identified through various surveys conducted before the date of the studies. Samples size varied between 40 (Chinese workers) and 45,241 (Korean workers) people (see Annex A).

Seven major activity sectors were covered by the selected studies: "extraction, energy production and distribution (coal, electricity, gas, steam)", "health care", "banks, public administration and defence", "chemical production (synthetic chemical compounds, diatomite, metals)", "manufacturing industry (leather, footwear, adhesive tape, paint ...)", "agriculture and food industry" and "transport and logistics (railway, dockyard, planes, bus ...)". Studies on these sectors included 37 articles, representing over 58% of the total studies. "Manufacturing industry" is the sector with the largest sample of workers represented, with 78,356 workers across 20 studies. "Health care" is the sector with the smallest sample of workers represented, with 1,348 workers in one study (see Fig. 2). The remaining studies ($n = 26$) did not focus on a specific sector, and some were based on several activity sectors, with workers drawn from national ($n = 19$ studies) or international ($n = 5$ studies) surveys, including a large number of people.

3.2. Multiple exposures

In the 63 selected studies, worker populations were exposed to three types of nuisances: chemical ($n = 35$ studies), physical-biomechanical ($n = 39$ studies), and psychosocial-organisational ($n = 27$ studies) nuisances, corresponding to 6 co-exposures scenarios: chemical, chemical/physical-biomechanical, chemical/psychosocial-organisational, physical-biomechanical, physical-biomechanical/psychosocial-organisational, and psychosocial-organisational. The chemical nuisances most studied were a combination of different solvents and xylene, reported in 10 and 8 studies, respectively. Among physical-biomechanical exposures,

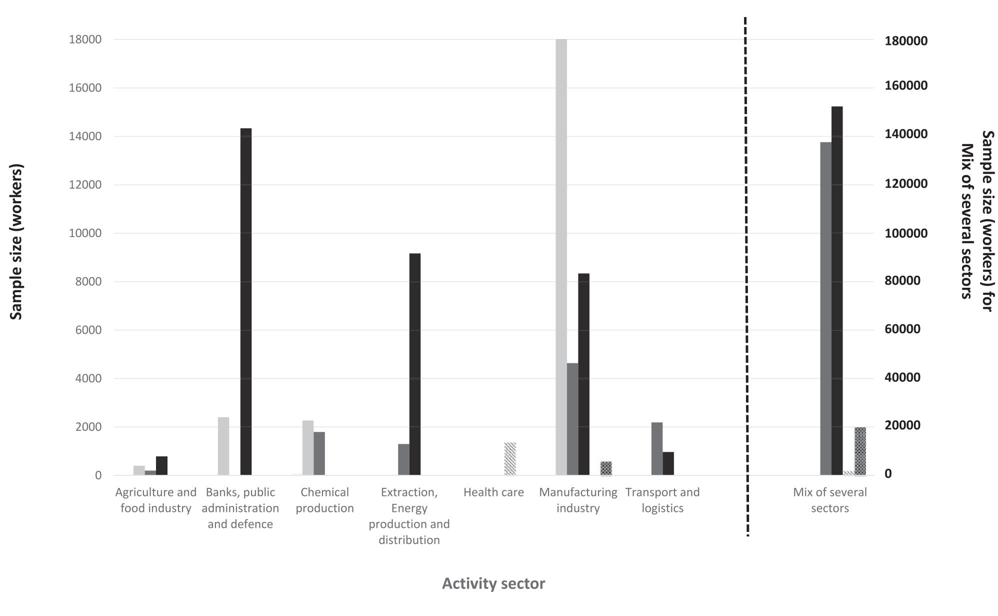

Fig. 2. Distribution of sample size for working populations and activity sector in the studies selected for review.

biomechanical exposures – repetitive movement, carrying heavy loads or static working positions – predominated ($n = 14$ studies). Other physical-biomechanical exposures, such as noise ($n = 13$ studies) and vibrations ($n = 7$ studies), were also studied. Another study looked at exposure to extremely low frequency magnetic fields.

Psychosocial-organisation exposures were often grouped under the same label, such as social support or decision latitude.

Exposure information was presented using study-specific ($n = 37$ studies), national ($n = 21$ studies) and international ($n = 5$ studies) surveys. In these studies, data collection protocols were based on different methods: exposures measurement, job-exposure matrix (JEM), occupation or self-reported exposures with or without trained interviewer (see Fig. 3).

3.3. Health effects

A variety of health effects were studied by the authors. They have been grouped into six categories based on target organs: nervous system, auditory system, mental health, respiratory tract, musculoskeletal system, and 'other systems'. The co-exposures and health effects were organised into six tables representing different co-exposure scenarios (see Tables 1–6). Only results concerning associations between at least two combined exposures and a health effect are presented. The absence of a correlation does not undermine the proven health effects of individual exposures. The term 'correlation' or 'correlated' used in the results systematically refers to statistically significant correlations. All combinations of exposures presented in the tables, whether correlated with a health effect or not, are detailed in the following sub-chapters.

3.3.1. Nervous system

Four studies focused on neurological problems: 3 of them deal with chemical co-exposure, and 1 with chemical/physical-biomechanical co-exposure. Four out of six co-exposures were correlated with neurological problems.

The health effects correlated with chemical co-exposures were quite varied:

- Postural imbalance was correlated with xylene and n-hexane co-exposure in 29 Asian men working in the leather and shoe production sector (average age around 50). Exposure was measured by metabolite concentration in urine samples before and after the work. The nervous system disorders frequency was compared with that of 22 unexposed workers in the private health sector by multiple regression (fixed variables method) [9].
- Neurobehavioral effects were correlated with a combination of organic solvents in 67 South African men working in paint manufacturing (average age around 46). The total combined exposure to solvents, calculated in a second article, was ≤0.72 of the workplace air limit value. The degree of central nervous system damage was measured. The Spearman R coefficient was used [10].

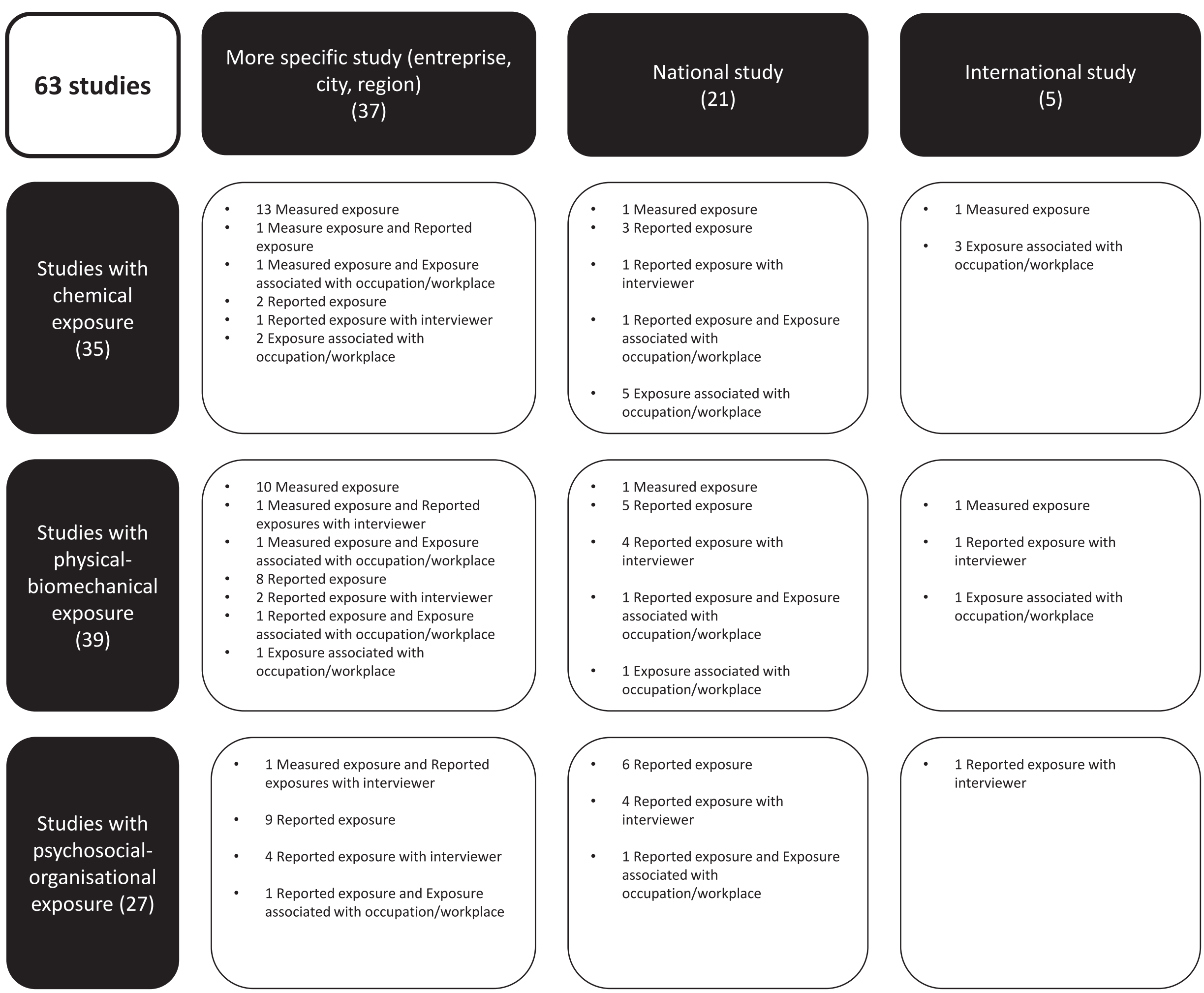

Fig. 3. Types of exposure and data-collection methods in the different studies.

Table 1
Summary of chemical effects observed in the studies included

Occupational exposure type 1 / Occupational exposure type 2	Health effect	Significant	Reference
Chemical			
• Xylene and N-hexane	Postural imbalance (sway)	Yes	[9]
• Organic solvents	Neurobehavioral effects	Yes	[10]
• Organochlorine insecticides • Nitriles herbicides	Parkinson's disease	Yes	[11]
• Metals (lead, cadmium, arsenic) and Solvents (toluene, xylene)	Permanent shift in hearing threshold	Yes	[21]
• BTEXS (benzene, toluene, ethylbenzene, xylene, styrene)	Small airway dysfunction	Yes	[32]
• Aromatics solvents • Gases and Fumes	Lung function decline	Yes	[33]
• Pesticide (organophosphates, pyrethroids, fungicides, herbicides)	Night cough	Yes	[34]
• Chromium-IV and Nickel	Laryngeal cancer	Yes	[35]
• Biocides and Synthetic metalworking fluid	Lung cancer	Yes	[36,37]
• Asbestos and Refractory ceramic fibres	Pleural mesothelioma	Yes	[38]
• Asbestos and Silica • Asbestos and Mineral wool			[38] [39]
• Crystalline silica and Asbestos	Lung cancer	No	[40]
• Benzene, Toluene, Xylene and N-hexane	Colour vision impairment	Yes	[63]
• Solvents (ethyl acetate, ethanol, and ketones)	Dyschromatopsia	Yes	[64]
• Silica and Asbestos	Bladder cancer	Yes	[66]
• Solvents and Oil	Dermatitis	Yes	[69]
• Pesticides (Insecticides, Herbicides, Fungicides)	Chronic lymphocytic leukaemia	Yes	[70]
• Toluene and Xylene, Styrene or Copper • Xylene and Styrene, Iron or Copper • Styrene and Lead, Copper or Antimony • TCE and Copper • Iron and Manganese or Copper • Manganese and Copper or Antimony • Lead and Copper	Metabolic syndrome	Yes	[71]

- Parkinson's disease was correlated with organochlorine insecticides and nitriles herbicides co-exposures in 224 French men and women cases working in the agricultural sector (aged 18–75). Information on exposure was collected through interviews with occupational physicians to reconstruct exposure history. Comparison was made with 557 control workers using conditional logistic regression [11].

In contrast, brain cancers (glioma and meningioma) were not correlated with metals/extremely low frequency magnetic fields (ELF) and solvents/ELF co-exposures. The population was drawn from the INTEROCC survey. The analysis was performed on men and women (average age around 50), including 2,054 patients with glioma, 1,924 patients with meningioma, and 5,601 controls. Exposures were estimated using a modified version of the Finnish JEM (FINJEM). A conditional logistic regression was used [12].

3.3.2. Auditory system

Nine studies focused on hearing-related problems: 8 of them deal with noise and solvents co-exposure, and one with chemical co-exposure. All the co-exposures (n = 10) were correlated with hearing problems.

Co-exposures to noise and solvents have been correlated with hearing loss in 7 studies involving several workers sub-populations:

- In Taiwanese men (average age around 45) exposed to carbon disulfide. Data were gathered for 131 rayon and viscose production workers exposed to both carbon disulfide and noise, 105 workers exposed to noise only, and 110 workers exposed to low noise levels (adhesive tape and electronic production and administration of the rayon plants workers). Exposures were measured on-site. Logistic regression was used [13].
- In Polish men and women (average age around 40) exposed to xylene isomers, ethyl benzene, ethyl acetate, butyl acetate, n-butanol, white spirit, and toluene. The analysis was conducted on 517 noise and solvent-exposed dockyards workers. Hearing levels were compared to those of 184 noise-exposed and 205 non-exposed workers. Exposures were measured on-site. Multiple linear and logistic regression models were used [14].
- In European men and women (aged 18–63) exposed to styrene. This sub-population is based on a European Commission 5th Framework Programme research project: NoiseChem. Hearing levels were compared to those of workers producing reinforced fibreglass (423 styrene-exposed, and 268 styrene and noise-exposed workers) and workers producing standard fibreglass or other products as well as office workers (359 noise-exposed and 354 non-exposed workers). Exposures were measured on-site. Multiple logistic regression was used [15].
- In Chinese men and women (average ages: around 35.8 for noise-exposed workers, 36.7 for solvent and noise-exposed workers) exposed to acetone, ethyl acetate, methyl ethyl ketone, benzene, toluene, butyl acetate, ethylbenzene, xylene, and styrene. The analyses were performed on 40 workers: 20 furniture-making workers, exposed to both solvents and noise, and 20 manufacturing workers exposed to noise only. Exposures were measured on-site [16].
- In Korean men (average age around 31) exposed to benzene, toluene, tetrachloroethylene, xylene, and acetone. The analysis was conducted on 328 avionics workers: 146 exposed to noise, 18 exposed to solvents, 13 exposed to both and 151 not exposed. A cumulative exposure index was calculated using an exposure index for noise or solvents obtained from data collected by work environment measurement. Multiple logistic regression was used [17].

Table 2
Summary of chemical and physical-biomechanical effects observed in the studies included

Occupational exposure type 1	Occupational exposure type 2	Health effect	Significant	Reference
Chemical	Physical-biomechanical			
• Metals (Cadmium, chromium, iron, lead, nickel, welding fumes) • Solvents (Aliphatic and alicyclic hydrocarbons, aromatic hydrocarbons, organic solvents, toluene)	• Extremely low frequency magnetic fields (ELF)	Glioma and Meningioma	No	[12]
• Carbon Disulfide • Organic solvents (Xylene isomers, ethyl benzene, ethyl acetate, butyl acetate, n-butanol, white spirit, and toluene) • Styrene • Solvents (acetone, ethyl acetate, methyl ethyl ketone, benzene, toluene, butyl acetate, ethylbenzene, xylene, and styrene) • Mixed solvents • Solvents (benzene, toluene, tetrachloroethylene, xylene, acetone) • Solvents (toluene, xylene, styrene, benzene) and JP-8 (jet fuel)	• Noise	Hearing loss	Yes	[13] [14] [15] [16] [17] [18] [19]
• Styrene, methanol and methyl acetate	• Noise	Upper limit of hearing	Yes	[20]
• Metals (lead, cadmium, arsenic) and Solvents (toluene, xylene)	• Noise	Permanent shift in hearing threshold	Yes	[21]
• Fumes or dust, toxic and dangerous products	• Noise, biomechanical exposures (standing, tiring position or movements, walking, heavy loads, vibrations, repetitive tasks, high biomechanical exposure)	Sleep disorders Major depressive episode	Yes	[24] [25]
• Fumes or dust, toxic and dangerous products	• Noise, biomechanical exposures (standing, tiring position or movements, walking, heavy loads, vibrations, repetitive tasks, high biomechanical exposure)	Generalized anxiety disorder	No	[25]
• Chemicals (Trichloroethylene, white spirit, cellulose thinners, paints and varnishes, inks and dyes, pesticides)	• Physicals (Effort, repetitive hand movements or pinching, vibrations transmitted to the hand, awkward wrist postures)	Carpal tunnel syndrome	Yes	[41]
• Solvents (Toluene, DMF) • Organic solvents (Benzene, toluene, xylene, acetone, tetrachloroethylene)	• Noise	Hypertension	Yes	[58] [59]
• Paper dust	• Noise	Mortality from ischemic heart disease and Ischemic stroke	Yes	[60]
• BTEXS	• Noise	Mild renal impairment	Yes	[67]
• Metalworking fluid	• Noise	Chronic kidney disease	Yes	[68]
• Toluene • Xylene • Iron • Copper	• Noise	Metabolic syndrome	Yes	[71]

Table 3
Summary of chemical and psychosocial-organisational effects observed in the studies included

Occupational exposure type 1	Occupational exposure type 2	Health effect	Significant	Reference
Chemical	Psychosocial-organisational			
• Toluene • Xylene • DMF • Manganese • Lead • Copper	• Night work	Metabolic syndrome	Yes	[71]

- In Turkish men and women exposed to benzene, toluene, xylene, acetone, and tetrachloroethylene. The analysis was conducted on 588 truck and bus manufacturing workers: 223 exposed to noise, 115 exposed to solvents, 131 exposed to both and 119 non-exposed. Solvent hazard index (mg/m^3) was calculated to measure the impact of each solvent exposure. Variance analysis and t-test were used [18].
- In the USA, men and women exposed to toluene, xylene, styrene, benzene and JP-8 (jet fuel). The analysis was conducted on 476 men and 27 women working in military aviation. Noise exposure was assigned based on historical information and measurements at sites with exposure ≥85 dB. Chemical exposures were linked to workplace records: if a chemical product was used (historical) or purchased, an exposure was considered. Logistic and linear regression were used [19].

Upper limit of hearing was correlated with solvents (styrene, methanol, methyl acetate) and noise co-exposure in Japanese men working in plastic button manufacturing. The analysis was performed on 18 workers exposed to noise only, 19 workers exposed to

Table 4
Summary of physical-biomechanical effects observed in the studies included

Occupational exposure type 1	Occupational exposure type 2	Health effect	Significant	Reference
Physical-biomechanical				
• Noise and Vibrations		Anxiety	Yes	[27]
• Noise and Awkward posture		Job stress	No	[28]
• Work rate, grip strength, neck, shoulder and arm posture, wrist and hand posture, tool/hand contact stress, segmental and whole-body vibration …		Musculoskeletal disorders	Yes	[42]
• Repetitive work, awkward postures, pushing and pulling, use of force …				[52]
• Awkward posture and Forceful exertions		Lateral epicondylitis	Yes	[43]
• Whole body vibration and Awkward posture		Low back pain	No	[49]
• Walking, standing; Arms above shoulder; Repetitive arm movement; Back twisted, bent; Lifting, carrying; Pushing, pulling; Kneeling, squatting		Neck-shoulder and low-back pain	Yes	[51]
• Continuous and impulse noise, and Physical workload		Coronary heart disease	Yes	[61]
• Noise and Vibrations		Eye Strain, headache	Yes	[65]

noise and solvents, and 11 non-exposed office workers. Solvent exposures were measured in the working environment and breathing zone air with 3 types of diffusive samplers. Noise exposure was recorded at 183 measurement points in the workplaces [20].

Permanent shift in hearing threshold was correlated with a combination of metals (lead, cadmium, arsenic) and solvents (toluene, xylene) but also in co-exposure to this combination and noise in men and women shipyard workers from USA. The analysis was performed on 37 noise-exposed workers, 294 workers exposed to metals and solvents, 644 workers exposed to noise and metals, 291 workers exposed to noise, metals and solvents, and 280 non-exposed workers. Chemical and noise exposures comes from the DOEHRS-IH database. Chemical values were compared to the respective OSHA action levels for lead (0.03 mg/m^3), cadmium (0.0025 mg/m^3), and arsenic (0.005 mg/m^3). Noise exposure was considered high when the value was $\geq$85 dBA. Logistic regression was used [21].

3.3.3. *Mental health*

Ten studies focused on mental health problems: 6 of them deal with psychosocial-organisational co-exposure, 2 with physical-biomechanical co-exposure, and 2 with psychosocial-organisational and chemical/physical-biomechanical co-exposures. 12 out of 15 co-exposures were correlated with mental health problems.

Depressive symptoms have been studied with:

- Combination of psychosocial-organisational exposures: The correlation with depressive disorders was observed in Danish workers population comprising 1,143 men and 1,015 women (average age of 48). Four psychosocial factors were defined using average scores for several items: quantitative demands, emotional demands, role conflict and workplace bullying. Depressive disorder was measured using the Major Depression Inventory. Logistic and Cox regression were used [22]. In another study, this correlation with was observed in 699 women from Republic of Korea working in call-centers with a maximum age of 40. 13 items from a short form of the Korean Occupational Stress Scale were used to assess exposures (job demands, job insecurity, emotional labor, etc.). Multivariable analysis were used [23]. The correlation with major depressive episode (MDE) was observed in a French population comprising 8,579 men and 11,851 women (aged 15–65). Workers responded to 79 questionnaire items relate to 21 psychosocial work factors (demands at work, work organisation and job satisfaction, etc.) and 10 questionnaire items related to 2 physical and 2 chemical work factors: fumes or dust, toxic and dangerous products, noise, and biomechanical exposure. Weighted logistic regression was used [25]. In contrast, the correlation with MDE was not observed in Canadian population with 2,021 men and 2,180 women (average age of 44.6). Workers responded to 25 questionnaire items from the job content questionnaire (JCQ) related to work stress. Generalised estimating equations time-lag was used [26].
- Combination of chemical products (fumes or dust, toxic and dangerous products) and physical-biomechanical exposures: The correlation with MDE was also observed in the Bertrais et al study [25].

Anxiety and stress disorders have been studied with:

- Combination of psychosocial-organisational (demands at work, work organisation, job content, etc.) exposures: The correlation with generalized anxiety disorder was observed in the same population that Bertrais et al study [25]. The collection method and statistical analysis are also the same [25].
- Combination of chemical products (fumes or dust, toxic and dangerous products) and physical-biomechanical exposures: The correlation with generalized anxiety disorder was not observed in the same population that Bertrais et al study [25]. The collection method and statistical analysis are also the same [25].
- Noise and vibrations: The correlation with anxiety was observed in Korean population comprising 21,612 men and 23,629 women from the fifth Korean Working Condition Survey (KWCS) cohort. Noise and vibrations were assessed using a frequency of exposure scale ranging from never (representing no exposure) to all the time. Logistic regression was used [27].
- Noise and awkward posture co-exposure: The correlation with job stress disorders was not observed in Iranian workers in the restoration sector, including 69 men and 131 women with an average age around 33 years. Noise was considered an exposure when it exceeded 85 decibels. Awkward posture was divided into four risk levels: low, moderate, high and very high risk. Two-way analysis of variance (ANOVA) was used [28].

Table 5
Summary of physical-biomechanical and psychosocial-organisational effects observed in the studies included

Occupational exposure type 1 Physical-biomechanical	Occupational exposure type 2 Psychosocial-organisational	Health effect	Significant	Reference
• Posture with arms above shoulder level	• Low social support	Upper-extremity musculoskeletal disorders	Yes	[44]
• Workload, vibration while sitting	• High mental demands, low job control, low social support	Hand or wrist disorders and Upper limb	Yes	[45]
• Tiring or painful positions, carrying or moving heavy loads, standing, working with computers, high temperatures …	• Dissatisfaction with working conditions, work in the evening, disagree with "I am well paid for the work I do" …	Lower limb pain	Yes	[46]
• Vibration, heavy weights, awkward postures	• Psychosocial demands (effort, reward, decision …)	Low back symptoms	Yes	[47]
• Repetitive movements, force exerted, body and arm posture, standing, walking, material handling, hand use	• Psychological demands, decision latitude, social support	Low back pain	No	[48]
• Awkward or tiring positions, awkward grip or hand movements, lifting, carrying out repetitive tasks, working at very high speed, standing, sitting, or using tools that vibrate	• Contact and cooperation with management, level and difficulty of work, hours of work, work organisation, job satisfaction	Musculoskeletal symptoms	Yes	[53]
• Ergonomic risk factors: Tiring or painful position, lifting or moving people, carrying or moving heavy loads, continuous standing, and repetitive hand or arm movements	• Long working hours			[55]
• Force used at work, work with the arm(s) elevated, repetitive work	• Job demands, job control, social support	Combined musculoskeletal pain in the upper and lower body	Yes	[54]
• Postural constraints (static-seated posture, inadequate neck alignment and angle of forearms above the horizontal; impossibility of taking regular breaks, static-seated posture and inadequate neck alignment)	• Job strain (Psychological demands: quantity of work, time constraints, level of intellectual effort required; Decision latitude: opportunities for learning, autonomy, and participation in the decision-making process)	Shoulder-neck, upper limbs and lower-back pain	Yes	[56]
• Physical effort, carrying heavy loads, rapid physical activity, awkward body postures, head, and arm positions	• Work control, decision latitude, social support (supervisor, colleagues)	Coronary heart disease	Yes	[57]
• Continuous and impulse noise	• Shift work			[61]
• Carrying heavy loads, working in crouching or kneeling positions, working regularly or in a prolonged manner with one or both arms above the shoulders, repeatedly bending …	• Decision latitude exposures, psychological demands exposures, ever reported high-strain work	Decline of the physical function	Yes	[62]
• Noise	• Night work	Metabolic syndrome	Yes	[71]

Table 6
Summary of psychosocial-organisational effects observed in the studies included

Occupational exposure type 1	Occupational exposure type 2	Health effect	Significant	Reference
Psychosocial-organisational				
• Job demands and Job decision		Depressive symptoms/disorders	Yes	[22]
• Job demand, job control, interpersonal conflict, job insecurity and Emotional labor				[23]
• Demands at work, work organisation and job content, interpersonal relationships and leadership, work-individual interface, workplace violence		Sleep disorders	Yes	[24]
• Administrative and organisational pressure, physical and psychological threat, and lack of support				[31]
• Demands at work, work organisation and job content, interpersonal relations and leadership, work-individual interface, workplace violence		Major depressive episode and Generalized anxiety disorder	Yes	[25]
• Job demand and control, effort-reward imbalance and work-family conflicts		Major depressive episode	No	[26]
• Low and medium job strain and Night work • High job strain and Night work • High job strain and Rotating night shift		Mental health	Yes	[29]
• Low job control, high job demands and high insecurity about job		Common mental disorder	Yes	[30]
• Psychological demands (quantity of work, time constraints, conflicting demands) and Decision latitude (opportunities to make decision, to be creative, to use and develop one's abilities)		Persistent back pain	No	[50]
• Pace of work, workload issues, quality of relationships with management or colleagues, reward and recognition …		Musculoskeletal disorders	Yes	[52]

Common mental disorders have been studied with:

- Job strain (low, medium and high) and shift work (night and rotating night shift) co-exposure: The correlation with general mental health was observed in Chinese railway workers population, comprising 1,242 men and 28 women (aged 20–60). Workers responded to 49 questionnaire items from JCQ related to job demands, job control and workplace social support. Logistic regression was used [29].
- Low job control, high job demands and high insecurity about job co-exposure: The correlation with common mental disorders was observed in Australian 645 men and 634 women (aged 40–46). Exposures were assessed using 19 items from the Whitehall II study. Logistic regression was used [30].

Sleep disorders related with anxiety and job stress have been studied with:

- Combination of psychosocial-organisational exposures: The correlation with sleep disorders was observed in the same population that Bertrais et al study [25]. The collection method is also the same. Analysis was performed by weighted Poisson regression [24]. In another study, the correlation with sleep disorders was observed in American police workers among the Buffalo Cardio-Metabolic Occupational Police Stress cohort (256 men and 100 women; average age 41). Like French workers, they responded to 60 questionnaire items related to administrative and organisational pressures, physical and psychological threats, and availability or lack of support. Responses were analysed by linear regression [31].
- Chemical and physical-biomechanical co-exposure: The correlation with sleep disorders was also observed in the Bertrais et al study [24].

3.3.4. *Respiratory tract*

Nine studies were interested in respiratory problems. All of them deal with chemical co-exposures. 9 out of 10 co-exposures were correlated with respiratory problems.

Respiratory function problems have been studied with:

- Benzene, toluene, ethylbenzene, xylene, and styrene co-exposure: The correlation with small airway dysfunction was observed in a Chinese population of 530 Men and 105 Women (average age 47) working in the petrochemical production sector. A generalised linear model was used [32].
- Gases and fumes co-exposure or Combination of aromatic solvents: The correlation with lung function decline was observed in an Australian working population in the Tasmanian Longitudinal Health Study (TAHS). The analysis concerned 382 men and 385 women (average age around 45). Exposures were estimated using the ALOHA plus JEM. Multiple linear regression was used [33].
- Combination of pesticides (main contributors: pyrethroids): The correlation with night cough was observed with in Mexican avocado farmworkers population comprising 391 men and 9 women (average age around 40). Exposure-intensity scores were estimated using five factors about the utilisation of the pesticides. Bayesian weighted quantile sum (BWQS) was used [34].

Respiratory system cancers have been studied with:

- Hexavalent chromium and nickel co-exposure: The correlation with laryngeal cancer was observed in mixed European and American populations included in the INHANCE (International Head and Neck Cancer Epidemiology) consortium. The analysis concerned 2,256 cases (2,053 men and 203 women) aged between 50 and 69 years. Hexavalent chromium and nickel co-exposure was estimated from SYN-JEM. The laryngeal cancer frequency was compared with that of 7,857 unexposed by an adjusted logistic regression model [35].
- Biocides and synthetic metalworking co-exposure: The correlation with lung cancer was observed in men and women automobile manufacturing workers from USA in two studies with 38,560 and 23,877 (1,137 exposed and 22,740 non-exposed) workers respectively. On inclusion, the median age was 24 and the mean age 36. The exposures were assessed using retrospective exposure assessment based on historical company records. Parametric models and cox proportional hazards regression were used respectively [36,37].
- Asbestos and refractory ceramic fibres co-exposure: The correlation with pleural mesothelioma was observed in 988 French men workers. Exposures were assessed by two JEMs. Workers were considered to be exposed when the probability of exposure was >5% for asbestos and >1% for refractory ceramic fibres. Unconditional logistic regression adjusted was used [38].
- Asbestos and silica co-exposure or Asbestos and mineral wool co-exposure: The correlation with pleural mesothelioma was observed in 1,199 French men workers (average age of 66.9). Exposures were assessed by several JEM with a consideration as an exposure with a non-zero probability. Logistic regression was used [39].
- Crystalline silica and asbestos co-exposure: The correlation with lung cancer was not observed in 2,266 American men working in diatomaceous earth production. Cumulative exposures to asbestos and crystalline silica were estimated for each worker according to their job. A Poisson regression was used to analyse data [40].

3.3.5. Musculoskeletal system

Sixteen studies focused on musculoskeletal problems: 9 of them deal with physical-biomechanical and psychosocial-organisational co-exposures, 4 with physical-biomechanical co-exposure, 2 with psychosocial-organisational co-exposure, and one with both mix independently. 14 out of 19 co-exposures were correlated with musculoskeletal problems.

Upper limb disorders have been studied with:

- Combination of chemical substances (trichloroethylene, white spirit, cellulose thinners, etc.) and physical-biomechanical exposures: The correlation with carpal tunnel syndrome was observed in a population of French workers (aged 18–65). The analysis concerned 711 men and 332 women working in the agricultural sector. Exposure were reported using 6 physical and 6 chemical questionnaire items. Weighted univariate logistic regression was used [41].
- Posture, repetitive work, vibrations and use of force co-exposure: The correlation with upper limb musculoskeletal disorders was observed in 1,174 American men and women working in automobile construction sector. Exposures were assessed using 8 questionnaire items. Robust multivariate regression was used [42].
- Awkward posture and forceful exertions co-exposure: The correlation with lateral epicondylitis was observed in American workers in manufacturing and service sector. Analyses performed on 312 men and 299 women (average age around 40). Both exposures were estimated by video. Forceful exertions were defined based on the literature. Survival analyses were used [43].
- Posture with arms above shoulder level and low social support co-exposure: The correlation with upper-extremity musculoskeletal disorders was observed in French workers comprising 734 men and 512 women (average age of 38). Posture and low social support were assessed using the European consensus criteria and the French version of the JCQ respectively. Multivariate models were used [44].
- Combination of physical-biomechanical (workload, vibrations while sitting) and psychosocial-organisation (high mental demand, low job control, low social support) exposures: The correlation with upper limb and hand or wrist disorders was observed in 450 men and 114 women from United Kingdom (aged 26–55). Exposures were assessed using a questionnaire. According to their response, workers were classified into 4 categories: low physical-biomechanical and psychosocial-organisation exposures, low physical-biomechanical and high psychosocial-organisation exposures, high physical-biomechanical and low psychosocial-organisation exposures, and high physical-biomechanical and psychosocial-organisation exposures. Unconditional multiple logistic regression was used [45].

Low back disorders have been studied with:

- Combination of physical-biomechanical and psychosocial-organisational exposures: The correlation with lower limb pain was observed in European workers aged over 15 years. The analysis concerned 17,466 men and 17,906 women from the fifth European Working Conditions Survey. Exposures were assessed using 352 questionnaire items relating to working conditions and quality of employment, in the presence of an interviewer. A logistic regression was used [46]. In another study, the correlation with low back symptoms was observed in Indonesian coal mining workers comprising 1,255 men and 39 women (median age of 26). Physical-biomechanical (vibration, heavy weights and awkward posture) and psychosocial-organisation (effort, reward, decision, etc.) exposure were assessed with a percent exposure scale and the JCQ respectively. Logistic regression was used [47]. In contrast, the correlation with low back pain was not observed in 392 men and 177 women from Brazil working in plastic factories. Physical-biomechanical (repetitive movements, force exerted, body and arm posture, etc.) exposures were assessed using a self-reported questionnaire with 11 items and 6-point scale. Psychosocial-organisation (psychological demands, decision latitude, social support) exposures were assessed using JCQ questionnaire. Logistic regression was used [48].
- Whole body vibration and awkward posture co-exposure: The correlation with low back pain was not observed in German drivers comprising 58 workers (10 bus and locomotive drivers, 19 crane operators, 20 earth moving machine operators and 9 forklift drivers) with an average age around 46 years. Whole body vibration was defined according to the ISO 2631-1 with 3 categories: low (<0.5 m/s^2), intermediate (≥ 0.5 m/s^2 and <1 m/s^2) and high (≥ 1 m/s^2). Awkward posture was also defined into 3 categories according to the ISO 11226: neutral, moderate and awkward. Regression was used [49].
- Combination of psychosocial-organisation exposures: The correlation with persistent back pain was not observed in Canadian white and blue collars workers comprising 483 men

and 366 women (average age around 39 and 38 respectively). Psychological job demands and job decision latitude were measured with a score calculated with 9 items respectively with a French version of JCQ. Workers are considered exposed of each when their respective scores are greater than 9 and less than 70. Multivariate models were used [50].

General musculoskeletal syndromes have been studied with:

- Combination of physical-biomechanical exposures: The correlation with neck-shoulder and low back pain was observed in 18,905 Danish workers (8,629 men and 10,276 women) who took part in more than one questionnaire of the Work environment and health in Denmark study (WEHD). Seven physical-biomechanical factors were measured using a frequency of exposure scale: walking or standing, arms above shoulder, repetitive arm movement, back twisted or bent, lifting or carrying, pushing or pulling and kneeling or squatting. K-means cluster and survey regression analyses were used [51]. In another study, the correlation with musculoskeletal pain was observed in an Australian health care sector population (average age around 40). The analysis involved 733 men and 601 women responding to 26 questionnaire items for psychosocial-organisation exposures and 12 questionnaire items for physical-biomechanical exposures. Generalised linear models assuming binary logistic regression were used [52].
- Combination of psychosocial-organisation exposures: The correlation with musculoskeletal pain was also observed in the Neupane et al study [52].
- Combination of physical-biomechanical and psychosocial-organisational exposures: The correlation with musculoskeletal symptoms was observed in New Zealand workers (median age of 45). The analysis involved 1,431 men and 1,572 women who estimated their working time in several situations with physical-biomechanical exposures using a frequency scale (from never to full-time) and who answered a modified version of the JCQ using a 5-point Likert scale for psychosocial-organisation exposures. Multivariable logistic regression was used [53]. In another study, the correlation with combined musculoskeletal pain in the upper and lower body was observed in 14,081 men and 20,173 Danish workers (average age around 40). Physical-biomechanical exposures were assessed by linking self-reported occupation to exposure estimates from two JEM. Psychosocial-organisation exposures were assessed using Karasek–Theorell three-factor model. Poisson regression was used [54].
- Combination of ergonomic exposures and long working hours: The correlation with musculoskeletal symptoms was observed in 20,212 men and 14,104 women (minimum age of 15) from the fifth KWCS. Information about exposures were collected by the KWCS questionnaire. Survey-weighted multiple logistic analysis was used [55].
- Postural constraint and job strain co-exposure: The correlation with shoulder-neck, upper limbs and lower-back pain was observed in 761 men and 1,093 women white collars from Canada (aged 18–60). Job strain were assessed using the French version of JCQ. Postural constraint were measured based on Health Canada ergonomic guidelines. Unconditional logistic regression was used [56].

3.3.6. Others systems

The selected studies reported problems with other physiological systems that can be subdivided into six categories: cardiovascular disorders, general decline of physical function, ocular disorders, renal and urinary tract disorders, skin disorders and biological disorders. Results are presented in supplementary material (see Annex B).

4. Discussion

This review is the first to take stock of what we know about the link between all occupational multiple exposures and workers' health. It highlights the associations between combinations of exposures and occupational diseases. Chemical/chemical and physical-biomechanical/chemical co-exposures are the most frequently studied.

Surprisingly, biological risks and some co-exposure scenarios known to have health effects like chemical substances/atypical working hours or ultraviolet rays/chemical substances were not identified in the literature mined for this review. However, this observation is quite consistent with the results presented in [72], where only two studies involving biological exposures are mentioned, with neither linked to occupational exposure (atopy and viral infection). Nevertheless, biological risks in occupational settings are studied, but no study met all the selection criteria for inclusion in our review: either the link with the health problem [73] or the multiple exposure aspect [74,75] were missing. In addition, most studies provide an unquantified estimate of exposure, indicating only the activity sector and assuming specific exposure linked to this sector. This is the case for example for sewage [76] or composting workers [77].

Regarding chemical co-exposure with atypical working hours, the result exposed by Smolensk et al [78], revealed the effects of some chemical substances on metabolism depending on the timing of exposure. For example, workers may be exposed to chemical substances outside typical working hours, such as during night work. Although this situation is quite common, further studies are required [79]. Another example of co-exposure not reported is ultraviolet rays and chemical substances (in particular polycyclic aromatic hydrocarbons), which can also be a common situation notably for outdoor occupations, such as road construction [4,80]. This type of co-exposure can have an effect on human skin [81].

For inclusion in this review, the studies had to meet strict selection criteria, which limited their number. Most of the studies excluded reported only co-exposure without relating it to a health effect [82,83]. For example, in Raffler et al (2010), combined exposure to whole-body vibration and uncomfortable postures was measured in the field for several drivers and on several machines. No links to physical effects were made. Similarly, in Bosson-Rieutort et al (2020), co-exposure was determined based on workplace measurements of chemical agents. Although co-exposures and recurrent agents were identified, the risks they pose to workers were not examined. In addition, several studies demonstrating an association between co-exposure and health outcomes are experimental, and the results obtained have not been confirmed in human populations [84,85]. Thus, in Suzuki et al (2014), the effects of inhalation of 1,2-Dichloropropane and dichloromethane individually and in combination were studied in mice. Co-exposure enhanced the genotoxic effects of 1,2-Dichloropropane measured in the liver. In Grytting et al (2022), co-exposure to diesel exhaust particles and mineral particles induced enhanced pro-inflammatory responses in vitro, in human bronchial epithelial cells. Other studies have shown an association between two exposures and a health effect but did not consider the possibility of interaction between the exposures. In this case, the effect of each exposure was observed individually on the health effect [86–88].

In addition, reviews and meta-analysis were deliberately excluded from this scoping review, as the diversity of combinations was prioritized over quantity. These reviews group together studies according to a specific health effect or combination of exposures, or both. The amount of information is therefore considerable, but it is also well-directed. Six of them met the initial selection criteria, however, the co-exposures presented are redundant with the articles selected: noise and solvents for hearing disorders [89,90], biomechanical factors for musculoskeletal disorders [91,92], chemical and shift work co-exposures [93], and psychosocial risks for mental health [94].

Although most of the studies included in this review report significant associations between co-exposure and a health problem, none have identified specific preventive measures for multiple exposures. Twenty studies provide information on prevention methods for reducing multiple exposures effects. Twenty-five studies offer traditional perspectives such as continuing research, highlighting the need for sampling strategies or studying occupational exposure using new or modified methods. Eight studies highlight the need to introduce protective measures adapted to the occupational situation studied, or to introduce screening methods for early detection of health problems. Ten studies do not give any advice on prevention. The prevention advice given focuses on the individual effects of each exposure in the combination, and there is no 100% solution for multiple exposure. Nevertheless, this absence of new safety measures can be seen as positive, particularly for companies that do not need to introduce a new type of safety system and can concentrate on existing measures. However, it is still necessary to identify the conditions of multiple exposure in order to improve the distribution of known measures.

One way of gaining a better understanding of multiple exposures in the workplace and identifying appropriate risk mitigation strategies could be to combine databases that provide information on populations, exposures and/or diseases, and to apply statistical models adapted to the data. In France, a study has been carried out to compare the complementarity of several French occupational health databases [95]. This work highlighted a degree of complementarity between the databases, with some information in common but also complementary information provided by individual databases. The merging of several sources of information is therefore an avenue worth exploring.

In conclusion, every year we learn more about concurrent or co-exposure to multiple occupational hazards, but we still do not know enough to get a definite idea of its impact on health. Some co-exposure scenarios and risks need to be more extensively studied in an occupational setting. New research strategies and new methods of analysis need to be developed for application with multiple exposures. The use of occupational health databases would also be a good way to identify co-exposure and its association with health effects in defined sectors or for particular occupations. Prevention to reduce the risks to workers' health is still underdeveloped in the case of multiple exposure. Few practices, regulations or advice have been put in place or explained to ensure a healthy work environment. Research into multiple exposure and related occupational health problems must be continued in order to improve prevention methods.

CRediT authorship contribution statement

Cassandra BARBEY: Writing – original draft, Methodology, Investigation, Formal analysis. **Nathalie BONVALLOT:** Writing – review & editing, Validation, Supervision, Methodology. **Frédéric CLERC:** Writing – review & editing, Validation, Supervision, Methodology.

Conflicts of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.shaw.2024.10.004.

References

[1] Bambra C, Gibson M, Sowden A, Wright K, Whitehead M, Petticrew M. Tackling the wider social determinants of health and health inequalities: evidence from systematic reviews. J Epidemiol Community Health 2010;64(4):284–91. 1 avr.
[2] Alla F. 3. Les déterminants de la santé. In: Traité de santé publique [Internet]. Lavoisier. 2016 [cité 26 juin 2023]. p. 15. Disponible sur: http://www.cairn.info/traite-de-sante-publique–9782257206794-page-15.htm.
[3] Pega F, Momen N, Streicher K, Nafradi B. WHO/ILO joint estimates of the work-related burden of disease and injury; 2021. p. 2000–16.
[4] Rider CV, Simmons JE. éditeurs. Chapter 16 -Chemical mixtures and combined chemical and nonchemical stressors: exposure, toxicity, analysis, and risk. Cham, Switzerland: Springer; 2018. 556 p.
[5] Fourneau C, Pernelet Joly V, Boulanger G, Bastos H. Plan Santé au Travail 2016-2020 - Action 1.11 Amélioration et prise en compte de la polyexposition. «Recensement des principales initiatives institutionnelles sur la poly-exposition en santé au travail »; 2018. 78 p.
[6] Fourneau C, Sanchez M, Perouel G, Frery N, Coutrot T, Boulanger G, Courrier B, Pernelet-Joly V, Bastos H. The French 2016-2020 National Occupational Health Plan: a better understanding of multiple exposures. Environ Risques Santé Août 2021;20(4):377–82.
[7] International Programme on Chemical Safety. Inter-Organization Programme for the Sound Management of Chemicals. Assessment of combined exposures to multiple chemicals : report of a WHO/IPCS international workshop on aggregate/cumulative risk assessment, 75; 2009.
[8] OECD. Considerations for assessing the risks of combined exposure to multiple chemicals [internet]. OECD [cité 4 juill 2023]. (OECD Series on Testing and Assessment). Disponible sur: https://www.oecd-ilibrary.org/environment/considerations-for-assessing-the-risks-of-combined-exposure-to-multiple-chemicals_ceca15a9-en 2018; 2018.
[9] Yokoyama K, Araki S, Murata K, Nishikitani M, Nakaaki K, Yokota J, Ito A, Sakata E. Postural sway frequency analysis in workers exposed ton-hexane, xylene, and toluene: assessment of subclinical cerebellar dysfunction. Environ Res Août 1997;74(2):110–5.
[10] Nell V, Myers J, Colvin M, Rees D. Neuropsychological assessment of organic solvent effects in South Africa: test selection, adaptation, scoring, and validation issues. Environ Res nov 1993;63(2):301–18.
[11] Elbaz A, Clavel J, Rathouz PJ, Moisan F, Galanaud J, Delemotte B, Alpérovitch A, Tzourio C. Professional exposure to pesticides and Parkinson disease. Ann Neurol oct 2009;66(4):494–504.
[12] Turner MC, Benke G, Bowman JD, Figuerola J, Fleming S, Hours M, Kincl L, Krewski D, McLean D, Parent M, Richardson L, Sadetzki S, Schlaefer K, Schüz J, Siemiatycki J, Tongeren M, Cardis E. Interactions between occupational exposure to extremely low frequency magnetic fields and chemicals for brain tumour risk in the INTEROCC study. Occup Environ Med nov 2017;74(11):802–9.
[13] Chang SJ, Shih TS, Chou TC, Chen CJ, Chang HY, Sung FC. Hearing loss in workers exposed to carbon disulfide and noise. Environ Health Perspect oct 2003;111(13):1620–4.
[14] Sliwinska-Kowalska M, Zamyslowska-Szmytke E, Szymczak W, Kotylo P, Fiszer M, Wesolowski W, Pawlaczyk-Luszczynska M, Bak M, Gajda-Szadkowska A. Effects of coexposure to noise and mixture of organic solvents on hearing in dockyard workers. J Occup Environ Med janv 2004;46(1):30–8.
[15] Morata TC, Sliwinska-Kowalska M, Johnson AC, Starck J, Pawlas K, Zamyslowska-Szmytke E, Nylen P, Toppila E, Krieg E, Pawlas N, Prasher D. A multicenter study on the audiometric findings of styrene-exposed workers. Int J Audiol oct 2011;50(10):652–60.
[16] Fuente A, Qiu W, Zhang M, Xie H, Kardous CA, Campo P, Morata TC. Use of the kurtosis statistic in an evaluation of the effects of noise and solvent exposures on the hearing thresholds of workers: an exploratory study. J Acoust Soc Am 2018;143(3):1704–10. 1 Mars.
[17] Kim J, Park H, Ha E, Jung T, Paik N, Yang S. Combined effects of noise and mixed solvents exposure on the hearing function among workers in the aviation industry. Ind Health 2005;43(3):567–73.
[18] Unlu I, Kesici G, Basturk A, Kos M, Yılmaz O. A comparison of the effects of solvent and noise exposure on hearing, together and separately. Noise Health 2014;16(73):410.
[19] Hughes H, Hunting K. Evaluation of the effects of exposure to organic solvents and hazardous noise among US Air Force Reserve personnel. Noise Health 2013;15(67):379.
[20] Morioka I, Miyai N, Yamamoto H, Miyashita K. Evaluation of combined effect of organic solvents and noise by the upper limit of hearing. Ind Health 2000;38(2):252–7.
[21] Schaal N, Slagley J, Zreiqat M, Paschold H. Effects of combined exposure to metals, solvents, and noise on permanent threshold shifts. Am J Ind Med Mars 2017;60(3):227–38.

[22] Lunen JC, Rugulies R, Sørensen JK, Andersen LL, Clausen T. Exploring exposure to multiple psychosocial work factors: prospective associations with depression and sickness absence. Eur J Public Health 2023;33(5):821–7. 10 oct.
[23] Cho SS, Kim H, Lee J, Lim S, Jeong WC. Combined exposure of emotional labor and job insecurity on depressive symptoms among female call-center workers: a cross-sectional study. Medicine (Baltimore). Mars 2019;98(12):e14894.
[24] Bertrais S, André N, Bèque M, Chastang J, Niedhammer I. Associations between multiple occupational exposures and sleep problems: results from the national French Working Conditions survey. J Sleep Res [Internet] juin 2021;30(3) [cité 24 févr 2023];Disponible sur: https://onlinelibrary.wiley.com/doi/10.1111/jsr.13101.
[25] Bertrais S, Mauroux A, Chastang J, Niedhammer I. Associations of multiple occupational exposures with major depressive and generalized anxiety disorders: findings from the French National Working Conditions Survey. Depress Anxiety Mars 2021;38(3):337–50.
[26] Nigatu YT, Wang J. The combined effects of job demand and control, effort-reward imbalance and work-family conflicts on the risk of major depressive episode: a 4-year longitudinal study. Occup Environ Med Janv 2018;75(1):6–11.
[27] Park M, Nari F, Jeong W, Park EC, Jang SI. Association between occupational noise and vibration and anxiety in the South Korean working population: a cross-sectional study. J Occup Med Toxicol Déc 2022;17(1):1.
[28] Chaharaghran F, Tabatabaei S, Rostamzadeh S. The impact of noise exposure and work posture on job stress in a food company. Work. 13 Déc 2022;73(4):1227–34.
[29] Jiang Y, Wu C, Hu T, Chen M, Liu W, Zhou Y, Chen Z, Xu X. Association for combined exposure to job strain, shift work on mental health among Chinese railway workers: a cross-sectional study. BMJ Open oct 2020;10(10):e037544.
[30] Too LS, Leach L, Butterworth P. Cumulative impact of high job demands, low job control and high job insecurity on midlife depression and anxiety: a prospective cohort study of Australian employees. Occup Environ Med juin 2021;78(6):400–8.
[31] Ma CC, Hartley TA, Sarkisian K, Fekedulegn D, Mnatsakanova A, Owens S, Gu JK, Tinney-Zara C, Violanti JM, Andrew ME. Influence of work characteristics on the association between police stress and sleep quality. Saf Health Work Mars 2019;10(1):30–8.
[32] Liao Q, Du R, Ma R, Liu X, Zhang Y, Zhang Z, Ji P, Xiao M, Cui Y, Xing X, Liu L, Dang S, Deng Q, Xiao Y. Association between exposure to a mixture of benzene, toluene, ethylbenzene, xylene, and styrene (BTEXS) and small airways function: a cross-sectional study. Environ Res Sept 2022;212:113488.
[33] Alif SM, Dharmage S, Benke G, Dennekamp M, Burgess J, Perret JL, Lodge C, Morrison S, Johns DP, Giles G, Gurrin L, Thomas PS, Hopper JL, Wood-Baker R, Thompson B, Feather I, Vermeulen R, Kromhout H, Jarvis D, Garcia Aymerich J, Walters EH, Abramson MJ, Matheson MC. Occupational exposure to solvents and lung function decline: a population based study. Thorax Juill 2019;74(7):650–8.
[34] Alcalá CS, Armendáriz-Arnez C, Mora AM, Rodriguez-Zamora MG, Bradman A, Fuhrimann S, Lindh C, Rosa MJ. Association of pesticide exposure with respiratory health outcomes and rhinitis in avocado farmworkers from Michoacán, Mexico. Sci Total Environ 2024;945:173855. 1 oct.
[35] Hall AL, Kromhout H, Schüz J, Peters S, Portengen L, Vermeulen R, Agudo A, Ahrens W, Boffetta P, Brennan P, Canova C, Conway DI, Curado MP, Daudt AW, Fernandez L, Hashibe M, Healy CM, Holcatova I, Kjaerheim K, Koifman R, Lagiou P, Luce D, Macfarlane GJ, Menezes A, Menvielle G, Polesel J, Ramroth H, Richiardi L, Stücker I, Thomson P, Vilensky M, Wunsch-Filho V, Yuan-Chin AL, Znaor A, Straif K. Olsson A. Laryngeal cancer risks in workers exposed to lung carcinogens: exposure–effect analyses using a quantitative job exposure matrix. Epidemiol Janv 2020;31(1):145–54.
[36] Garcia E, Picciotto S, Neophytou AM, Bradshaw PT, Balmes JR, Eisen EA. Lung cancer mortality and exposure to synthetic metalworking fluid and biocides: controlling for the healthy worker survivor effect. Occup Environ Med oct 2018;75(10):730–5.
[37] Mehta AJ, Malloy EJ, Applebaum KM, Schwartz J, Christiani DC, Eisen E. Reduced lung cancer mortality and exposure to synthetic fluids and biocide in the auto manufacturing industry. Scand J Work Environ Health nov 2010;36(6):499–508.
[38] Lacourt A, Rinaldo M, Gramond C, Ducamp S, Gilg Soit Ilg A, Goldberg M, Pairon JC, Brochard P. Co-exposure to refractory ceramic fibres and asbestos and risk of pleural mesothelioma. Eur Respir J 1 Sept 2014;44(3):725–33.
[39] Lacourt A, Gramond C, Audignon S, Ducamp S, Févotte J, Soit Ilg AG, Goldberg M, Imbernon E, Brochard P. Pleural mesothelioma and occupational coexposure to asbestos, mineral wool, and silica. Am J Respir Crit Care Med 2013;187(9):977–82. 1 mai.
[40] Checkoway H, Heyer NJ, Demers PA, Gibbs GW. Reanalysis of mortality from lung cancer among diatomaceous earth industry workers, with consideration of potential confounding by asbestos exposure. Occup Environ Med 1 Sept 1996;53(9):645–7.
[41] Roquelaure Y, Jégo S, Geoffroy-Perez B, Chazelle E, Descatha A, Evanoff B, Garlantézec R, Bodin J. Carpal tunnel syndrome among male French farmers and agricultural workers: is it only associated with physical exposure? Saf Health Work Mars 2020;11(1):33–40.
[42] Gold J, Punnett L, Cherniack M, Wegman D. Digital vibration threshold testing and ergonomic stressors in automobile manufacturing workers: a cross-sectional assessment. Ergon Janv 2005;48(1):66–77.
[43] Fan ZJ, Silverstein BA, Bao S, Bonauto DK, Howard NL, Smith CK. The association between combination of hand force and forearm posture and incidence of lateral epicondylitis in a working population. Hum factors J hum factors ergon soc. Févr 2014;56(1):151–65.
[44] Nambiema A, Bodin J, Stock S, Aublet-Cuvelier A, Descatha A, Evanoff B, Roquelaure Y. Proportion and number of upper-extremity musculoskeletal disorders attributable to the combined effect of biomechanical and psychosocial risk factors in a working population. Int J Environ Res Public Health 7 avr 2021;18(8):3858.
[45] Devereux JJ, Vlachonikolis IG, Buckle PW. Epidemiological study to investigate potential interaction between physical and psychosocial factors at work that may increase the risk of symptoms of musculoskeletal disorder of the neck and upper limb. Occup Environ Med Avr 2002;59(4):269–77.
[46] Garcia MG, Graf M, Läubli T. Lower limb pain among workers: a cross-sectional analysis of the fifth European Working Conditions Survey. Int Arch Occup Environ Health oct 2017;90(7):575–85.
[47] Widanarko B, Legg S, Devereux J, Stevenson M. Interaction between physical and psychosocial work risk factors for low back symptoms and its consequences amongst Indonesian coal mining workers. Appl Ergon Janv 2015;46:158–67.
[48] Fernandes RDCP, Carvalho FM, Assunção AÁ, Silvany Neto AM. Interactions between physical and psychosocial demands of work associated to low back pain. Rev Saúde Pública Avr 2009;43(2):326–34.
[49] Raffler N, Rissler J, Ellegast R, Schikowsky C, Kraus T, Ochsmann E. Combined exposures of whole-body vibration and awkward posture: a cross sectional investigation among occupational drivers by means of simultaneous field measurements. Ergonomics 2 nov 2017;60(11):1564–75.
[50] Leroux I, Dionne CE, Bourbonnais R. Psychosocial job factors and the one-year evolution of back-related functional limitations. Scand J Work Environ Health Févr 2004;30(1):47–55.
[51] Andersen LL, Vinstrup J, Sundstrup E, Skovlund SV, Villadsen E, Thorsen SV. Combined ergonomic exposures and development of musculoskeletal pain in the general working population: a prospective cohort study. Scand J Work Environ Health 2021;47(4):287–95. 1 mai.
[52] Neupane S, Nygård CH, Oakman J. Work-related determinants of multi-site musculoskeletal pain among employees in the health care sector. Work. 26 Juill 2016;54(3):689–97.
[53] Widanarko B, Legg S, Devereux J, Stevenson M. The combined effect of physical, psychosocial/organisational and/or environmental risk factors on the presence of work-related musculoskeletal symptoms and its consequences. Appl Ergon nov 2014;45(6):1610–21.
[54] Sommer TG, Frost P, Svendsen SW. Combined musculoskeletal pain in the upper and lower body: associations with occupational mechanical and psychosocial exposures. Int Arch Occup Environ Health nov 2015;88(8):1099–110.
[55] Park JW, Kang MY, Kim JI, Hwang J, Choi SS, Cho SS. Influence of coexposure to long working hours and ergonomic risk factors on musculoskeletal symptoms: an interaction analysis. BMJ Open mai 2022;12(5):e055186.
[56] Lapointe J, Dionne CE, Brisson C, Montreuil S. Interaction between postural risk factors and job strain on self-reported musculoskeletal symptoms among users of video display units: a three-year prospective study. Scand J Work Environ Health mars 2009;35(2):134–44.
[57] Clays E, Casini A, Van Herck K, De Bacquer D, Kittel F, De Backer G, Holtermann A. Do psychosocial job resources buffer the relation between physical work demands and coronary heart disease? A prospective study among men. Int Arch Occup Environ Health nov 2016;89(8):1299–307.
[58] Chang T, Wang V, Hwang B, Yen H, Lai J, Liu C, Lin S. Effects of Co-exposure to noise and mixture of organic solvents on blood pressure. J Occup Health Juill 2009;51(4):332–9.
[59] Attarchi M, Golabadi M, Labbafinejad Y, Mohammadi S. Combined effects of exposure to occupational noise and mixed organic solvents on blood pressure in car manufacturing company workers. Am J Ind Med Févr 2013;56(2):243–51.
[60] Torén K, Neitzel RL, Eriksson HP, Andersson E. Occupational exposure to noise and dust in Swedish soft paper mills and mortality from ischemic heart disease and ischemic stroke: a cohort study. Int Arch Occup Environ Health Sept 2023;96(7):965–72.
[61] Virkkunen H, Härmä M, Kauppinen T, Tenkanen L. The triad of shift work, occupational noise, and physical workload and risk of coronary heart disease. Occup Environ Med Juin 2006;63(6):378–86.
[62] Sabbath EL, Glymour MM, Descatha A, Leclerc A, Zins M, Goldberg M, Berkman LF. Biomechanical and psychosocial occupational exposures: joint predictors of post-retirement functional health in the French GAZEL cohort. Adv Life Course Res déc 2013;18(4):235–43.
[63] Zendehdel R, Parsarad M, Asgari Gandomani E, Panjali Z, Rafieepour A, Mohammadi Z, Moradpour Z, Vahabi M, Mohammad Alipour M, Gholamiarjenaki R. Risk assessment of chemical mixtures by benchmark dose-principle component analysis approach in occupational exposure. Environ Sci Pollut Res nov 2021;28(41):58781–6.
[64] Gonzalez M, Velten M, Cantineau A. Increased acquired dyschromatopsia among solvent-exposed workers: an epidemiology study on 249 employees of an aluminum-foil printing factory. Int Arch Occup Environ Health 28 Juill 1998;71(5):317–24.
[65] Kim J, Lee W, Won JU, Yoon JH, Seok H, Kim YK, Lee S, Roh J, Fuh J. The relationship between occupational noise and vibration exposure and

headache/eyestrain, based on the fourth Korean Working Condition Survey (KWCS). Fuh JL, éditeur. PLOS ONE 23 mai 2017;12(5):e0177846.
[66] The Canadian Cancer Registries Epidemiology GroupLatifovic L, Villeneuve PJ, Parent MÉ, Kachuri L, Harris SA. Silica and asbestos exposure at work and the risk of bladder cancer in Canadian men: a population-based case-control study. BMC Cancer Déc 2020;20(1):171.
[67] Chen Q, Deng Q, Liu Y, Long Z, Li S, Liu Q, Lv Y, Qin J, Yang A, Huang Y, Tan Z, Wang D, Xing X, Xiao Y. Co-exposure of petrochemical workers to noise and mixture of benzene, toluene, ethylbenzene, xylene, and styrene: impact on mild renal impairment and interaction. Environ Pollut avr 2024;346:123628.
[68] Zhou L, Wu B, Tang M, Li G, Chan W, Song L, Wang J, Zhu L, Lin L, Lian Y. Association between exposure to metalworking fluid aerosols, occupational noise and chronic kidney disease: a cross-sectional study in China. BMC Public Health 4 juin 2024;24(1):1495.
[69] Coenraaos PJ, Foo SC, Phoon WO, Lun KC. Dermatitis in small-scale metal industries. Contact Dermatitis. Mars 1985;12(3):155–60.
[70] Benavente Y, Costas L, Rodríguez-Suarez MM, Alguacil J, Santibáñez M, Vila J, Robles C, Alonso E, De La Banda E, Gonzalez-Barca E, Dierssen-Sotos T, Gimeno Vazquez E, Aymerich M, Campos E, Jiménez-Moleón JJ, Marcos-Gragera R, Castaño-Vinyals G, Aragonés N, Pollan M, De Sanjose S, Kogevinas M, Tardón A, Casabonne D. Occupational exposure to pesticides and chronic lymphocytic leukaemia in the MCC-Spain study. Int J Environ Res Public Health 2020;17(14):5174. 17 juill.
[71] Kang D, Lee ES, Kim TK, Kim YJ, Lee S, Lee W, Sim H, Kim S. Association with combined occupational hazards exposure and risk of metabolic syndrome: a workers' health examination cohort 2012–2021. Saf Health Work Sept 2023;14(3):279–86.
[72] Fox MA, Niemeier RT, Hudson N, Siegel MR, Dotson GS. Cumulative risks from stressor exposures and personal risk factors in the workplace: examples from a scoping review. Int J Environ Res Public Health 29 mai 2021;18(11):5850.
[73] Heldal KK, Barregard L, Larsson P, Ellingsen DG. Pneumoproteins in sewage workers exposed to sewage dust. Int Arch Occup Environ Health janv 2013;86(1):65–70.
[74] Donham KJ, Cumro D, Reynolds SJ, Merchant JA. Dose-response relationships between occupational aerosol exposures and cross-shift declines of lung function in poultry workers:: recommendations for exposure limits. J Occup Environ Med Mars 2000;42(3):260–9.
[75] Heldal K, Madsø L, Eduard W. Airway inflammation among compost workers exposed to actinomycetes spores. Ann Agric Environ Med 2015;22(2):253–8. 11 mai.
[76] Muzaini K, Yasin SM, Ismail Z, Ishak AR. Systematic review of potential occupational respiratory hazards exposure among sewage workers. Front Public Health 8 Mars 2021;9:646790.
[77] Poole CJM, Basu S. Systematic Review: occupational illness in the waste and recycling sector. Occup Med 2 déc 2017;67(8):626–36.
[78] Smolensky MH, Reinberg AE, Sackett-Lundeen L. Perspectives on the relevance of the circadian time structure to workplace threshold limit values and employee biological monitoring. Chronobiol Int 26 nov 2017;34(10):1439–64.
[79] Caetano G, Gautier MA, Weibel L, Patrascu C. Polyexpositions entre substances chimiques et travail en horaires atypiques : Introduction à la « Chronotoxicologie ». Réf En Santé Au Trav 2023;174:15–36.
[80] Hopf NB, Spring P, Hirt-Burri N, Jimenez S, Sutter B, Vernez D, Berthet A. Polycyclic aromatic hydrocarbons (PAHs) skin permeation rates change with simultaneous exposures to solar ultraviolet radiation (UV-S). Toxicol Lett Mai 2018;287:122–30.
[81] Von Koschembahr A, Youssef A, Béal D, Calissi C, Bourgart E, Marques M, Leccia M, Giot J, Maitre A, Douki T. Solar simulated light exposure alters metabolization and genotoxicity induced by benzo[a]pyrene in human skin. Sci Rep 2 oct 2018;8(1):14692.
[82] Raffler N, Hermanns I, Sayn D, Göres B, Ellegast R, Rissler J. Assessing combined exposures of whole-body vibration and awkward posture — further results from application of a simultaneous field measurement methodology. Ind Health 2010;48(5):638–44.
[83] Bosson-Rieutort D, Sarazin P, Bicout DJ, Ho V, Lavoué J. Occupational Co-exposures to multiple chemical agents from workplace measurements by the US occupational safety and health administration. Ann Work Expo Health 30 Avr 2020;64(4):402–15.
[84] Suzuki T, Yanagiba Y, Suda M, Wang R. Assessment of the genotoxicity of 1,2-dichloropropane and dichloromethane after individual and Co-exposure by inhalation in mice. J Occup Health mai 2014;56(3):205–14.
[85] Grytting VS, Chand P, Låg M, Øvrevik J, Refsnes M. The pro-inflammatory effects of combined exposure to diesel exhaust particles and mineral particles in human bronchial epithelial cells. Part Fibre Toxicol 21 Févr 2022;19(1):14.
[86] Barro D, Olinto MTA, Macagnan JBA, Henn RL, Pattussi MP, Faoro MW, Garcez ADS, Paniz VMV. Job characteristics and musculoskeletal pain among shift workers of a poultry processing plant in Southern Brazil. J Occup Health. Sept 2015;57(5):448–56.
[87] Abareshi F, Salimi F, Farnia F, Fallahi M, Rastaghi S. The impact of mental workload, work-related and socio-demographic factors on job burnout among emergency medical staff. Work. 11 Août 2022;72(4):1269–77.
[88] Behrens T, Ge C, Vermeulen R, Kendzia B, Olsson A, Schüz J, Kromhout H, Pesch B, Peters S, Portengen L, Gustavsson P, Mirabelli D, Guénel P, Luce D, Consonni D, Caporaso NE, Landi MT, Field JK, Karrasch S, Wichmann H, Siemiatycki J, Parent M, Richiardi L, Simonato L, Jöckel K, Ahrens W, Pohlabeln H, Fernández-Tardón G, Zaridze D, McLaughlin JR, Demers PA, Świątkowska B, Lissowska J, Pándics T, Fabianova E, Mates D, Bencko V, Foretova L, Janout V, Boffetta P, Bueno-de-Mesquita B, Forastiere F, Straif K, Brüning T. Occupational exposure to nickel and hexavalent chromium and the risk of lung cancer in a pooled analysis of case-control studies (SYNERGY). Int J Cancer 2023;152(4):645–60. 15 févr.
[89] Hormozi M, Ansari-Moghaddam A, Mirzaei R, Dehghan Haghighi J, Eftekharian F. The risk of hearing loss associated with occupational exposure to organic solvents mixture with and without concurrent noise exposure: a systematic review and meta-analysis. Int J Occup Med Environ Health 2017;30(4):521–35.
[90] Warner R, Fuente A, Hickson L. Jet fuel, noise, and the central auditory nervous system: a literature review. Mil Med Sept 2015;180(9):950–5.
[91] Jahn A, Andersen JH, Christiansen DH, Seidler A, Dalbøge A. Occupational mechanical exposures as risk factor for chronic low-back pain: a systematic review and meta-analysis. Scand J Work Environ Health 2023;49(7):453–65. 1 oct.
[92] Jahn A, Andersen JH, Seidler A, Christiansen DH, Dalbøge A. Hip osteoarthritis and occupational mechanical exposures: a systematic review and meta-analysis. Scand J Work Environ Health 2024;50(4):244–56. 14 Mars.
[93] Lie JAS, Zienolddiny-Narui S, Bråtveit M. Effects of the combined exposure to chemicals and unusual working hours. Ann Work Expo Health 8 Juill 2024;68(6):647–56.
[94] Stansfeld S, Candy B. Psychosocial work environment and mental health—a meta-analytic review. Scand J Work Environ Health déc 2006;32(6):443–62.
[95] Rollin L, Andujar P, Bloch J, Chatelot J, Coutrot T, Dewitte JD, Homere J, Léonard M, Leroyer A, Memmi S, Nisse C, Rosankis E, Tone F, Vongmany N. Quelle complémentarité pour les dispositifs en santé travail (Evrest, MCP, Sumer, RNV3P) : un exemple à partir des métiers de l'aide à domicile chez les femmes? Arch Mal Prof Environ Mai 2021;82(3):261–76.